Cambridge Intellectual Property and Information Law

Gene Patents and Collaborative Licensing Models

Patent Pools, Clearinghouses, Open Source Models and Liability Regimes

Edited by
Geertrui Van Overwalle

CAMBRIDGE

Gene Patents and Collaborative Licensing Models

Concerns have been expressed that gene patents might result in restricted access to research and health care. The exponential growth of patents claiming human DNA sequences might result in patent thickets, royalty stacking and, ultimately, a 'tragedy of the anticommons' in genetics.

The essays in this book explore models designed to render patented genetic inventions accessible for further use in research, diagnosis or treatment. The models include patent pools, clearinghouse mechanisms, open source structures and liability regimes. They are analysed by scholars and practitioners in genetics, law, economics and philosophy.

The volume looks beyond theoretical and scholarly analysis by conducting empirical investgation of existing examples of collaborative licensing models. Those models are examined from a theoretical perspective and tested in a set of operational cases. This combined approach is unique in its kind and prompts well-founded and realistic solutions to problems in the current gene patent landscape.

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Society of Human Genetics (2002–4) and the Dutch Society of Human Genetics (1993–2000) and Editor-in-chief of the European Journal of Human Genetics (1997–present). He is present and past member of several National, EU and HUGO committees in the fields of Genetics, Innovative Health Care, Genomics, Bioinformatics, Ethics and IP aspects. He is the Director and Principal Investigator of the Center for Medical Systems Biology (CMSB), one of the four Centers of Excellence established in 2003 by the Netherlands Genome Initiative. The CMSB is a joint activity of Leiden University Medical Center, Leiden University, Free University Medical Center and Free University in Amsterdam, TNO Leiden and Erasmus MC Rotterdam, aiming to improve diagnosis, therapy and prevention of common diseases and rare variants thereof.

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Preface

At present the genetics community is increasingly concerned that patents might lead to restricted access to research and health care. Thoughtful observers are increasingly expressing concerns that the exponential growth of patents claiming human DNA sequences may lead to patent thickets, royalty stacking and, ultimately, to a 'tragedy of the anticommons' in the genomic field. An anticommons effect may also arise from blocking patents. Concerns have also been voiced with regard to downstream research as new genetic inventions might not find their way into products and a translational gap might emerge.

In an attempt to capture and comprehend these recent developments, and to reflect on potential remedies, the Centre for Intellectual Property Rights of the University Leuven (Belgium) organised a two-day international workshop on '*Gene Patents and Clearing Models: From Concepts to Cases*' on 8–9 June 2006. This workshop took place in the framework of a research project on 'Gene Patents and Public Health' sponsored by the Fund for Scientific Research Flanders (FWO, Belgium – Grant number G.O120.04), EuroGenTest (a Network of Excellence set up under the European Union Framework Programme 6 – Contract number 512148) and the Vancraesbeeck Fund (K.U.Leuven, Belgium). For the research that led to the workshop and the present book, as well as for the workshop, we are very grateful to those organisations.

The workshop aimed at exploring models designed to render patented genetic inventions accessible to further use in research and to diagnosis and/or treatment in further depth, and to investigate alternative models. The models include patent pools, clearinghouse mechanisms, open source models and liability regimes. There is a clear need to examine in more depth to what extent these schemes can be tailored to meet the needs of promotion and protection of innovation in human genetics.

The workshop aimed at combining both theoretical concepts and practical issues involved in applying these models in genetics, by inviting academics as well as business people and practitioners. The workshop equally aimed at developing a multidisciplinary point of view, by

confronting the views of legal scholars, geneticists, economists and philosophers.

The present book contains all papers presented at the workshop, as well as a few contributions by scholars not present, which were added later. In covering the various models the same format is followed in the first four parts of the book. First, the model is described and the concepts underlying the model are explored in depth. Then, a few cases are offered where the model has been put to work in practice. Finally, a critical analysis of the potential of the model for application in the genetic field is developed. In the fifth chapter the various models are examined from a wide panoply of perspectives: a clinical geneticist's view, a patent practitioner's perspective, through the lens of competition law, an economic perspective and an institutional perspective. The sixth and last chapter recapitulates the major findings and tests them against a set of pre-assumptions.

The present book moves beyond theoretical and scholarly analysis into empirical investigation of existing examples. Collaborative licensing models are first examined from a theoretical perspective, whereupon the findings are tested in a set of operational cases. This combined approach is unique in its kind and may prompt both well founded and realistic solutions to the current problems in the current gene patent landscape.

We hope that this volume thus reflects our ambition to step 'beyond the veil of ignorance'[1] into open, reflective, critical and constructive 'model mongering',[2] an enticing exercise in which we would like to invite all our readers to participate.

GEERTRUI VAN OVERWALLE

[1] Rai, A.K., Reichman, J.H., Uhlir, P.F. and Crossman, C., 'Pathways across the valley of death. Novel intellectual property strategies for accelerated drug discovery', Chapter 17 of this volume p. 270.

[2] Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume p. 172, with reference to John Braithwaite.

Foreword

Some thoughts on the multidisciplinary approach to the study of patents and health care

At the start of this enticing book, allow me to take you through a few considerations, which may be more philosophical than genetic.

The first thing is to agree on definitions. Indeed, this is more than semantics. If you want to be understood by people from other disciplines you must be sure to speak the same language. To give you an example: the contributions in the present book all deal with 'patents'. For me as a medical doctor, patent means open as in a patent foramen ovale, a hole in the heart. I understand that in IPR circles, patent also mean open, but did this book not come about in an attempt to keep them patent to access?

Anyway, '*interdisciplinarity* is a type of academic collaboration in which specialists drawn from two or more academic disciplines work together in pursuit of common goals' (a definition found in Wikipedia). Interdisciplinary programmes may arise from a shared conviction that the traditional disciplines are unable or unwilling to address important problems. They can also arise from new research developments, such as nanotechnology, which cannot be addressed without combining the approaches of two or more disciplines. In our field, bioinformatics is a nice example, since it combines molecular biology with computer science.

Interdisciplinary research should be distinguished from *transdisciplinary* research. According to the Swiss National research fund, it is intended to make a contribution towards solving socially relevant issues and involves practitioners from beyond the realm of science. I guess what we are doing in the Eurogentest Network of excellence is transdisciplinary, since we involve patient and family representatives in our activities.

Now, there are varying degrees of interdisciplinarity. In *multidisciplinarity*, researchers from two or more disciplines work together on a common problem, but without altering their disciplinary approach or developing a common conceptual framework.

True interdisciplinarity can only be claimed when researchers from two or more disciplines pool their approaches and **modify them** so

that they are better suited to the problem at hand. There is a holistic aspect in true interdisciplinarity. Indeed the researchers accept from the outset the idea that all the properties of a given system (biological, chemical, social, legal etc.) cannot be determined or explained by the sum of their component parts alone. The system as a whole determines in an important way how the parts behave. Aristotle already recognised this when he said: 'The whole is more than the sum of the parts.' A holistic approach has become a necessity in many disciplines. In biology, we know that cells, tissues and organs are more than the genes and pathways which they express. *Systems biology* has indeed become a trendy phrase. In philosophy, sociology and psychology holistic approaches are also well known. In medicine *holism* is almost synonym of psychosomatic medicine. Alternative medicine has capitalised on this since it recognises that emotional, mental, spiritual and physical elements of each person comprise a system, and that the whole person must be treated, the symptoms as well as the causes of the illness.

Reductionism is the opposite of holism. Scientists may need to have a reductionist approach to extract a particular mechanism from a complex biological problem. This is a well-known successful approach in science. Nevertheless, in the back of their minds, good scientists will remain aware of this necessary, but temporary reductionist approach.

Let us go back then to inter- and multi-disciplinarity and analyse how these principles are being applied in the present collection and in the genetics field in general. Does the study of IPR issues in genetics by lawyers and geneticists constitute an example of multidisciplinary or a true interdisciplinary approach?

If we consider the sex of the investigators, we have to conclude that the approach is definitely multidisciplinary. Females and males work on the same issues. Their perspective, timing, emotions and approaches will be different. To become truly interdisciplinary the investigators would have to learn to find a common ground and appreciate the qualities and shortcomings of the sex of their colleagues. For obvious reasons I will not go into this issue any further.

The second issue is the difference in scientific approach. Geneticists place emphasis on qualitative and quantitative 'rigour' and as a result may think that their approach is 'more scientific' than that of their colleagues from the humanities. In addition, they are used to face the unexpected outcome from an experiment. Lawyers may associate quantitative approaches with an inability to grasp the broader dimensions of the problem. On the other hand their approach is just to make sure that the unexpected is covered by the texts.

While geneticists are very keen to determine the sequence of a piece of DNA with great accuracy, by repeating the exercise a few times, they will readily accept that a well-written scientific text has a clear and obvious meaning. They have a kind of holistic approach when it comes to interpreting texts. Lawyers on the other hand make a living finding different interpretations of the same word, the same sentence or the same text. It is not clear, however, whether at the end the patent still covers what it is supposed to cover. One also wonders sometimes if a patent could ever be written and submitted if more than one lawyer worked on it. One also wonders why some patent applications, written by geneticists, could stand any challenge by lawyers.

A third issue is the difference in autonomy that the two parties may enjoy. Biomedical research is known to be expensive and to drain a good part of the budgets reserved for research. Legal investigations, with the exception of the legal fees, are cheap, require access to a library and a PC and are funded accordingly. As in other situations in society, the rich and the poor may not have the same ambitions and goals.

Is a multidisciplinary or even true interdisciplinary approach of IPR issues in genetics/diagnostics therefore even possible? It is clear that if left only to geneticists or lawyers, we may end up as already said: with something quite useless. 'To be aware of one's shortcomings, is the first step towards improving oneself,' as Socrates used to say. Therefore, combining the expertise, even in a 'multidisciplinary' approach, will create a more holistic approach, which will be much more useful to all parties involved and to the aim of the collaboration.

One has to keep in mind, however, that even if multi- and interdisciplinarity is very trendy in our universities, it may be less obvious when one applies for funding. We all know examples, where multidisciplinary projects have not received the expected financial support. The quantitative scientist will have judged that the project is too descriptive, while the qualitative scientists will have found it poorly written or not understandable.

In conclusion, I guess there is only one way in which this collaboration could become truly interdisciplinary and that is by becoming a *discipline* itself. If it succeeds, it might even solve the problem of its research funding, make even its own tenure and promotion decisions. Other examples of such integrations do exist: neuroscience, biomedical engineering and bioinformatics, to cite only a few examples, have been successful in this, here or in other places in the world. Whether the academic authorities will follow in this particular topic, I would not be too optimistic.

In any case, I would like to congratulate all contributors to the present book in trying to talk to each other and even to try to understand each other's language, and to grow into a multidisciplinary approach. Of course my congratulations also go to the organiser of the workshop and the editor of the present volume, Geertrui Van Overwalle, for being the necessary catalyst in this process.

JEAN-JACQUES CASSIMAN

Abbreviations

3GPP	3rd Generation Partnership Project
ACMG	American College of Medical Genetics
AD	Alzheimer Disease
AFLP	Amplified Fragment Length Polymorphism
AFJ2	Second Amended Final Judgment
AI	artificial intelligence
AIDS	Acquired Immunodeficiency Syndrome
AIPPI	Association Internationale pour la Protection de la Propriété Industrielle
ALRC	Australian Law Reform Commission
ASCAP	American Society of Composers, Authors and Publishers
ASTP	Association of European Science & Technology Transfer Professionals
AUTM	Association of University Technology Managers
BCLC	Breast Cancer Linkage Consortium
BSD	Berkeley Software Distribution
BIEM	Bureau International des Sociétés Gérant les Droits d'Enregistrement et de Reproduction Mécanique
Biotechnology Directive	EU Directive on the Legal Protection of Biotechnological Inventions, 1998
BiOS	Biological Innovation for Open Society
BMI	Broadcast Music, Inc.
BRCA	Familial Breast and Ovarian Cancer (gene)
BRT	Belgische Radio- en Televisieomroep
BSD	Berkeley Software Distribution
BUMA	Dutch Association for Performance Rights
B2B	business-to-business

CAMBIA	Centre for Applications of Molecular Biology in International Agriculture
CBD	Convention on Biological Diversity
CC	Creative Commons
CCS	Copyright Collection Societies
cDNA	complementary DNA
CF	Cystic Fibrosis (Mucoviscidosis in some languages)
CFTR	Cystic Fibrosis Transmembrane Conductance Regulator (gene and protein)
CGIAR	Consultative Group on International Agricultural Research
CH	clearinghouse
CIMMYT	International Maize and Wheat Improvement Centre
CISAC	Confédération Internationale des Sociétés d'Auteurs et Compositeurs
CJ	Court of Justice (EU)
CMM (detection)	Chemical Mismatch (detection)
CMT-1A	Charcot-Marie-Tooth disease, type 1A
CPC	Community Patent Convention
CRO	Collective Rights Organisation
CRUK	Cancer Research UK
CSCE	Conformation Sensitive Capillary Electrophoresis
DArT	Diversity Array Technology
DG	Directorate General
DGGE	Denaturing-Gradient Gel Electrophoresis
DH	Department of Health (UK)
DHPLC	Denaturing High-Pressure Liquid Chromatography
DMD	Duchenne Muscular Dystrophy (disease, protein and gene)
DNA	Desoxyribonucleic Acid
DOJ	Department of Justice (US)
DRM	Digital Rights Management
EBI	European Center for BioInformatics
EBoA	Enlarged Board of Appeal (EPO)
ECJ	European Court of Justice
EC Treaty	Treaty of the European Communities
EEA	European Economic Area
EGE	European Group on Ethics in Science and New Technologies

EMD	Enzymatic Mismatch Detection
EMEA	European Agency for the Evaluation of Medicinal Products
EPC	European Patent Convention, 1973
EPIPAGRI	European Collective Management of Public Intellectual Property for Agricultural Biotechnologies
epo	Erythropoietin
EPO	European Patent Office
ESGH	European Society of Human Genetics
EST	Expressed Site Tag
EU	European Union
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration (US)
FIPC	French Intellectual Property Code
FMF	familial Mediterranean fever
FRAND	Fair Reasonable and Non-Discriminatory
FS	free software
FSF	Free Software Foundation
FTC	Federal Trade Commission (US)
FTO	freedom to operate
GATT	General Agreement on Tariffs and Trade (WTO)
GBIF	Global Biodiversity Information Facility
GBS	Global Bio-Collecting Society
GCP	Good Clinical Practice
GEMA	German Gesellschaft für musikalische Aufführungs – und mechanische Vervielfältigungsrechte (Germany)
GFP	Green Fluorescent Protein
GM	genetically modified
GMS	Genetic Microsystems
GNU	recursive acronym for '*G*NU's *N*ot *U*nix', the name for the complete Unix-compatible *operating system*
GNU/Linux	Linux kernel (see 'Linux') together with other *operating system* elements supplied by the GNU-project
GPL	General Public License
GRDC	Grains Research and Development Corporation
Guidelines EPO	Guidelines for Examination in the European Patent Office
GUS	glucuronidase

GVL	Gesellschaft zur Verwertung von Leistungsschutzrechten (Germany)
GWAS	Genome-Wide Association Studies
HART	Homologous Allelic Recombination (or Replacement) Technologies
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HD	Huntington Disease
HGS	Human Genome Sciences
HH	Hereditary Hemochromatosis
HIV	Human Immunodeficiency Virus
HKU	Hong Kong University
HLA	Human Leukocyte Antigens
HLA tissue typing	Examination of Human Leukocyte Antigens (HLA) in a patient. Tissue typing is done for all donors and recipients in transplantation to help match the donor and recipient. Human Leukocyte Antigens
HNPCC	Hereditary Non-Polyposis Colorectal Cancer
HUGO	Human Genome Organisation
HTS	High-throughput screening
IBM	International Business Machines Corporation
ICS	incomplete contract structure
ICT	information and communication technology
IFPI	International Federation of the Phonographic Industry
IND	Investigation New Drug application
INSDC	International Nucleotide Sequence Database Collaboration (more commonly known as GenBank)
INPI	Institut National de la Propriété Industrielle (France)
IP	intellectual property
IP Australia	Australian Intellectual Property Office
IPRs	intellectual property rights
IT	information technology
ITPRGFA	International Treaty on Plant Genetic Resources for Food and Agriculture
JASRAC	Japanese Society for Rights of Authors, Composers and Publishers

LINUX	contraction of 'Linus' Minix', the name the developer (Linus Torvald) chose to refer to the *kernel* of the GNU/Linux operating system
MCPS	Mechanical Copyrights Protection Society
MLI	Molecular Libraries Initiative
MLS	Multilateral System
MRI	magnetic resonance imaging
mRNA	messenger RNA
MGH	Michigan General Hospital
MIT	Massachusetts Institute of Technology
MMR	mismatch repair
MPEG	Moving Picture Experts Group
MPEG LA	MPEG Licensing Authority
MS	mass spectrometry
MTA	material transfer agreement
NAS	National Academy of Sciences
NCBI	National Center for BioInformatics
NCE	new chemical entity
NDA	new drug application
NHS	National Health Services (UK)
NIH	National Institutes of Health (US)
NOS	Nederlandse Omroep Stichting (the Netherlands)
NSF	National Science Foundation
OECD	Organization for Economic Co-operation and Development
OJ EPO	*Official Journal of the European Patent Office*
OJ	*Official Journal of the European Communities*
OSD	open source definition
OSFS	open source free software
PAHO	Pan American Health Organization
PCR	Polymerase Chain Reaction
PCT	Patent Cooperation Treaty
PGD	Pre-implantation Genetic Diagnosis
PIPRA	Public Intellectual Property Resource for Agriculture
PKU	Phenylketonuria
PLoS	Public Library of Science
PLC	Patenting and Licensing Committee (ESHG)
PLT	Patent Law Treaty
PPPC	Public and Professional Policy Committee (ESHG)

PRCCH	Patent Royalty Collection Clearinghouse
PRS	Performing Rights Society (UK)
PSTC	Predictive Safety Testing Consortium
Pty Ltd/PL	Proprietary Limited
RAND	Reasonable And Non-Discriminatory
RDF	Resource Description Framework
RFLP	Restriction Fragment Length Polymorphism
RNA	ribonucleic acid
SABAM	Société Belge des Auteurs, Compositeurs et Éditeurs (Belgium)
SACEM	Société des Auteurs, Compositeurs et Éditeurs de Musique (France)
SARS	Severe Acute Respiratory Syndrome
SCA1	Spinocerebellar Ataxia, type 1
SDNY	United States District Court of the Southern District of New York
SSCP (analysis)	Single-Strand Conformation Polymorphism (analysis)
SENA	Stichting ter Exploitatie van Naburige Rechten (the Netherlands)
SESAC	Society of European Stage Authors & Composers
SIR	Statutory Invention Registration
SLA	simple letter agreement
SME	small- and medium-sized enterprise
SMTA	standard material transfer agreement
SNP	single nucleotide polymorphism
SSR	simple sequence repeat
STEMRA	Dutch foundation for mechanical reproduction rights (the Netherlands)
TBoA	Technical Board of Appeal
TIGR	The Institute for Genome Research
TKT	Transkaryotic Therapeutics (company name)
TRIPs	Agreement on Trade-Related Aspects of Intellectual Property Rights, 1995
TTBER	Commission Block Exemption Regulation (EC) No. 772/2004 on Technology Transfer Agreements (EU)
TTG	Transfer Technology Guidelines (EU)
UBMTA	Uniform Biological Material Transfer Agreement
UK	United Kingdom
UN	United Nations

UPA	Utility Patent Act
US	United States
USPTO	United States Patent and Trademark Office
VC	venture capital
WBCSD	World Business Council for Sustainable Development
WFCC	World Federation of Culture Collections
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organisation

Part I

Patent pools

1 Patent pooling for gene-based diagnostic testing

Conceptual framework*

Birgit Verbeure

1.1 Introduction

The presence of a patent thicket in a certain technology inevitably leads to a high number of licenses required to gain access to the patented technology. Consequently, this may result in the accumulation of royalties to be paid (royalty stacking). Such a situation may cause hindrance of access to and subsequent under-use of the technology, which is described in literature as the anticommons effect.[1] When access and use to a certain technology are hindered by the existence of multiple patents, held by multiple patent owners (a patent thicket),[2] a patent pool might be a useful model to facilitate access.

Patent thickets have arisen in technical fields other than the genetic area and patent pools have emerged to deal with overlapping patents for a long time.[3] One of the first patent pools was formed in 1856, by sewing machine manufacturers Grover, Baker, Singer, Wheeler and Wilson, all accusing the others of patent infringement. They met in Albany, New York to pursue their suits. Orlando B. Potter, a lawyer and president of the Grover and Baker Company, proposed that, rather than sue their profits out of existence, they pool their patents. In 1917, an aircraft pool

* The present paper builds further on a previous publication by the author: Verbeure B., van Zimmeren E., Matthijs G., and Van Overwalle G., 'Patent pools and diagnostic testing', 24(3) *Trends in Biotechnology*, 2006, 115–20.

[1] Heller, M.A. and Eisenberg, R.S., 'Can patents deter innovation? The anticommons in biomedical research', **280** *Science*, 1998, 698–701.

[2] Shapiro defined patent thicket as an overlapping set of patent rights requiring that those seeking to commercialize new technology need to obtain licenses from multiple patentees. Shapiro, C. (2001) 'Navigating the Patent Thicket: Cross Licenses, Patent Pools and Standard Setting', in Jaffe, E., Lerner, J. and Stern, S. (eds), *Innovation Policy and the Economy*, volume I, MIT Press, 119–150.

[3] Merges, R. (2001) 'Institutions for intellectual property transactions: the case of patent pools', in Dreyfuss, R., Leenheer Zimmerman, D. and First, H. (eds), *Expanding the Boundaries of Intellectual Property* Oxford University Press, 123–166.

was privately formed encompassing almost all aircraft manufacturers,[4] which was crucial to the US government entering World War I. In the late 1990s several patent pools were formed in the ICT branch starting with the MPEG-2 pool in 1997 for inventions relating to the MPEG-2 standard[5] with others to follow.[6, 7, 8]

According to a recent study under the auspices of NAS's Science, Technology and Economic Policy Board and Committee on Science, Technology and Law,[9] there is no real or substantial evidence for a patent thicket or a patent blocking problem in the field of genetics at present. However, it should be noted that the report is strongly focused on the influence of IP on research activities. At the same time, one is cautioned about the future: this lack of evidence is associated with a general lack of awareness or concern among the technology users on the one hand, and growing assertiveness of patent holders in asserting their rights on the other hand. Similar findings resulted from the European PATGEN project.[10] Nevertheless, cases of restrictive licensing or refusals to license practices have generated widespread controversy and disapproval because of the potential adverse effects on public health. Such studies were mainly reporting on problems relating to gene-based diagnostic testing, the reason why we further investigate to what extent a patent pool could alleviate the pains in this field.

Although there seems to be little evidence to suggest that there is an anticommons problem in the biotechnology industry in general, and in the genetics in particular, the biotech industry does have several characteristics that make it fertile ground for an anticommons. For example, a proliferation of patents held by a large number of market participants and an occasional tendency by companies to accumulate

[4] Dykman, H.T., 'Patent licensing within the Manufacturer's Aircraft Association', **46** *Journal of the Patent Office Society*, 1964, 646.

[5] Klein, J.I. 'Business review letter to Gerrard R. Beeney regarding MPEG-2', 1997, Department of Justice, Antitrust division.

[6] Klein, J.I. 'Business review letter to Gerrard R. Beeney regarding licensing of DVD technology', 1998, Department of Justice, Antitrust division.

[7] Klein, J.I. 'Business review letter to Carey R. Ramos regarding licensing of DVD technology', 1999, Department of Justice, Antitrust division.

[8] James, C.A. 'Business review letter to Ky P. Ewing regarding 3G platform' 2002, Department of Justice, Antitrust division.

[9] National Research Council of the National Academies, 'Reaping the benefits of genomic and proteomic research: intellectual property rights, innovation, and public health', 2005, National Academies Press.

[10] Hopkins, M.M., Mahdi, S., Thomas, S.M., Patel P. 'The patenting of human DNA: global trends in public and private sector activity (The PATGEN Project)', *Report on a European Commission's 6th Framework programme* 2006.

IP could indicate the emergence of a patent thicket and/or issues to gain access to the technology. Like in ICT, the biotech industry is characterized by rapid growth, a high level of complexity and a tendency to attach high importance and value to IP. But contrary to the IT industry, the attitude in biotech is much more protective. It is the aim of this chapter to review patent pooling as a concept (1.2) and to assess to what extent the concept could offer a facilitating effect on the licensing of IP for gene-based technology, in particular genetic testing (1.3).

1.2 Patent pools: the concept

Introduction

Definition

In order to overcome an anticommons effect, a patent pool provides for an agreement between two or more patent owners to license one or more of their patents to one another, and together as a package to third parties. As illustrated in Figure 1.1 two major licensing techniques are involved in the patent pool setup. On the one hand, a multiparty agreement is set up between the patent owners who license their patents as a package to one another and form a pool (lines within circle). On the other hand, a bilateral license agreement, usually in the form of a standard out-licensing agreement, provides for access of third parties to that package of patents (lines outside circle). As a consequence, a patent pool allows interested parties to gather in one instance all the necessary tools to practice a certain technology, i.e. "all-in-one license", rather than obtaining licenses from each patent owner individually.

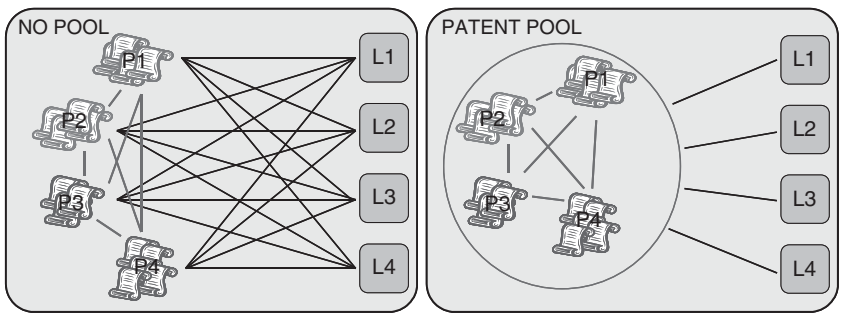

Figure 1.1 Comparative illustration of the different licenses needed in the absence or presence of a patent pool.

Motivation

Over the last hundred years, the reasons for setting up a patent pool have changed considerably. Roughly, two periods can be distinguished. From the introduction of the first patent pools in late nineteenth century and mainly during the first two decades of the twentieth century, patent pools were market based. They were set up to clear blocking patent positions and to cease patent hostilities, often after government intervention. Also the creation of a market division among horizontal competitors, naked price-fixing and other anti-competitive goals incensed some of the early patent pools. However, due to growing concern for and criticism of such uncompetitive behaviour, apart from some exceptions, no new patent pools were formed between approximately 1920 and the 1990s.[11]

Nevertheless, in the 1990s, the patent pool model was picked up again but the incentives for pool formation differed considerably. At this point in history, patent pools were typically designed to deal with substantial patent thickets for technologies that were essential to one and the same technical standard, which led to standard-based patent pools. Standards are technical specifications relating to a product or an operation, which are recognized by a large number of manufacturers and users.[12] Typically, such standards-driven patent pools are the ones we know from the ICT sector which set off with the MPEG-2 patent pool. This new approach to patent pooling shed a different light on the possible impact of patent pools on competition. By bringing together essential patents in a one-package license, the access to technologies essential to implement a standard was facilitated, bringing strong pro-competitive effects in the balance. As can be read in the Guidelines issued by the US Department of Justice and US Federal Trade Commission (FTC) in 1995,[13] it was recognized that cross-licensing arrangements and patent pooling "may provide pro-competitive benefits by integrating complementary technologies, reducing transaction

[11] This growing concern with regard to anticompetitive licensing conduct eventually led to a rigid approach of the US Department of Justice to licensing arrangements, identifying particular practices that it considered to be forbidden as the "Nine No-Nos" of intellectual property licensing. *See* Bruce B. Wilson, Deputy Assistant Attorney General, 'Remarks before the Fourth New England Antitrust Conference, Patent and Know-How License Agreements: Field of Use, Territorial, Price and Quantity Restrictions', 1970.

[12] European Commission Communication COM (92) 445 final of 27 October 1992 on Intellectual Property Rights and Standardisation.

[13] US Department of Justice and Federal Trade Commission (1995) 'Antitrust Guidelines for the Licensing of Intellectual Property'.

costs, clearing blocking positions and avoiding costly infringement litigation."[14]

Set-up

The establishment of a patent pool is a long, complex, multi-step process. In view of the varied issues and interests at stake, expertise and joint collaboration of highly qualified patent attorneys, technical experts in the relevant field and legal advisors both in the field of patent law and competition law are required.

A patent pool may be and usually is formed upon the initiative of the patentees, acting as shareholders of the pool and as financiers of the licensing entity. Consequently, to a certain extent the patentees preserve authority over the licensing conditions. Third-party licensing may occur directly by patentees to licensees, e.g. by appointment of one of the partners of the pool. Alternatively, third-party licenses may be administered indirectly through a new entity specifically set up for the pool administration, a separate independent licensing authority.[15, 16, 17, 18]

The first situation will generally apply to patent pools with a relatively limited number of participating patent holders. In such organizations whereby one of the patent owners manages the patent pool, some safeguards with respect to its independence and confidentiality of business information should clearly be built in. The administration of larger pools puts a large burden on the administering body and will in general be transferred to an independent licensing authority.

Based on the nature of the patent pool initiators and the complexity of the pool's structural organization, three types of patent pools can be distinguished.[19] "Joint licensing schemes" are initiated by a group

[14] I*bid*. §5.5

[15] Shapiro, C., (2001) 'Navigating the patent thicket: cross licenses, patent pools and standard setting', in Jaffe, E., Lerner, J. and Stern, S. (eds), *Innovation Policy and the Economy,* volume I, MIT Press, 119–150.

[16] Clark, J. 'Patent Pools: a Solution to the Problem of Access in Biotechnology patents?' in a White Paper commissioned by Q. Todd Dickinson, the Under Secretary of Commerce for Intellectual Property and Director of the US Patent and Trademark Office, 2000.

[17] Klein, J.I., (1997) 'Cross licensing and antitrust law', *An Address to the American Intellectual Property Law Association* May 2, 1997.

[18] Merges, R. (2001) 'Institutions for intellectual property transactions: the case of patent pools', in Dreyfuss, R., Zimmerman, D.L. and First, H. (eds), *Expanding the Boundaries of Intellectual Property,* Oxford University Press, 123–166.

[19] Bekkers, R., Iversen, E., Blind, K. 'Patent pools and non-assertion agreements: coordination mechanisms for multi-party IPR holders in standardization', paper for the EASST 2006 Conference, Lausanne, Switzerland, 23–26 August 2006.

of (usually larger) licensors of a particular technology (or standard). One of them may act as an agent for the joint licensing contract. Most of these pools are eventually open to any holder of essential IPR to the standard in question. Nevertheless, they started as an activity of a small group.

"Patent pools with a licensing administrator" start off with an open call for essential patents for a certain standard by an independent body. Subsequently, the independent licensing administrator has a patent evaluation carried out (preferably by an independent third party) to determine essentiality to the standard in question. A priori, the licensors that decide to join such a pool do not know who the other licensors will be that will become a member of the pool. Well-known examples of such independent bodies acting as licensing authorities/administrators for several patent pools covering a diversity of technical standards at the same time are MPEG LA[20] or ViaLicensing.[21] The licensing administrator sets, in dialogue with the licensors, the royalty rate for the pool, and collects the royalties and redistributes them given a pre-agreed scheme.

In the case of "patent platforms", an organizational approach is adopted that deals flexible with multiple technologies (standards) and multiple product groups (employing one or more patents that are essential to a certain standard). It also aims to be more flexible towards the actual agreements between licensors and licensees. In the patent platform, there is one overall umbrella organization, as well as multiple entities which each develop licensing programmes for specific standards. The aim is to have a standard offer (bundle) available. However, within the context of the patent platform, licensors and licensees may also agree upon other arrangements, possibly involving cross licensing, licensing of non-essential patents, and so on. To date, the 3rd Generation Partnership Project (3GPP)[22] is the only example of such an approach. One could argue that there is little or no difference between the 3G platform model and an organization like MPEG LA or Vialicensing on the basis of organization or administration. We do however want to stress the importance of a particular feature of this third model. The platform deals with partly integrating technologies in a flexible approach tailored to the particular needs of different licensees. Licensing administrators dealing with multiple pools may adopt a more or less flexible approach within one patent pool, but will still treat these different pools independently. As will be discussed in more detail

[20] www.mpegla.com [21] www.vialicensing.com [22] www.3g.org

in part 1.3 of this chapter, it is exactly the flexibility within seemingly a single technology that justifies its separate classification, especially for the purpose of this paper.

Benefits and risks

From the experience in ICT, we learn that patent pools may have significant benefits which make for a pro-competitive counterweight for possible anti-competitive effects, which largely account for the critical opinions with respect to the patent pool model. A major beneficial effect to begin with is the elimination of stacking licenses. The licensing transaction costs are reduced by the introduction of a system of "all-in-one licensing" for non-member licensees instead of having to negotiate and acquire separate licenses directly from each of the patent owners individually (see Figure 1.1). At the darker/down side of this model, one has at the same time to take into account that the initial cost of setting up and negotiating a pool agreement will often be high. Another benefit is a decrease in patent litigation and its associated high cost. A patent pool also leads to the institutionalized exchange of technical information not covered by patents through a mechanism for sharing technical information relating to the patented technology, which would otherwise be kept as a trade secret. This is reflected by an exchange of know-how brought along by the set-up of a patent pool, thereby further facilitating innovation and efficient use of resources. However, from competition law point of view, such exchange should be limited to technical information only. The exchange should not extent to exchange of business information between competitors which risks resulting in cartel formation.

Patent pools may also offer an interesting instrument for government policy, in the sense that it is better to encourage companies to establish patent pools rather than for example to force them into a compulsory licensing scheme. However, one should not overlook that it was exactly those early patent pools created after government intervention that raised antitrust concerns. A major prerequisite for establishing patent pools is the voluntary participation of all patent holders, whereas the compulsory licensing mechanism is exactly intended for creating access in a situation where patent holders do not voluntarily wish to enter into (reasonable) licensing negotiations. In the past however, "non-voluntary patent pools" have been set up, i.e. patent pools initiated on the basis of government intervention. An early example of such non-voluntary patent pool was the airplane patent pool created by the US Government

in 1917.[23] More recently, attempts were made in the biomedical field to create access to HIV drugs for developing countries by setting up the "Essential Patent Pool for AIDS".[24]

One should be wary of some additional potential risks as well. Patent pools might shield invalid patents[25] and entail the risk of inequitable remunerations although expert valuation could settle disagreements on the value of the patents.[26] The major criticism is the danger of covering for a cartel and subsequent anti-competitive effects.[27, 28, 29]

Economics

As originally studied by Cournot back in 1838,[30] the creation of a patent pool is typically attractive when at least two entities hold blocking patents. Cournot's theory of the complements nicely illustrates that the inefficiency associated with multiple blocking positions can be eliminated by pooling patents and joint licensing. When individual patentees join forces and offer their IP in a single license as a package, the price of such package license is less then the cumulative price of the individual components when priced separately. Both the patentees and licensees fare better under such a regime. Because of the availability of a license

[23] As the US contemplated the needs of entering and fighting in World War I, the problems associated with the development, manufacture, supply availability, innovation and cost of airplanes were brought to the forefront. In the early days of aviation, the Wright brothers and Curtiss company, whilst also litigating each other on their patents, retarded innovation in the aircraft industry. The National advisory committee for aeronautics was created which recommended "the formation of the Aircraft Manufacturers Association among all aircraft manufacturers to manage a patent pool". The US Congress passed a law to enable the Secretary of War and the Secretary of the Navy to secure by purchase, condemnation, donation or otherwise essential patents as they may consid er necessary to the development and manufacture of aircraft in the US for governmental and civil purposes. Eventually, the AMA's patent pool was created. The level of allocation of royalties was forced upon the patent owners under threat of the government to take over the patents.

[24] See www.essentialinventions.org/docs/eppa.

[25] Aoki, R. 'The Consortium Standard and Patent Pools' 55(4) *The Economic Review*, 2004, 345–356.

[26] Bekkers et al. 'Patent pools and non-assertion agreements'.

[27] Aoki, R. 'The Consortium Standard and Patent Pools' 55(4) *The Economic Review*, 2004, 345–356.

[28] Versaevel, B., Dequiedt, V. 'Patent Pools and the Dynamic Incentives to R&D' *Cahiers de Recherche, Working Papers No 2009/6*, available at www.em-lyon.com/ressources/ge/documents/publications/wp/2006-09.pdf

[29] See note 23, above.

[30] For a brief description of Cournot's original work on complements, and modern extensions, *see* Shapiro, C. (1989), 'Theories of Oligopoly Behavior', in Schmalensee R. and Willig, R. (eds.), *Handbook of Industrial Organization*, Elsevier Science Publishers, 330–414, at 339.

that covers all, there is a higher chance on effective marketing of market products which in turn results in higher revenue for the patentees on their IP. At the other side, since the package license is available at a more reasonable price, the public fares better by having a market product available with a lower royalty burden. More recent economic modelling studies on the patent pool concept, confirm Cournot's early findings.[31]

More recently, more complex studies have been conducted to evaluate the effect of the formation of a patent pool on welfare, thereby aiming at better understanding which characteristics of patent pool arrangements lead to pro-competitive effects, and therefore indicating which patent pools should be authorized by the regulator. A clear outcome of these studies highlights the importance of the essentiality of the patents included in the pool. The foregoing analyses evaluate the impact of a pool on welfare after the formation of that pool, i.e. *ex post* perspective.[32]

A new approach to the economic study of the patent pool model looks at the perspective before the formation of a patent pool and reveals additional interesting observations. This *ex ante* approach[33] led to the conclusion that the perspective of joining a patent pool would have a positive impact on R&D activity, i.e. higher R&D investment and enhanced speed of R&D. In other words, the prospect of patent pooling has an innovation stimulating effect. More in particular, it is perceived as crucial to be part of the pool initiators. However, this phenomenon gives rise to the observation of two distortions. On the one hand there is the risk for pre-pool overinvestment in order to be participant in the pool formation. But on the other hand, there may well be a risk for underinvestment after pool formation. Hence there might be a negative effect on further innovation once the pool has been set up.

This theoretical determination of the incentives effect of the prospect of a patent pool is also reflected in the setup of patent pools in a context of cooperative standard setting. Ironically, exactly the role of standard setting bodies in the set-up of patent pools as such may raise anti-trust concerns. Standard setting bodies almost always coordinate standard setting by competitive or potentially competitive business

[31] Lerner, Josh and Tirole, Jean, 'Efficient Patent Pools' (5 August 2002). Available at SSRN: http://ssrn.com/abstract-322000.

[32] Aoki, R. 'The consortium standard and patent pools' **55**(4) *The Economic Review*, 2004, 345–356.

[33] Versaevel, B., Dequiedt, V. 'Patent Pools and the Dynamic Incentives to R&D', *Cahiers de Recherche, Working Papers No 2009/6*, available at www.em-lyon.com/ressources/ge/documents/publications/wp/2006-09.pdf.

entities whereas true competition is considered to be best encouraged if business decisions by the market players are made independent from each other. The risk of improper collusion in a standard setting process is therefore never far away. Such improper collusion where business decisions are made by competitors working together may be reflected in price fixing, market division and allocation or joint market monopolization, product restrictions etc.[34, 35, 36] Careful assessment of the impact of the formation of a pool is therefore needed. The possible pro-competitive effects of a patent pool once the pool has been set up counterbalance these fears. By clearing the intellectual property rights (IPRs) covering a certain technology, the facilitated access to the technology may open up the technology for wide-spread use and for further research and innovation.

Legal aspects[37]

Applicable law

As indicated, the US antitrust agencies but also the European Commission as well as the Japanese Fair Trade Commission have established guidelines in an attempt to deal with potential anti-competitive effects of (multiparty) licensing agreements. In the US, the Federal Trade Commission (FTC) and Antitrust Division of the Department of Justice (DOJ) have developed *Antitrust Guidelines for the Licensing of Intellectual Property (IP Licensing Guidelines)*. The principles laid down in the IP Licensing Guidelines cover both the multiparty licensing agreements to set up a patent pool and bilateral licensing agreements between the pool and third parties. Upon request, the federal antitrust agencies may review both types of licensing agreements. The IP Licensing Guidelines specifically refer to the potential pro-competitive effects of patent pool agreements "by integrating complementary technologies, reducing transaction costs, clearing blocking positions, and avoiding costly infringement litigation".

[34] Shapiro, C. 'Setting Compatibility Standards: Cooperation or Collusion?', in Dreyfuss, R., Zimmerman, D.L., First, H. (eds), *Expanding the Boundaries of Intellectual Property – Innovation Policy for the Knowledge Society*, Oxford University Press, 2001, 81–102.

[35] Wellford, H.B. 'Antitrust issues in standard setting', address at the 2nd Annual Seminar on IT Standardization and Intellectual Property China, Electronics Standardization Institute Beijing, China, 29 March, 2007.

[36] Lemley, Mark A., 'Intellectual Property Rights and Standard-Setting Organizations', **90** *California Law Review*, 2002, 1889–1980.

[37] With special thanks to Esther van Zimmeren on whose work this section is based, manuscript on file with the author.

In the European Union the major competition rules related to technology licensing are laid down in the *Commission Block Exemption Regulation* (EC) No. 772/2004 on *Technology Transfer Agreements* (TTBER).[38] However, the TTBER only deals with bilateral agreements, not with multiparty agreements like patent pools. Nevertheless, the licensing agreements between a patent pool and a third party are seen as regular license agreements which may fall within the scope of the TTBER. To further clarify the scope and application of this regulation, supplementary *Transfer Technology Guidelines* (TTG)[39] were established in April 2004. Unlike the TTBER, the TTG does provide guiding principles for the set-up of a multiparty licensing agreement to set up a patent pool. It is noteworthy to mention that the TTG do not use the term "IP pools" or "patent pools" but "technology pools'. Such technology pools are defined as "arrangements whereby two or more parties assemble a package of technology which is licensed not only to contributors to the pool but also to third parties" (TTG 210). A technology pool can thus not only encompass patents, but also copyrights, trademarks and the like.

Conditions

Close examination of foregoing guidelines, regulations and related decisions provides valuable information on the attitude of US and European authorities towards patent pools. In short, patent pools should avoid causing anti-competitive restraints and will most likely be accepted if they meet the following conditions.[40]

Evidently, the patents taken up by the pool should be *valid*. A patent is valid from the date of grant until the date of expiration defined by law, which usually is twenty years from the date of filing, provided the maintenance fees are being paid.

The technologies covered by the patents included in a patent pool should be *essential and complementary*. A technology or patent is deemed to be essential if the technology in question constitutes a necessary part of the package of technologies for the purposes of producing the product(s) or carrying out the process(es) to which the pool relates,

[38] Commission Regulation (EC) No. 772/2004 of 27 April 2004 on the application of Article 81 (3) of the Treaty to categories of technology transfer agreements, *OJ* 2004 No L123, 11. This Regulation replaces Commission Regulation (EC) No. 240/96 of 31 January 1996 on the application of Article 85 (3) of the Treaty to certain categories of technology transfer agreements, *OJ* 1996 L31, 2.

[39] Commission Guidelines on the application of Article 81 of the EC Treaty to technology transfer agreements *OJ*, 2004 No. C101, 2.

[40] Verbeure, B., van Zimmeren, E., Matthijs, G. and Van Overwalle, G., 'Patent pools and diagnostic testing', **24**(3) *Trends Biotechnology,* 2006, 115–20.

and, if there are no substitutes for that technology inside or outside the pool.[41] Hence, provided a technology meets the essentiality requirement, that technology is necessarily also complementary to the other technologies included in the pool. In the currently established patent pools, essentiality is usually measured against a standard. In order to guarantee validity of the patents and essentiality of the pooled technology, validity of the patents and the weight of each of these patents, a system of *independent patent expert evaluation* is required.

Regarding *royalties* paid by third-party licensees, undertakings setting up a pool are in principle free to negotiate and fix royalties for the technology package and each technology's share of the royalties. These royalties paid to the pool by the licensees as well as other licensing terms should be *fair, reasonable and non-discriminatory* (the so-called "FRAND-terms") and licenses granted by the pool should be *non-exclusive*. A license is non-exclusive when one or more licensees are granted the right to use the licensed technology covered by the patent(s) during the term of the license and when the licensor retains the right to use the licensed technology and associated patent(s) as well.

As for the patent pool agreement, *licenses from patent owners to the pool should also be non-exclusive*. This leaves the opportunity for licensing of the patent independently from the pool, e.g. when a licensee is not interested in a full pool package, or for the licensing of a technology for an application not envisaged in the pool. At the same time, royalties paid by licensees to the patent pool should be distributed amongst the licensors according to an agreed *royalty allocation formula* set forth in the patent pool arrangement.

With respect to further innovation on the basis of the pooled technology, a licensee may be obliged to grant the licensor *non-exclusive licenses for improvements of the licensed technology*. Such clause in the license agreement is also referred to as a "grant back" provision. This should be limited to essential patents and be settled on reasonable terms in order not to discourage further innovation. However, licensees are *free to develop and use alternative technologies*.

Safeguards for sensitive business information should be provided. Competitively sensitive business information on the licensee is safeguarded in case auditing mechanisms for the management of the royalties are established.

And finally, it has been suggested that an independent and therefore neutral *dispute resolution mechanism* is desirable in the agreements setting up the pool.

[41] Commission Guidelines on Technology Transfer Agreements (TTG).

1.3 Patent pools for gene-based diagnostics?

Introduction

Unlike gene-based drug development, the development of a gene-based diagnostic test based on the fundamental finding of the link between a particular nucleic acid sequence and the aetiology of a disease does not involve the same enormous investment. A principal argument for patenting biomedical inventions is the fact that typically, post-invention development costs far exceed pre-invention research expenditures, and firms are unable to make this substantial investment without protection from competition. Patents therefore facilitate transfer of technology to and within the private sector by providing exclusive rights to preserve the profit incentives of innovating firms. Additionally, for drug development based on genomic knowledge one could envisage parallel but different routes to obtain a drug. In other words, in contrast to diagnostic testing, for drug development there is still some room for inventing around. The justification of a right to exclude others from exploitation of the technology seems therefore less obvious and acceptable with regard to gene-based diagnostic testing as for drug development.

Currently, more than a thousand genetic diseases can be diagnosed through available tests. Although some of the associated genes are free of patents, most are not. According to Jensen and Murray 20% of human genes are explicitly claimed as US IP. Within this group of genes, specific regions are identified as "hot spots" of heavy patent activity, usually with a one-gene-many-patents scenario.[42] A European study identified 15,000 patent families seeking to claim human DNA patents between 1980 and 2003, of which just fewer than 6,000 contained one or more patents granted at the main patent offices (United States Patent and Trademark Office (USPTO); European Patent Office (EPO); Japanese Patent Office (JPO)) by 2005. Remarkably, significant regional differences in DNA patenting activity were observed: 94% of these families contain a USPTO patent grant compared to only 13% at the EPO. Several reasons are brought forward to account for this difference, such as a popularity of the USPTO due to the size of the market and low cost of gaining a US patent in comparison, as well as a more stringent patent examination at the EPO.[43] Still, when the IP

[42] Jensen, K. and Murray, F., 'Intellectual Property Landscape of the Human Genome', **310** *Science* 2005, 239–240.

[43] Hopkins, M.M., Mahdi, S., Thomas, S.M., Patel P. 'The patenting of human dna: global trends in public and private sector activity (The PATGEN Project)' *Report on a European Commission's 6th Framework programme* 2006.

rights necessary to arrive at a commercial end product such as a kit for diagnostic testing are held by patentees too numerous or heterogeneous to agree on licensing terms, an anticommons effect to the detriment of the public (the patients) may emerge for which a patent pool could be the answer.

Policy incentives

The USPTO suggested in a white paper in 2000 that the solution to some gene patent problems might be the use of patent pools. In the words of Q. Todd Dickinson, the Under Secretary of Commerce for Intellectual Property and Director of the US Patent and Trademark Office at that time:

> Biotechnology is heavily dependent on patent protection to maintain viability. While most biotechnology companies are responsible corporate citizens, offering reasonable access to their patented inventions, one concern about broad patenting in biotechnology, especially regarding genomic inventions, is the ease and cost of licensing multiple patents. Patent pools can allow reasonable access to patented genomic inventions, thereby promoting research and development while also promoting competition through patenting.

The Organization for Economic Co-operation and Development (OECD, 2002) considers the patent pool concept to be interesting for biotechnology, but has some doubts as to whether the technologies and markets for genetic inventions are amenable to pools and called for further study. Also the Australian Law Reform Committee carefully studied issues relating to gene patenting and human health. In their report dating back from 1999, patent pools are mentioned as a viable option to facilitate gene-patent licensing.[44]

Inspiring case studies

There is currently no widespread use of the patent pool approach in the biomedical area, although some inspiration on how a collaborative arrangement might function in this field can be found and will be discussed briefly.

Golden Rice. Golden Rice is an instructive case on patterns of protection and on negotiation through patent thickets in the field of agricultural biotechnology. Potrykus succeeded in genetically enriching

[44] The report is available at www.austlii.edu.au/au/other/alrc/publications/reports/99/.

rice grains with β-carotene, the precursor to vitamin A,[45] as a result of which the grains are yellowish in colour and called "Golden Rice". Potrykus wanted to transfer the Golden Rice materials to developing countries for further breeding in order to introduce the trait in local varieties consumed by poor people. However, a freedom-to-operate survey uncovered seventy patents belonging to thirty-two different companies and universities embedded in Golden Rice.[46] The six key patent holders were approached and an agreement was reached that allowed Potrykus to grant licenses, free of charge, to developing countries, with right to sub-license.[47, 48, 49] A Humanitarian Board ("HumBo") was established as a voluntary association to assist in governance and decision making.[50] Around twenty "master licenses" have been granted so far to developing country institutions in Asia (Personal communication Anatole F. Krattiger).

The Golden Rice case is an example of how private and public organizations in a combined effort dealt with the patent thicket by creating a non-profit humanitarian patent pool in the form of a single licensing authority.[51, 52, 53, 54]

SARS pool. A recent case where a situation of overlapping patents is emerging and where laboratories try to remove the thicket by way of a

[45] Beyer, P., Al-Babili, S., Ye, X., Lucca, P., Schaub, P., Welsch, R. and Potrykus, I. 'Golden Rice: introducing the beta-carotene biosynthesis pathway into rice endosperm by genetic engineering to defeat vitamin A deficiency', **132**(3) *The Journal of Nutrition* 2002, 506S-510S.

[46] Kryder, R.D., Kowalski, S.P. and Krattiger, A.F. 'The intellectual and technical property components of pro-vitamin A rice (Golden rice TM): A preliminary freedom to operate review', *ISAAA Briefs* No. 20, 2000.

[47] Zeneca (now Syngenta) press release: 'Golden Rice collaboration brings health benefits nearer', 16 May 2000.

[48] Zeneca (now Syngenta) press release: 'International Rice Research Institute begins testing Golden Rice', 22 January 2001.

[49] Zeneca (now Syngenta) press release: 'Syngenta to donate Golden Rice to Humanitarian Board', 14 October 2004.

[50] Dubock, A.C. 'Public goods and public policy for agricultural biotechnology', *7th ICABR International Conference*, Ravello (Italy), 29 June to 3 July, 2003.

[51] Graff, G. and Zilberman, D. 'Towards an intellectual property clearinghouse for Ag-Biotechnology. An issues paper.', **3** *IP Strategy Today* 2001.

[52] Graff, G., Bennett, A., Wright, B. and Zilberman, D. 'Towards an intellectual property clearinghouse for Ag-Biotechnology. Summary of an industry.', Academia and International Development Round Table, **3** *IP Strategy Today* 2001.

[53] Graff, G.D., Cullen, S.E., Bradford, K.J., Zilberman, D. and Bennett, A.B. 'The public-private structure of intellectual property ownership in agricultural biotechnology', **21** *Nature Biotechnology* 2003, 989–995.

[54] Parish, R. and Jargosch, R. 'Using the industry model to create physical science patent pools among academic institutions', *Journal of the Association of University Technology Managers* 2003, 65–79.

pool, relates to the biomedical field, namely to the SARS corona virus.[55] In response to the outbreak of Severe Acute Respiratory Syndrome (SARS), the World Health Organization (WHO) set up a network of laboratories to help control the disease, which led to the isolation of the causative virus and the sequencing of its genome. Apparently two groups discovered the SARS genome independently from each other.[56, 57] Several of the contributing laboratories filed patent applications incorporating SARS genomic sequence data and further research led to the filing of additional patent applications by both public and private sector entities.[58] The WHO set up a SARS consultation group which proposed "that a strategy be developed, in consultation with stakeholders, to address potential SARS corona virus related IP issues and thus enhance development of intervention approaches".

At present, the relevant parties have been identified and principal agreement has officially been gained by the signing of a letter of intent. Highly qualified technical and legal experts assist the parties during the chain of negotiations.[59]

Green Fluorescent Protein. Sometimes also referred to as a biotech patent pool is the GFP pool. Green Fluorescent Protein (GFP) is a fluorescent reporter molecule with a wide spectrum of applications in life science research. For example, GFP is used in molecular biological research to elucidate the molecular mechanisms of cell biology, in pharmaceutical compound screening to monitor either protein behaviour or gene activation in response to treatment with test compounds, incorporated within the genome of transgenic organisms etc. The intellectual property (IP) associated with Aequorea victoria GFP (AvGFP) is complex. Via a series of strategic alliances, GE Health care acquired the rights to offer sub-licenses to AvGFP IP thus enabling users to obtain these rights from a single source. Upon closer analysis of the situation, the GFP pool is rather an example of aggregation of patent rights with subsequent out-licensing of the technology. As can be read

[55] Simon, J.H.M., Claassen, E., Correa, C.E. and Osterhaus A.D.M.E. 'Managing severe acute respiratory syndrome (SARS) intellectual property rights: the possible role of patent pooling', **83**(9) *Bulletin of The World Health Organisation* 2005, 641–720.

[56] Rota, P.A. *et. al.* 'Characterization of a novel coronavirus associated with severe acute respiratory syndrome', **300** *Science* 2003, 1394–1399.

[57] Marra, M. A. *et. al.* 'The genome sequence of the SARS-associated coronavirus', **300** *Science* 2003, 1399–1404.

[58] Simon et al. 'Managing severe acute respiratory syndrome (SARS) intellectual property rights: the possible role of patent pooling'.

[59] A more profound insight into the current state of affairs of the SARS patent pool will be given by Carmen Correa from Vironovative, one of the patentees involved in the setup of this pool, see Chapter 3 of this volume.

on their website, the GFP License offered by GE Health care includes the rights covered by European, US and Japanese patents covering different mutations that greatly enhance the properties of AvGFP. As a particularity, it should be noted that not just one license is offered covering the full portfolio, but a wide range of licenses are available, offering considerable flexibility and ensuring the most cost-effective solution, by purchasing only the rights that are required. When purchasing a GFP product, the user automatically acquires a license for use of the AvGFP technology for the use for which the product is intended. Besides the AvGFP License, they also provide a license for the basic GFP claims held by Columbia University.

SNP Consortium. In 1999, the SNP Consortium[60] was organized with inputs from both private and public players in the field, and as a non-profit foundation to provide public data on single nucleotide polymorphisms (SNPs). The SNP Consortium has already been referred to as a patent pool, but could more appropriately be named "intellectual property pool". It is not the intention here to refer to the SNP Consortium as an example of a proper patent pool. Though there is an interesting aspect to the SNP Consortium with respect to the feasibility, in particular the possible incentives, to set up a patent pool in the area of genetics. The SNP Consortium initiative demonstrates the openness within the genetics community (ranging from academic research institutes to large pharmaceutical entities) vis-à-vis sharing IP under conditions that are acceptable for all parties involved. A major incentive hereto that may be derived from this example is to further or facilitate research in a cooperative way. Contrary to for example the Human Genome Project, strict rules governed the IP generated within the consortium to ensure free access for all at the end of the ride. Provisional patent applications were filed as new SNPs were discovered and prior to release into the public domain, thereby maintaining the priority date of discovery of the SNP for use as prior art. The provisional applications were later converted into US utility patent applications and instead of prosecuting to grant, the applications were then converted into statutory invention registrations.[61] In order to prevent the facilitation of patenting of the

[60] Holden A.L. 'The SNP consortium: summary of a private consortium effort to develop an applied map of the human genome', **26** *Biotechniques Supplement* 2002, 22–24.

[61] In US patent law, a statutory invention registration (SIR) is a publication of an invention by the USPTO at the request of the applicant (i.e. inventor(s) or assignee(s)). Statutory invention registrations were used by applicants for publishing patent applications they no longer felt they could get patents on. By publishing the patent applications, they helped insure that the inventions were in the public domain and no one else could subsequently get a patent on them. As of the 1999 American Inventors

same SNPs by third parties, the identified SNPs were only released to the public when mapping had been achieved. The IP policy of the SNP Consortium was set up in order to maximize the number of SNPs that (1) enter the public domain at the earliest possible date, and (2) are free of third-party encumbrances such that the final SNP map can be used by all without financial or other IP obligations.

Patents in genetic testing: technology specific versus diagnosis specific patents

Two types of patents can be identified when looking at genetic testing: technology specific patents and diagnosis specific patents.[62]

Technology specific patents encompass general molecular biological technologies such as amplification, labelling or detection of nucleic acid fragments. The technology used can be the same for different diagnostic tests. Additionally, different technologies may be used for a particular diagnostic test. For example, if an amplification step is needed, this can be achieved using Roche's polymerase chain reaction technology (PCR). When looking back at the entry of PCR in the market, there was concern about the cost and access to the technology due to the licensing. Over time a system was set up by Roche to value its PCR inventions through licenses to the technology as such or through the development and sale of instrumentation and biologicals. Alternatively, other methods such as Gen-Probe's transcription-mediated amplification, Becton Dickenson's strand displacement amplification, Biomerieux's nucleic acid sequence-based amplification or the branched DNA technology from Bayer can be used. In other words, PCR was subject to a competition-driven environment where alternatives were available or possible, urging the patentee to competitive licensing terms in order to create revenue.

Diagnosis specific patent protection is specific for the diagnosis of a certain defect or disease. Examples of such patented subject matter include the specific nucleic acid sequences, mutations or polymorphisms correlated with that certain defect or disease (disease gene

Protection Act, however, most patent applications filed in the US have been published 18 months after they were filed. These published patent applications serve a similar purpose to a statutory invention registration. Once an application is published, an inventor need only let their application go abandoned in order to give up their right to a patent and dedicate the invention to the public. Also see www.uspto.gov/web/offices/pac/mpep/documents/appxl_35_U_S_C_157.htm.

[62] Vlassak, K. and Schüller, K. (2007) 'The effect of patents on research and development of diagnostic kits', in Van Overwalle, G. (ed.), *Gene Patents and Public Health*, Bruylant, 99–113, at 104.

patents). These patents are not only different for each diagnosis performed. They are also essential to the gene-based diagnosis of that particular disease, essential in the same way as patented technology should be essential for a standard in the formation of a patent pool. Contrary to technology specific IP, there is no alternative to possibly circumvent such an essential patent when performing genetic testing for the particular disorder.

Within the group of diagnosis specific patents on which we will be focusing, two types of "overlapping" rights, and thus in a more extreme scenario, two types of patent thickets may emerge. These two types of overlapping rights could raise different issues with respect to the interpretation of essentiality in the framework of a patent pool and with respect to incentives for patent owners to cooperate. First, due to the cumulative nature of research, a thicket may be vertically oriented. A first patent may be granted on the initially unravelled diagnostic gene-disease link, while at a later stage of the research additional patents may be filed for example on specific mutations within that gene. These types of patents centre on a single gene and exhibit a high degree of interdependence urging patent owners to cooperate. A second type of thicket would be horizontally oriented. Such could be the case with multi-trait or multi-gene based disorders. One disease may be caused by defects caused by different genes, independently or cooperatively. In such a situation, interdependence of different patents is less obvious which leaves more room for patent owners to act independently.

Anticommons effect for gene-based diagnostics: blocking positions and patent thickets

Under this heading, we aim to paint a picture of the patent situation for genetic testing and resulting licensing issues. Based on these observations, some of the requirements imposed by competition law for the patent pool model to be an appropriate model to deal with licensing issues in this field can be evaluated.

A blocking patent position is a patent covering all or part of the technology that is essential to a certain activity. Due to its essentiality, one must get the permission from the patentee to use the technology. As defined above, a patent thicket occurs when multiple patents cover the same application or technology. An anticommons effect, understood as restricted access to a technology due to restricted access – because of a patent thicket or because of a single blocking position – and therefore under-use of appropriated technology, can be the result of a blocking position and/or patent thicket. When caused by one blocking position,

report has it that there is a refusal to license a key patent (at a reasonable price). Within the field of genetic testing, several reports caution for an anticommons effect of gene patents, i.e. restricted availability of testing for the patent. In most of these reports, the reason given is restrictive licensing behaviour that patentees display regarding these (diagnostic) gene patents.[63]

There are some well-known examples that nicely illustrate the broad spectrum of possible licensing strategies that are pursued in the field of gene-based diagnostic testing with respect to gene patents.

At the most restrictive end of the range of licensing policies for diagnostic testing is located the well-known and much debated approach of Myriad Genetics with regard to the testing for early-onset familial breast and ovarian cancer on the basis of BRCA1 and BRCA2. After a joint effort of several laboratories (Breast Cancer Linkage Consortium), Skolnick and co-workers at the University of Utah were the first to announce they had identified a gene at the basis of the predisposition to hereditary breast cancer and named it BRCA1. Patents were filed and eventually granted. The exclusive rights to the patents were assigned to Myriad Genetics. Soon after, a second gene also at the basis of the predisposition to hereditary breast cancer, BRCA2, was identified and patented.[64] The Myriad business model is to license the test for BRCA exclusively to a limited number of commercial genetic laboratories within specific geographic regions. However, these laboratories may only be licensed to perform limited testing of the BRCA genes, with complete sequence analysis performed only by Myriad in Salt Lake City (Utah, USA) at the cost of $2,580.[65]

At the other extreme end of the range of possible enforcement strategies is the IP management on the testing for Huntington Disease (HD) located. James Gusella and collaborators identified the location of the Huntington's gene on human Chromosome 4 in 1983, a discovery that was hailed as one of the most important advances in human genetics. It took another ten years of hard work to clone the HD gene itself. When Gusella and the Michigan General Hospital (MGH) filed for patents on the genetic testing for HD based on their findings, their main concern

[63] Cho M.K., Illangasekare, S., Weaver, M.A., Leonard, D.G. B. and Merz, J.F. 'Effects of patents and licenses on the provision of clinical genetic testing services', **5**(1) *Journal of Molecular Diagnostics* 2003, 3–8.

[64] For an overview of the BRCA1 and BRCA2 patents, see Verbeure, B., Matthijs, G. and Van Overwalle, G. 'Analysing DNA patents in relation with diagnostic genetic testing', **14** *European Journal of Human Genetics* 2006, 26–33.

[65] Walpole, I.R., Dawkins, H.J.S., Sinden, P.D. and O'Leary P.C. 'Human gene patents: the possible impacts on genetic services health care', **179** *Medical Journal of Australia* 2003, 256–283.

was that the technology not be used inappropriately. They believed they might use the exclusionary right of the patents to control the testing process thereby ensuring the quality of HD testing. To date, MGH has not exerted its own patent rights or licensed the patents to others for financial gain.

Somewhere in between the previous two approaches is located the licensing policy with regard to Cystic Fibrosis and the delta F 508 deletion held by the Hospital for Sick Children of Toronto and the University of Michigan. The cystic fibrosis (CFTR) gene and the delta F 508 deletion were identified in 1989 and patent applications were filed.[66] The patent is exploited by collecting royalties on gene-based commercial test kits only. Otherwise, non-exclusive (free) in-house diagnostic testing licenses are granted for use of the technology.

Leonard has reported more examples of restrictive licensing practices with regard to genetic testing.[67] Most of the currently tested genetic diseases that are reportedly restricted by gene patents are single gene diseases. And at present, the problems perceived seem to be mainly the consequence of one blocking patent (or patents owned by a single patent owner), not the presence of a patent thicket. According to Cournot's theory, the creation of a patent pool is an economically attractive model especially in an area with blocking patents. However, this viewpoint starts from the premise that there are at least two players holding blocking positions, a situation that is not always applicable to disease-specific patents for genetic testing, and willingness to license. It is therefore questionable whether the patent pool model is the appropriate solution to the problematic access to some of these patents when caused by restrictive licensing.

However, the situation could be of a different nature in case of polymutational or multi-gene based diseases. For example, the diagnosis of Hereditary Non-Polyposis Colorectal Cancer (HNPCC) in a particular family is in part based on molecular genetic testing for germ line mutations in one of the mismatch repair (MMR) genes. Typically, patients are being tested for two or more of four genes (MLH1, MSH2, MSH6, and PMS2) but other genes involved in the MMR pathway have been reported to be associated with HNPCC (e.g. MLH2, MLH3, PMS1, MSH3, MSH5, MYH). The number of identified genes involved in familial colorectal cancer is expected to grow even more. Some of these newly identified genes may soon be on the shortlist for "routine testing".

[66] WO 91/02796.

[67] Document available at www7.nationalacademies.org/step/Leonard_presentation_October_proteomics.ppt.

Possibly, overlapping patents may emerge on the genetic data necessary in testing for HNPCC as various patent holders filed patents.[68] Might a patent thicket arise, an HNPCC pool encompassing the essential gene patents could help to eliminate the thicket and render proprietary genomic data more accessible for use. Additionally, the patent pool is to be considered a dynamic model, both with regard to size and use. As to size, the pool will differ over time. Additional patents that are essential to the pool, once granted, can enter the pool (e.g. on other genes with a role in the same pathology and on particular mutations in those genes); other will disappear when no longer valid. As to use, licenses to a subset of patents should be possible. Some genetic laboratories, offering testing for the clinical condition as a whole, might be interested in the entire pool. Other laboratories might only be interested in a license to a subset of patents in the pool: a subset of disease genes or mutations, which are of specific interest in view of the geographical heterogeneity of the distribution of mutations; a specific gene, or even a particular mutation for the development of an antibody or another therapeutic or research tool.

In line with poly- or multi-gene-based diseases, other situations abound in the field of genetic diagnostics that may give rise to a patent thicket with several blocking patents, for example in pharmacogenomics and DNA array technology. Pharmacogenomics is characterized by the analysis of differential gene expression to provide molecular subtype information for disease prognosis and treatment choice. They usually involve many different genes and variants that alter protein expression or function, a characteristic they have in common with the genetics underlying complex diseases.

With growing knowledge of pharmacogenetics and multi-trait disorders uncovering an entanglement of all kinds of genetic variation possibly spread over multiple genes, also the complexity of the IP related to the development of a diagnostic assay grows. As shown in the hypothetical case of HNPCC and further supported by the studies on economic effects of patent pool formation, patent pooling could be an attractive model for dealing with complementary, yet essential DNA patents. To allow a certain degree of flexibility regarding which gene patents would be needed for the implementation of a certain application – a defined panel of genes to be tested for a certain disease, or a set of patents needed for producing a particular pharmacogenomics chip – the patent

[68] European patent applications have been identified for example for MSH2, MLH1, PMS2 and MSH5. Patent holders include Human Genome Sciences, John Hopkins University, Oregon Health Sciences University and Dana-Farber Cancer Institute.

platform could provide for an appropriate model. Within a patent platform for genetics, individual patent pools could be narrowly defined around single genes comprising vertically oriented patents. These individual patent pools may then be associated in a platform, thereby providing access to horizontally oriented thickets.

Incentives, benefits and doubts

The initial idea for patenting an invention is to award original research and recuperate investment in return for making public the invention. A return on investment is achieved through revenue coming from the exploitation of the invention, whether this is by putting the technology itself to work or through royalties. For third parties, different licensing schemes may be envisaged for legitimately accessing a patented technology whereby the inventor or patent owner is appropriately rewarded.[69] In this section, we aim to identify potential incentives for patent owners to set up a pool or platform; resulting benefits and potential issues will be assessed.

Standards

An important aspect in the success of ICT patent pools is standard setting. Standards can be an important trigger to set up a pool, as illustrated in the ICT sector. In the field of genetics, a standard could present itself as a set of genes or mutations to be screened, which are recognized by the international scientific community, or which reflect national or international best practice guidelines for genetic testing for a particular disease such as the standards and guidelines issued by the American College of Medical Genetics for Cystic Fibrosis[70] or Huntington's disease.[71, 72] Such guidelines could serve as an authoritarian guidance in the establishment of corresponding patent pools for the determination of essentiality and judgement on which IP should be included in the pool. The OECD already indicated that "if a limited field of application

[69] Van Overwalle, G., van Zimmeren, E., Verbeure, B. and Matthijs, G. 'Models for facilitating access to patents on genetic inventions', **7** *Nature Reviews Genetics* 2006, 143–154.

[70] Richards, C.S. *et. al.* 'Standards and guidelines for CFTR mutation testing', **4** *Genetics in Medicine* 2002, 379–391.

[71] Potter, N.T., Spector, E.B., Prior, T.W. 'Technical standards and guidelines for Huntington disease testing', **6** *Genetics in Medicine* 2004, 61–65.

[72] Ebersole, T.J., Guthrie, M.C. & Goldstein, J.A. 'Patent pools and standard setting in diagnostic genetics', **23** *Nature Biotechnology* 2005, 937–938.

and the essential patents can be defined in biotechnology, the patent pool model is worthy of consideration".[73]

Nevertheless, although it seems that a standard could be defined in genetics, it is not likely that such a standard could play a similar role in the setup of a patent pool as it does for ICT. In ICT a standard is set to guarantee interoperability of essential devices to a certain product, and to some extend, an ICT standard is based on arbitrary choice and – for evident reasons – all players want their technology to be part of the standard. Additionally, all players want reasonable access to complementary technologies in that standard. A standard for genetics on the contrary is a definition of the essentials of a gene-based disorder based on the knowledge build up over years of research. The way a standard for genetic testing is defined here, it might serve the role of quality control of testing services while it is dictated by natural occurrence, not by human choice, whereas an ICT standard rather defines the technology based on parameters set by the community. In genetics, there is not the need for the same type of interoperability, there is no such arbitrary decision involved defining a standard for genetic testing.

Potential revenue

One of the burning questions as to the feasibility of patent pools for genetics will be whether the creation of a patent pool levers the patentee an appropriate or expected revenue. The potential revenue from a (diagnostic) gene patent will ultimately depend on the total number of patients eligible for a genetic test. However, the actual revenue will be determined by the amount of diagnostic kits sold by the manufacturers and the number of tests effectively carried out in diagnostic testing centres. At present, owners of genetic patents mainly license to companies developing commercial kits and to large diagnostic laboratories. Patent pools may raise visibility and accessibility towards smaller or public genetic laboratories and thus may increase the actual amount of collected royalties by increasing its mass, thereby bridging the gap between potential and actual revenue. For example, several laboratories are still using "home brew" methods for cystic fibrosis testing, although several appropriate kits are commercially available. For other genes the diagnostic method is less amenable to a commercial product in the format of a kit for detection of a selected number of mutations. This is presently the case for e.g. the breast and ovarian cancer, tuberous

[73] OECD (2002) 'Genetic Inventions, Intellectual Property Rights and Licensing Practices – Evidence and Policies', document available at www.oecd.org/dataoecd/42/21/2491084.pdf.

sclerosis or neurofibromatosis. In both instances, litigation is difficult since data about the number of tests being performed are hard to find and litigation is costly and the amount of money to grasp small in comparison. The introduction of "all-in-one" licenses via the establishment of patent pools may promote a spontaneous registration by the users, and ease the collection of license fees.

A patent pool comprising the scattered rights on diagnostic genes could well lower the barrier of entry for users, e.g. the molecular diagnostic labs, and help them to adjust to the emerging phenomenon of patents in their practice and to facilitate the regularization of their service by creating clarity and legal certainty. For similar reasons, a gene pool can remove the reluctance to enter into research and incite innovation and test development, both from the perspective of pre- and post-pool formation.

However, to assess the potential overall economic benefit, not only the revenue of the patent pool but also the cost has to be considered. In order for a patent pool to be an effective solution, a right balance has to be achieved between the cost of creating and administering a pool and the prospect of adequate revenue generated by royalties on the end product. It remains to be seen whether a diagnostic gene patent pool covering only one disease syndrome will reach such a balance and to what extent small-size pools will prove to be viable. Extending those pools to a wider range or all genetic disorders in the form of a patent pool platform (*vide supra*) could prove to be more useful from an economic or a "clearing" point of view. Costs related to the set up of the individual patent pools and subsequent administration of the licensing could be substantially reduced when dealt with by a joint administering body in the framework of a patent platform.

Still, patent pools rely on the *voluntary* engagement of the patent owners. Conceptually, patent pools do not offer a solution in cases where patent holders do not wish to grant (reasonable) licenses. In both the Golden Rice and the SARS case, voluntary negotiations involving all essential patent owners appeared to be successful. One can only hope that the same would be true in future cases. To avoid the problem of holdout of essential patents, i.e. patent owners would purposely not contribute an essential patent to the patent pool, a grant-back clause might be included in the third-party standard licensing agreement. The grant-back clause would pertain to all patents essential to the technology and would not be strictly limited to essential patents covering further improvements of the pooled patents. The patent holder refusing to grant a license would be denied access to the other essential patents when not allowing access to his own. However, relevant to the scope

of the clause, such a clause could be seen as anticompetitive by the authorities.

Another way to approach an absence of voluntary engagement might be to resort to a compulsory licensing mechanism. Although compulsory licenses should be the last resort in a competitive environment, a "compulsory patent pool" in which a patent pool entity would seek a compulsory license from a patent holder of essential technology who does not voluntarily engage in the pool could be further investigated. However, it remains to be seen whether IP and competition law allow these measures. For example, problems might arise due to the prohibition of sub-licensing of patent rights acquired by the pool entity on such terms.[74]

On the other hand, instead of considering these more coercive actions to motivate patent owners, the SNP Consortium project proves that the perceived economic value of participation in a patent pool is not necessarily directly measurable in terms of licensing fees and royalty collection. The SNP Consortium is an example where pooled IP and pooled technical effort, resulted in both a cost-effective and very pro-competitive outcome. The specific IP policy of the SNP Consortium allowed for patenting any downstream invention made using the SNPs and the SNP map without any additional payment to or license from the consortium. One could say that the SNP Consortium is an IP pool, effective in clearing the thicket by anticipation.[75] Most remarkably, it was largely made possible by the initiative and substantial financial input from the pharmaceutical industry, otherwise perceived as the biggest obstacle towards creating access in the biomedical field.

1.4 Concluding remarks

Patent pools are designed to settle the stacking of *multiple* patents and *multiple* patent holders. Hence, pools are not applicable when one or more patents belonging to a *single* patent holder is controlling the genetic testing for a particular disease. Problems presently perceived as restricted access due to patents are mainly related to such a blocking position and not to a patent thicket. For example, one patent owner holds the different patents covering Hemochromatosis diagnosis.[76] On the contrary, all

[74] See TRIPS, Art 31.

[75] Grassler, F. and Capria, M.A. 'Patent pooling: uncorking a technology transfer bottleneck and creating value in the biomedical research field', **9**(2) *Journal of Commercial Biotechnology* 2003,111–118.

[76] Merz, J.F., Kriss, A.G., Leonard, D.G. and Cho, M.K. 'Diagnostic testing fails the test', **415** *Nature* 2002, 577–579.

putative patent pool cases discussed – Golden Rice, SARS, GFP and the hypothetical example of HNPCC – encompass multiple patents belonging to two or more patent holders. Also the SNP Consortium was incited by the otherwise high degree of fragmentation of IP.

However, given research developments in the genetics sector, setting up patent pools might turn out to be helpful in the area of genetic testing in the future to clear patent thickets, especially for disorders caused by multiple defects in a single gene (vertical thicket), diseases provoked by one or more defects in multiple genes, or, for the more common, multifactorial diseases for which often complex genetic associations are being discovered and consequently for which a patent thicket could emerge (horizontal thicket).

In the case a patent thicket would present itself, the emerging standards for good practice in medical and laboratory genetics can prove to be helpful in setting up patent pools. Vice versa, the thorough scientific evaluation of the patent portfolio in the framework of a patent pool could help to establish or to adjust those standards.

Still, seen the limited scope of a pool centred on a single disorder for which clinical testing is done at present (mostly single-gene disorders, or disorders based on a handful of genes), it might be hard to achieve a positive cost–benefit balance in the set-up of a patent pool. However, patent pool projects for different disorders may be set up by a joint administrative body creating a patent pool platform thereby reducing the cost compared to individual set up.

Additionally, although the patents may lack a high level of interdependence in the way it is known in the ICT sector, the SNP Consortium shows that the true economic incentive should perhaps be sought beyond the direct return in license fees and royalties, in a facilitating effect on innovation or in a concern for assurance or improvement of the quality of health care services, thereby benefiting all parties involved.

REFERENCES

Aoki, R. and Nagaoka, S. 'The consortium standard and patent pools', **55**(4) *The Economic Review* 2004, 345–356.

Bekkers, R., Iversen, E. and Blind, K. 'Patent pools and non-assertion agreements: coordination mechanisms for multi-party IPR holders in standardization', paper for the EASST 2006 Conference, Lausanne, Switzerland, 23–26 August 2006.

Beyer, P., Al-Babili, S., Ye, X., Lucca, P., Schaub, P., Welsch, R. and Potrykus, I. 'Golden Rice: introducing the beta-carotene biosynthesis pathway into rice endosperm by genetic engineering to defeat vitamin A deficiency', **132**(3) *The Journal of Nutrition* 2002, 506S-510S.

Cho M.K., Illangasekare, S., Weaver, M.A., Leonard, D.G. B. and Merz, J.F. 'Effects of patents and licenses on the provision of clinical genetic testing services.', **5**(1) *Journal of Molecular Diagnostics* 2003, 3–8.

Clark, J., Piccolo, J., Stanton, B. and Tyson, K. 'Patent pools: a solution to the problem of access in biotechnology patents?', in a White Paper commissioned by Q. Todd Dickinson, the Under Secretary of Commerce for Intellectual Property and Director of the US Patent and Trademark Office, 2000.

Dubock, A.C. 'Public goods and public policy for agricultural biotechnology', *7th ICABR International Conference*, Ravello (Italy), 29 June to 3 July 2003.

Dykman, H.T., 'Patent licensing within the Manufacturer's Aircraft Association', **46** *Journal of the Patent Office Society* 1964, 646.

Ebersole, T.J., Guthrie, M.C. and Goldstein, J.A. 'Patent pools and standard setting in diagnostic genetics', **23** *Nature Biotechnology* 2005, 937–938.

European Commission Communication COM (92) 445 final of 27 October 1992 on Intellectual Property Rights and Standardisation.

Graff, G. and Zilberman, D. 'Towards an intellectual property clearinghouse for Ag-Biotechnology. an issues paper', **3** *IP Strategy Today* 2001.

Graff, G., Bennett, A., Wright, B. and Zilberman, D. 'Towards an intellectual property clearinghouse for Ag-Biotechnology. Summary of an industry.', Academia and International Development Round Table, 3 *IP Strategy Today* 2001.

Graff, G.D., Cullen, S.E., Bradford, K.J., Zilberman, D. and Bennett, A.B. 'The public-private structure of intellectual property ownership in agricultural biotechnology', **21** *Nature Biotechnology* 2003, 989–995.

Grassler, F., Capria, M.A. 'Patent pooling: uncorking a technology transfer bottleneck and creating value in the biomedical research field', **9**(2) *Journal of Commercial Biotechnology* 2003,111–118.

Heller, M.A. and Eisenberg, R.S., 'Can patents deter innovation? The anticommons in biomedical research', **280** *Science* 1998, 698–701.

Holden A.L. 'The SNP consortium: summary of a private consortium effort to develop an applied map of the human genome', **26** *Biotechniques Supplement* 2002, 22–24.

Hopkins, M.M., Mahdi, S., Thomas S.M., and Patel P. 'The patenting of human DNA: Global trends in public and private sector activity (The PATGEN Project)', *Report on a European Commission's 6th Framework programme* 2006.

James, C.A. 'Business review letter to Ky P. Ewing regarding 3G platform', 2002, Department of Justice, Antitrust division.

Jensen, K. and Murray, F., 'Intellectual property landscape of the human genome', **310** *Science* 2005, 239–240.

Klein, J.I. 'Business review letter to Carey R. Ramos regarding licensing of DVD technology', 1999, Department of Justice, Antitrust division.

'Business review letter to Gerrard R. Beeney regarding MPEG-2', 1997, Department of Justice, Antitrust division.

'Business review letter to Gerrard R. Beeney regarding licensing of DVD technology', 1998, Department of Justice, Antitrust division.

(1997) 'Cross licensing and antitrust law', *An address to the American Intellectual Property Law Association,* 2 May 1997.

Kryder, R.D., Kowalski, S.P. and Krattiger, A.F. 'The intellectual and technical property components of pro-vitamin A rice (Golden rice TM): A preliminary freedom to operate review', *ISAAA Briefs* No. 20, 2000.

Lemley, M.A., 'Intellectual property rights and standard-setting organizations', **90** *California Law Review* 2002, 1889–1980.

Marra, M. A. *et. al.* 'The genome sequence of the SARS-associated coronavirus.', **300** *Science* 2003, 1399–1404.

Merges, R. 'Institutions for intellectual property transactions: the case of patent pools', in Dreyfuss, R., Zimmerman, D.L. and First, H. (eds), *Expanding the Boundaries of Intellectual Property*, (Oxford University Press, 2001), 123–166.

Merz, J.F., Kriss, A.G., Leonard, D.G. and Cho, M.K. 'Diagnostic testing fails the test', **415** *Nature* 2002, 577–579.

National Research Council of the National Academies, 'Reaping the benefits of genomic and proteomic research: intellectual property rights, innovation, and public health', 2005, National Academies Press.

OECD (2002), 'Genetic inventions, intellectual property rights and licensing practices – evidence and policies', document available at www.oecd.org/dataoecd/42/21/2491084.pdf.

Parish, R. and Jargosch, R. 'Using the industry model to create physical science patent pools among academic institutions.', *Journal of the Association of University Technology Managers* 2003, 65–79.

Potter, N.T., Spector, E.B., Prior, T.W. 'Technical standards and guidelines for Huntington disease testing', **6** *Genetics in Medicine* 2004, 61–65.

Richards, C.S., Bradley, L.A., Amos, J., Allitto, B., Grody, W.W., Maddalena, A., McGinnis, M.J., Prior, T.W., Popovich, B.W., and Watson, M.S. 'Standards and Guidelines for CFTR Mutation Testing', **4** *Genetics in Medicine* 2002, 379–391.

Rota, P.A. *et. al.* 'Characterization of a novel coronavirus associated with severe acute respiratory syndrome', **300** *Science* 2003, 1394–1399.

Shapiro, C., 'Theories of oligopoly behavior', in Schmalensee R. and Willig, R. (eds.), *Handbook of Industrial Organization*, (Elsevier Science Publishers, 1989), 330–414, at 339.

'Navigating the patent thicket: cross licenses, patent pools and standard setting', in Jaffe, E., Lerner, J. and Stern, S. (eds), *Innovation Policy and the Economy*, volume I, (MIT Press, 2001), 119–150.

'Setting Compatibility Standards: Cooperation or Collusion?', in Dreyfuss, R., Zimmerman, D.L., First, H. (eds) In *Expanding the Boundaries of Intellectual Property – Innovation Policy for the Knowledge Society*, (Oxford University Press, 2001), 81–102.

Simon, J.H.M., Claassen, E., Correa, C.E. and Osterhaus A.D.M.E. 'Managing severe acute respiratory syndrome (SARS) intellectual property rights: the possible role of patent pooling', **83**(9) *Bulletin of The World Health Organisation* 2005, 641–720.

US Department of Justice & Federal Trade Commission (1995) 'Antitrust Guidelines for the Licensing of Intellectual Property'.

Van Overwalle, G., van Zimmeren, E., Verbeure, B. and Matthijs, G. 'Models for facilitating access to patents on genetic inventions', **7** *Nature Reviews Genetics* 2006, 143–154.

Verbeure B., van Zimmeren E., Matthijs G., and Van Overwalle G., 'Patent pools and diagnostic testing', **24**(3) *Trends in Biotechnology*, 2006, 115–20.

Verbeure, B., Matthijs, G. and Van Overwalle, G. 'Analysing DNA patents in relation with diagnostic genetic testing', **14** *European Journal of Human Genetics* 2006, 26–33.

Verbeure, B., van Zimmeren, E., Matthijs, G. and Van Overwalle, G., 'Patent pools and diagnostic testing', **24**(3) *Trends Biotechnology*, 2006, 115–20

Versaevel, B. and Dequiedt, V. 'Patent Pools and the Dynamic Incentives to R&D', *Cahiers de Recherche, Working Papers No 2009/6*, available at www.em-lyon.com/ressources/ge/documents/publications/wp/2006-09.pdf.

Vlassak, K. and Schüller, K. 'The effect of patents on research and development of diagnostic kits', in Van Overwalle, G. (ed.), *Gene Patents and Public Health*, (Bruylant, 2007), 99–113, at 104.

Walpole, I. R., Dawkins, H. J. S., Sinden, P. D. and O'Leary P. C. 'Human gene patents: the possible impacts on genetic services health care', **179** *Medical Journal of Australia* 2003, 256–283.

Wellford, H. B. 'Antitrust issues in standard setting' an address at the 2nd Annual Seminar on IT Standardization and Intellectual Property China, Electronics Standardization Institute Beijing, China, 29 March 2007.

2 Case 1. The MPEG LA® Licensing Model

What problem does it solve in biopharma and genetics?

Lawrence A. Horn

2.1 Introduction

Consumer electronics, telecommunications, computer and related industries have successfully employed a patent licensing model that encourages innovation through marketplace competition by balancing patent holders' expectation of reasonable return on their intellectual property (IP) with marketplace desire for widespread availability of technology. The model pioneered by MPEG LA[1] offers fair, reasonable, non-discriminatory access to essential IP from multiple patent holders under a single license as an alternative to separate licenses. The MPEG LA® Licensing Model has worked well where it solved a problem. But, what problem does it solve in biopharma and genetics?

2.2 Background

A patent is the grant of a property right covering an invention. The right conferred by the patent gives its owner the right to exclude others from making, using, offering for sale, selling or importing the invention in the absence of a license. Where standards and other technology platforms consist of many patents owned by many patent owners, the number of licenses required of users may be too costly and inefficient for users to negotiate. This is often referred to as a patent thicket.[2] By increasing uncertainty and conflict and restricting freedom of movement surrounding use of a technology, a patent thicket may impede its adoption, interoperability and use.

In the 1990s the MPEG-2 standard, which is required for DVD, satellite, cable and other digital video applications, faced a patent thicket.

[1] See www.usdoj.gov/atr/public/busreview/215742.htm; www.mpegla.com.
[2] See, for example, Shapiro, C., 'Navigating the patent thicket: cross licenses, patent pools and standard setting,' http://haas.berkeley.edu/~shapiro/thicket.pdf.

The single biggest challenge to MPEG-2 adoption was access to essential patents. MPEG-2 patents owned by many parties made it virtually impossible for the standard to be used. MPEG LA offered an alternative as a solution addressing the market's need for transactional efficiency. As a convenience to users, the licensing model pioneered and employed by MPEG LA enables multiple MPEG-2 users to acquire essential patent rights from multiple patent holders in a single transaction as an alternative to negotiating separate licenses. MPEG-2 became the most successful standard in consumer electronics history, and the MPEG LA® Licensing Model (see Figure 2.1) has become the template for addressing other patent thickets.[3]

Wherever an independently administered one-stop patent license would provide a convenient alternative to assist users with implementation of their technology choices, the MPEG LA® Licensing Model may provide a solution. MPEG LA is granted a nonexclusive sublicense to essential intellectual property rights (IPRs) owned by multiple essential IPR owners, offers users a single license incorporating them on fair, reasonable non-discriminatory terms, collects and distributes royalties for the benefit of essential patent owners, and receives an administrative fee out of royalties collected. MPEG LA is an independent licensing administrator; it is not related to any standards agency and is not itself a user or owner of patents under license or an affiliate of a patent owner.

By balancing patent users' interest in reasonable access with patent owners' interest in reasonable return, MPEG LA creates the opportunity for adoption of new technologies and fuels innovation. Today MPEG LA clears patent thickets in licensing programs consisting of essential patents in fifty-seven countries.[4] Additional licensing programs are in development.[5]

2.3 Elements of the MPEG LA® Licensing Model

Where many users require many licenses under many interdependent patents owned by multiple patent holders, a patent pool license may be useful in promoting technological innovation and use, permitting freedom of technological movement, reducing the potential for conflict and providing a realistic alternative to traditional bilateral licenses. The following summarizes various legal, marketing and organizational elements.

[3] See www.mpegla.com. [4] See www.mpegla.com. [5] See www.mpegla.com/pid/.

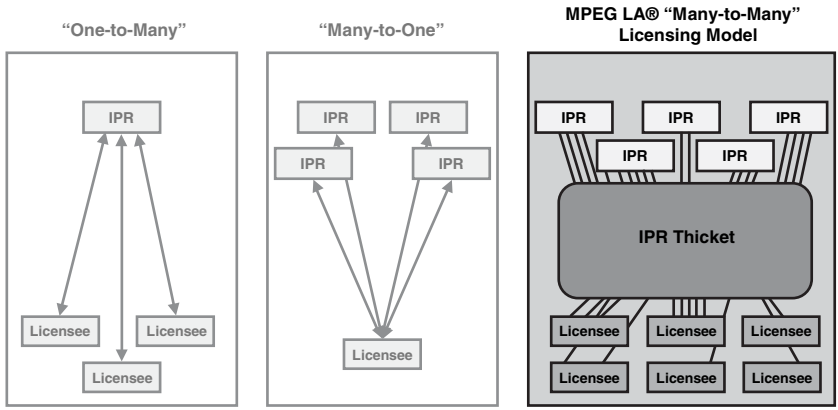

Figure 2.1 MPEG LA® Licensing Model

Marketability

A license must be responsive to marketplace needs and to variations on the MPEG LA® Licensing Model suited to meet them. Without both buyers and sellers, a license is unmarketable. Among other things, licenses should: resolve patent thickets (critical mass of essential patent holders with a critical mass of essential patents) that favor a pool license as an alternative to bilateral licenses; the subject technology should be of value to a mass market; royalty products should be readily identifiable; and the license should reflect a balance of royalty, revenue, administrative fee and other incentives that realize reasonable return to patent holders, reasonable access for licensees, reasonable profit for a licensing administrator, and necessary compliance and enforcement efforts.

Legal tenability

A patent pool license offers fair, reasonable, non-discriminatory access to essential IP, with the goal of including as much IP as possible for the convenience of the market. The patent pool administrator employs independent patent experts to evaluate patents for their essentiality to the defined technology, offers a standard license agreement with the same terms to everyone, actively markets the license and takes responsibility for enforcing contractual compliance.

Essentiality and a defined field of use

A patent may not be included unless it is infringed by use of the defined technology. This communicates clearly to both licensors and licensees the rights granted by the joint license and why patents are included or excluded. As a legal matter, it assures that the joint license is precise enough to include what a licensee needs to practice the particular technology and that competent competitive implementation options are neither favored nor foreclosed.

Nonexclusivity

Alternative (e.g. direct) licensing options are not precluded either to licensors or licensees.

Independence

The licence administrator is neither licensor nor licensee (nor an affiliate of any); both are customers, thus assuring impartial administration of the joint licence with a goal of balancing reasonable access for users with reasonable return to patent owners. Each licensing program is administered separately, fairly and impartially.

Licensor protections

Licensors share in reasonable allocation of royalties commensurate with their contributions to the licence. The independent patent evaluation process and openness of the joint licence to as many essential patents as possible assure fairness, value and competition law compliance.[6] In addition, to prevent licensees from using the joint licence to protect themselves from lawsuit in order to sue others on their own patents and to encourage negotiation and innovation in support of the technology platform, a patent holder may remove its patents from coverage as to a particular licensee if the licensee brings a lawsuit or other proceeding for infringement of an essential or related patent against the licensor and has refused to grant the licensor a licence on fair and reasonable terms and conditions under such patents on which the lawsuit is based.

[6] For example, the MPEG-2 Patent Portfolio Licence has grown from the original 8 patent owners and 100 essential patents to include more than 825 essential patents in 57 countries owned by 25 patent owners. There are approximately 1,500 licensees. See www.mpegla.com.

Licensee protections

Licensee data is protected as confidential from both patent holders, licensees and others. In addition, licensors are required to include all of their essential patents to the defined technology. Licensees are assured most favourable royalty rates and pay the same royalties to MPEG LA whether or not they are patent owners. To assure that a licensee does not take advantage of the joint licence yet refuse to license its own patents on fair and reasonable terms, any licensee (or affiliate) may add essential patents to the joint licence on the same terms and conditions as other patent holders. But, if a licensee chooses not to do so, it agrees to grant back a licence similar in scope to the joint licence rights granted to the licensee on fair and reasonable terms under any essential patents that the licensee and its affiliates may own. In addition, a clear, up-to-date list of licensed patents is maintained, and in the interest of including as much essential IP as possible for licence convenience, the joint licence must remain open for the continuing submission, evaluation and inclusion of essential patents.

Professional management

The licensing administrator provides a seamless worldwide connection among patent owners, users and technology. This requires a financially sound and motivated organisation with expertise in identifying joint licensing products the market can use; building consensus among fiercely independent patent holders each with its own expectations of value; the development of joint licence products that meet patent holders' interest in a reasonable return and the interest of the marketplace in access to fundamental technology under fair, reasonable terms; IP, anti-trust, contract drafting and administration and taxation; licensing and marketing; website management; transaction fulfilment and auditing; and international tax mitigation and reconciliation.

2.4 Biopharma and genetics: Where is the problem?

Since inception, MPEG LA has evangelized about the utility of the MPEG LA® Licensing Model to address patent thickets in industries outside of consumer electronics, telecommunications, computer and related industries. With expertise also in biopharma and genetics, MPEG LA has actively tried to identify problems there in which the MPEG LA licensing model may provide a solution and has written

articles[7] and attended worldwide conferences[8] in pursuit of that objective. Based on research commissioned by MPEG LA,[9] biopharma and genetics differ from consumer electronics, telecommunications, computer and related industries in ways that alter the value equation and therefore, may affect the feasibility of one-stop technology platform licensing:

Standards

Biopharma and genetics are not largely standards-driven.

Interoperability

In biopharma and genetics, interoperability and non-exclusivity may be desirable and appropriate for early-stage research (upstream development) technology that is ready to use, and certain diagnostic applications, but the value of upstream development is limited by research exemption,[10] difficulty of tracking infringement violations and lack of reach-through patent claims[11] that limit patent values.[12] In general, the business–legal ecosystem supports an environment in which academic institutions do basic research, biotech companies are in the target business, pharmaceutical companies conduct clinical trials and commercialize, and the law protects each in its own sphere. Even generic manufacturers are

[7] Horn, L. 'Alternative approaches to IP management: One-stop technology platform licensing', **9**(2) *Journal of Commercial Biotechnology,* January 2003, 119–127.

[8] Lee, P. 'Alternative one-stop platform technology patent licenses', Presentation at the Gene Patents and Clearing Models workshop sponsored by the Fund for Scientific Research (FWO, Flanders, Belgium), EuroGentest, the Centre for Intellectual Property Rights and the Centre for Human Genetics, K.U. Leuven, Leuven, Belgium, 8 June 2006; Horn, L., 'Alternative one-stop platform technology patent licenses', Presentation at the OECD Workshop on Collaborative IPR Mechanisms – Patents Pools, Clearinghouses, Washington, DC, 8–9 December 2005; Horn, L. 'Patent pools and business' Panel Presentation at Licensing Executives Society International Conference, Paris, France, 29 March 2004; Horn, L., 'Novel approaches to IP management: one-stop technology platform licenses', Presentation at the OECD Workshop Genetic Conventions, Intellectual property Rights and Licensing Practices, Berlin, Germany, 24 January 2002.

[9] The research was conducted by Campbell Alliance Group, Inc. of Raleigh, NC in spring 2005.

[10] *Merck KGaA* v. *Integra Lifesciences, Ltd.*, 545 U.S. US 193 (2005), *Whittemore* v. *Cutter,* F. Cas. 1120 (C.C.D. Mass. 1813), The 1984 Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98–417, 98 Stat. 1585.

[11] *Univ. of Rochester* v. *G.D. Searle & Co., Inc.*, 249 F. Su 2d 216 (W.D.N.Y. 2003), aff'd, 358 F.3d 916 (Fed. Cir. 2004), cert. denied, 543 US 1015 (2004).

[12] The so-called Cohen-Boyer patents for recombinant DNA and a patent for polymerase chain reaction (PCR) techniques for amplifying specific DNA segments have proved valuable despite certain of these limitations.

permitted by law to start their testing before patents expire in order to shorten lag time to market.

Branding

In consumer electronics, telecommunications, computer and related industries, the same technology has many users, and it is branding that creates value. But, patent pool licences that do not offer serious alternatives to bilateral licences are not valued by the marketplace. In biopharma and genetics, IP is the value, and exclusivity at the end (downstream development) part of the therapeutic product development chain is key.

Alternatives

In biopharma and genetics, a potential licensee faced with royalty-stacking issues often pursues less expensive opportunities, invents around the problem, ignores it at its own risk, waits and/or uses other tools such as public databases.[13]

Litigation

Litigation for infringing use of early research tools does not appear to be a widespread occurrence in biopharma and genetics – at least not yet.

2.5 Conclusion

The MPEG LA® Licensing Model has proven utility where there is a problem to be solved. As in other industries, to identify problems in biopharma and genetics, one must look to where the market's need for ease of access and avoidance of conflict intersect.

First, there must be a market need by many users for IPRs held by multiple owners of interdependent patents covering parts of a product, manufacturing method or process in a defined application or field of use.

[13] The SNP Consortium making available single nucleotide polymorphisms (SNPs) and an SNP map is one example. See Grassler and Capria, 'Patent Pooling: Uncorking a technology transfer bottleneck and creating value in the biomedical research field,' **9**(2) Journal *of Commercial Biotechnology,* January 2003, 113–14.

Second, incentives and expectations must be balanced for patent owners, licensees and licensing administrator and in the public interest of expanding innovation. Patent pool licences that do not offer a serious alternative to bilateral licences will not be valued and will not be profitable. In the event of a compulsory licence, there may be no alternative.

Third, the problem must be such that professional patent pool licensing administration – in the form of proactive pool licence development, licensing and marketing efforts, proven royalty disbursement infrastructure and critical mass volumes – is required to solve it. Patent pools around targets (e.g. signalling protein or cellular surface protein pathways for purposes of developing agonists to stimulate desirable reactions or antagonists to block undesirable ones) where researchers could be granted licenses for a broad range of associated patent thickets may offer one such opportunity.[14] Diagnostic genetics may offer another. Drug structure platforms common to a wide array of drugs may offer yet another.[15]

Where the market's need for ease of access and avoidance of conflict intersect and there is a problem in need of an appropriate solution, the MPEG LA® Licensing Model is available to assist.

REFERENCES

Grassler and Capria, 'Patent pooling: Uncorking a technology transfer bottleneck and creating value in the biomedical research field', **9**(2) *Journal of Commercial Biotechnology*, January 2003, 113–14

Horn, L. 'Alternative approaches to IP management: One-stop technology platform licensing', **9**(2) *Journal of Commercial Biotechnology*, January 2003, 119–127

'Alternative one-stop platform technology patent licenses' presentation at the OECD workshop on collaborative IPR mechanisms – patents pools, clearinghouses', Washington, DC, 8–9 December 2005

'Patent pools and business', Panel presentation at Licensing Executives Society International Conference, Paris, France, 29 March 2004

'Novel approaches to IP management: One-stop technology platform licenses', Presentation at the OECD Workshop Genetic Conventions, Intellectual property Rights and Licensing Practices, Berlin, Germany, 24 January 2002

[14] See also Grassler and Capria, 'Patent Pooling: Uncorking a technology transfer bottleneck and creating value in the biomedical research field,' **9**(2) *Journal of Commercial Biotechnology,* January 2003, 115.

[15] Horn, L., 'Alternative approaches to IP management: One-stop technology platform licensing,' **9**(2) *Journal of Commercial Biotechnology*, January 2003, 119–127.

Lee, P. 'Alternative one-stop platform technology patent licenses', Presentation at the Gene Patents and Clearing Models workshop sponsored by the Fund for Scientific Research (FWO, Flanders, Belgium), EuroGentest, the Centre for Intellectual Property Rights and the Centre for Human Genetics, K.U. Leuven, Leuven, Belgium, 8 June 2006

Shapiro, C., 'Navigating the patent thicket: cross licenses, patent pools and standard setting', http://haas.berkeley.edu/~shapiro/thicket.pdf

3 Case 2. The SARS case

IP fragmentation and patent pools

Carmen E. Correa

3.1 Introduction

In the last ten years diverse entities have filed for patents in the field of genomics. The race for patenting DNA sequences started around 1980 growing steadily until reaching its peak by the late nineties. Nowadays, the race seems to have slowed down and the number of patents actually granted in the field of genomics is not significantly high in proportion to the number of applications.[1] However, despite of the possibility that the patenting of DNA decreases due to the increase of patenting thresholds and, the fact that many patent applications are dropped as they prove to lack commercial viability (30% of US patents granted by the 1990s were abandoned by 2005),[2] the amount of patents claiming DNA seems still relevant enough to raise concerns regarding access to the covered technology for further development.

The entities filing patents on DNA sequences range from big pharmaceutical companies to academic institutions. This diversity has resulted in IP fragmentation (one technology/many owners). This fragmentation has originated different concerns and controversy as to whether it represents a problem to R&D and how it may affect public health.[3]

This paper briefly explains the effects of IP fragmentation. It continues with the presentation of patent pools as a solution to the negative effects of IP fragmentation. Finally, it discusses whether a patent pool represents an option for the SARS case.

[1] Hopkins, M. et al., 'DNA patenting: the end of an era?' **25**(2) *Nature Biotechnology*, February 2007,185–7.
[2] Hopkins, 'DNA patenting: the end of an era?', 2007.
[3] Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', see Chapter 1 of this volume.

3.2 IP fragmentation

IP fragmentation has an important economic impact in business: as much as the needed technology has become more fragmented, the revenues decrease. The erosion of revenues is due to licensing cost and royalty stacking.[4] In summary, "Developing commercial biomedical products requires access to many different IP rights and negotiating access with different patent owners is prohibitively difficult and costly."[5]

The fragmentation of IP rights may create several different problems in the R&D of health solutions. It may frustrate or delay development of products or, the cost of resolving the IP landscape may result in more expensive products.[6]

Moreover, the risk of a blocking position arises with IP fragmentation if one of the essential technologies is licensed on exclusive terms so third parties cannot have access to part of the technology deemed necessary to manufacture a product.[7, 8, 9, 10]

3.3 Patent pool as a potential solution

Among other proposals, the concept of patent pools has been analyzed as a potential solution to the negative impact of IP fragmentation. However, in the area of biotechnology there are very few operational examples.

Some of the patent pool options that have been put in practice to solve IP fragmentation problems are the so-called "force cooperation" and "cooperative pooling".[11] Force cooperation represents pools formed via government intervention and has the disadvantage to discourage innovation. The idea of patent rights aims to create an advantage for the inventor to exclude others from practicing its invention. However, when inventors cannot have the autonomy to decide in what

[4] Verbeure, see Chapter 1 of this volume.
[5] Gaule, P. 'Towards Patent Pools in Biotechnology?', ***2(2)*** *Innovation Strategy Today,* 2006, 123–34.
[6] Simon, J. 'Patent Pools in Biotechnology setting a precedent with SARS', OECD Workshop on Management of IPR 8 December, 2005.
[7] Verbeure, see Chapter 1 of this volume.
[8] Simon, J. 'Patent Pools in Biotechnology setting a precedent with SARS'.
[9] Goldstein, J. et al. 'Patent pools as a solution to the licensing problem of diagnostic genetics. United States and European perspectives'. *Drug Discovery World*. Spring 2005. 87–91.
[10] Simon, J. et al. 'Managing severe acute respiratory syndrome (SARS) intellectual property rights: the possible role of patent pooling', **83**(9)*Bulletin of the World Health Organization*, September 2005, 707–10.
[11] Krattiger, A. et al. 'Intellectual property management strategies to accelerate the development and access of vaccines and diagnostics: case studies on pandemic influenza, malaria and SARS', **2**(2) *Innovation Strategy Today*, 2006, 67–122.

type of agreement they may engage, such advantage may no longer be granted and innovation loses incentive. Cooperative pools, on the other hand, are formed on a voluntary basis by IP owners to maximize the advantage of patent rights, with the benefit that they create incentive to innovation and, also it facilitates entry to the market and cost reduction by increasing competition.[12]

Lessons can be learned from the successful experiences in the DVD-ROM and DVD-Video industry of cooperative patent pools formed around 1997.[13]

In the biotechnology industry, where the IP fragmentation landscape, may result in very high cost or, even in a barrier to development, a patent pool arrangement can facilitate downstream development because the companies that need to assemble technology from several IP owners would have a "one stop shop"[14] to license all the essential technology to develop their products.

The one stop shop results in a reduction of their licensing transaction cost, and eliminates the risk of a blocking position as the pool clears blocking scenarios.

3.4 The SARS case

Now, let's explore whether a pool arrangement is an option to resolve the SARS IP fragmentation.

In 2002, when the first outbreak of SARS happened, the WHO set up a network among several institutions to determine the cause of the disease. As a result, several of those institutions and other entities filed patent applications to cover part or the whole genetic sequence of the SARS-coronavirus.[15]

[12] Simon, J. et al 'Managing SARS intellectual property rights: the possible role of patent pooling'. Also, Krattiger, A. 'IP management strategies to accelerate the development and access of vaccines and diagnostics: case studies on pandemic influenza, malaria and SARS'.

[13] Krattiger, A. 'IP management strategies to accelerate the development and access of vaccines and diagnostics: case studies on pandemic influenza, malaria and SARS'. Also see, Gaule, P. 'Towards Patent Pools in Biotechnology?'; Simon, J. et al. 'Managing SARS intellectual property rights: the possible role of patent pooling'.

[14] Krattiger, A. 'IP management strategies to accelerate the development and access of vaccines and diagnostics: case studies on pandemic influenza, malaria and SARS'. Also see, Gaule, P. 'Towards Patent Pools in Biotechnology?'; Simon, J. 'Managing SARS intellectual property rights: the possible role of patent pooling'; Verbeure, see Chapter 1 of this volume.

[15] Simon, J. et al. 'Managing SARS intellectual property rights: the possible role of patent pooling'.

These patents have been named "primary" patents because such patents most likely will be needed to produce a large range of products for SARS.[16] Also, many other patent applications have been filed for different aspects of the SARS technology to cover diagnostic, antivirals etc. that most likely will need to be combined with the technology covered by the primary patents.[17]

The uncertainty over patent rights represents a challenge to product development because companies willing to develop any SARS-related product need to deal with several IP applicants holding primary patents, but they do not know from which they will get a license, or if they will require to license from all such patent holders. This uncertainty adds to the complexity to assemble a license, which translates in additional costs and time to the product development. Together with the challenge to decide whether to invest at such a high cost when they are not even sure whether a market will develop for their products[18] – no significant outbreaks since 2003 – setting up a patent pool is a real challenge.

This uncertainty may remain for years, delaying development that could help us to be prepared efficiently for any next outbreak.

However, if a patent pool is arranged, everyone in the economic-development chain wins in what can be called a "win-win-win" situation:[19]

1. Licensors, who will close deals with licensees, in a manner that allows access in a non discriminatory basis to all interested licensees. Besides, blocking positions are cleared and infringement litigation reduced. Also, IP holders will license among themselves the IP, which allows them to continue research in the field without overlapping efforts.
2. Potential licensees will reduce their licensing transaction cost and have access to the technology they need to develop a product, giving the manufacturers tools to innovate and compete downstream.
3. And, finally, public health is also better off because solutions to SARS can be efficiently brought into the market.

To form a patent pool several steps need to be completed:

1. Identify the relevant IP holders.
2. Negotiations shall lead to the execution of a letter of intent wherein the parties agree to go forward and to submit their patent applications in confidence to an independent evaluator.

[16] Simon, J. 'Patent pools in biotechnology setting a precedent with SARS'.
[17] Ibid.
[18] Simon, J. et al. 'Managing SARS intellectual property rights: the possible role of patent pooling'.
[19] Simon, J. 'Patent pools in biotechnology setting a precedent with SARS'.

3. Evaluation by an independent evaluator shall determine which patents are suitable for the pool (essentiality and complementation of patents, together with the issue of validity of the patents are the main core of issues this expert need to clarify). In parallel an operating model for the pool shall be negotiated and exchanged with the regulatory authorities in order to seek for an advisory opinion.
4. Execution of a final agreement for the practical operation of the pool shall be completed.

In respect of the prospective SARS patent pool the following steps have been taken:

- ViroScope[20] (formerly known as CoroNovative) and other patent holders (British Columbia Cancer Agency, Centre for Disease Control and Prevention and Versitech Limited[21]) that are expected to hold a significant number of primary patents have been identified. Subsequently, negotiations led to the execution of a letter of intent; therefore, the parties have submitted their patent applications to the independent evaluator to determine their suitability in the SARS patent pool. In parallel, exchange with the regulatory authorities has been initiated with the advice of experts in antitrust law. Furthermore, an operating model is in the process of been discussed.
- Once all this work is completed, a full agreement will be executed in due consideration of the results of the expert evaluation and the advisory opinion of the antitrust authorities, and an entity shall be appointed as the pool manager.

Generally, antitrust guidelines provide similar requirements (the most relevant of such guidelines have been issued by the DOJ, FTC in the US and the EU Commission in Europe) with the aim to determine whether a patent pool is considered pro-competitive. In summary, these guidelines basically require that the patent pool:

1. Results in the reduction of licensing transaction cost. Despite the criticisms associated with the high cost of setting up a patent pool,[22] such cost may be lower than the cost associated with individual licensing, and over-weighted by the avoidance of blocking positions. In the specific case of SARS, the associated cost of setting up the

[20] ViroScope is a spin-off company of Erasmus MC Rottterdam, www.viroscope.com.
[21] Versitech is a company affiliated to Hong Kong University.
[22] Gaule, P. 'Towards patent pools in biotechnology?' Also see Krattiger, A. 'IP Management Strategies to Accelerate the Development and Access of Vaccines and Diagnostics: Case Studies on Pandemic Influenza, Malaria and SARS'.

pool is minimized by the fact that most legal and technical advice has been obtained on a *pro bono* basis.[23]

2. Clears blocking position. No exclusive license shall be granted within and outside the pool, this requirement shall be incorporated in the patent pool agreement.
3. Permits the dissemination of technology and stimulates innovation. In the SARS case, this requirement will be fulfilled because certainly more licensees would be able to have access to the technology and competition to bring a product, first, into the market would speed up development.
4. Includes only essential and complementary patent technology. Determination by the independent evaluator is pending in the SARS case.
5. Shall not shield any invalid patents. This is one of the criticisms that frequently arise by the formation of a patent pool. This requirement can be fulfilled by providing in the patent pool agreement a special mechanism to revise the patent pool to exclude any patent that becomes invalid at any time. This mechanism shall also provide for the proportional reduction of royalties in lieu of the exclusion of the patent that has become invalid and the establishment of the fair rate in consideration to the valid patents that integrate the pool. The effect for the licensees shall be similar as to the effect that it would have the termination of any individual license in the assembly of the technology in absence of the pool, with the advantage that the patent pool serves as a control, which allows to ensure that the licensing efforts are limited to the patents that are actually valid and necessary, which overall cost is lower than the sum of individual licenses.

Analyzing the potential SARS patent pool, it seems possible to predict that most of those guidelines will be covered. And, the SARS case can be viewed as a unique opportunity for pooling genomic patents because:

1. The IP holders have agreed to move forward in this direction.
2. The patents have a similar stage of maturity.
3. Legal advice is given by specialized professionals in the relevant fields, which has facilitated:
   (a) the appointment of an independent evaluator to determine essentiality, complementarities and prospective validity of the patents that would integrate the pool; and

[23] Drinker, Biddle & Reath (patent) and Morgan, Lewis & Bockius (antitrust).

(b) the patent pool agreement, including mechanisms in compliance with antitrust guidelines is being drafted.

4. Several health organizations, such as WHO, Health Canada and NIH, support the idea.[24]

Regarding validity of the patents, concerns may arise because the SARS patent pool is actually a pool of patent applications rather than a pool of granted patents. However, the fact that patent applications confer to the applicants, as from the time of publications, the provisional right[25] to royalties, and therefore, licenses can be executed prior to the time such patents are granted. Similarly, a patent application shall be allowed in a pool, unless the independent evaluator has reasonable doubts to propose exclusion of a patent application from the pool, as far as the pool agreement provides the proper mechanism to exclude such technology upon the decision not granting the corresponding patent, or its invalidity is declared, or the decision of granting the patent limits its claims to those that make the patent no longer compatible with the pool (e.g. lack of essential and complementary characteristics). The solution shall be similar as to the case that a valid patent in the pool is declared invalid upon its challenge. Therefore, any concerns regarding whether or not a patent pool can be formed by patent applications may seem irrelevant.

3.5 Conclusions

The concept of patent pools may be a solution to IP fragmentation, but still difficult to determine whether it will be an attractive option for the biotech industry.[26] Specific issues arise due to the characteristics of the biotech industry. Although, I will not further discuss these issues it is worth mentioning one important one: contrary to the electronics industry, there are no standards to comply with, which make it particular difficult to determine which patents are essential and complementary. However, some attempts exist to provide standards in the area of diagnostics which may facilitate the task in such an arena.[27]

Also, the valuation of a company in the biotechnology industry depends heavily on its IP, which is of particular relevance in the case of small companies or start-ups. This makes companies very cautious to

[24] Simon, J. et al. 'Managing SARS intellectual property rights: the possible role of patent pooling'.
[25] 35 USC §§154 (US) and similar provision exists in other jurisdictions.
[26] Verbeure, see Chapter 1 of this volume.
[27] Verbeure, see Chapter 1 of this volume. Also see, Goldstein, J. 'Patent pools as a solution to the licensing problem of diagnostic genetics. US and European perspectives'.

enter into arrangements that in their view may compromise the valuation of the company.[28]

Finally, patent pools may not be a solution for all IP fragmentation cases, but they represent a suitable solution in many cases and are worth exploring; and, very likely, could be a solution to the SARS IP landscape as has been explained earlier. This experience would also serve as a valuable precedent and may promote consideration of changes to adapt legal guidelines to the specific needs of the industry that may prove necessary in the course of its implementation.

REFERENCES

Hopkins, M.; Mahdi, S.; Patel, P & Thomas, S. 'DNA patenting: the end of an era?', **25**(2) *Nature Biotechnology*, February 2007. www.nature.com/naturebiotechnology

Gaule, P. 'Towards patent pools in biotechnology?', **2**(2) *Innovation Strategy Today*, 2006, 123–34 www.biodevelopments.org/innovation/index.htm

Goldstein, J.; Ebersole, T.; Guthrie, M.; Hirschfeld, A. & van den Broek, B 'Patent pools as a solution to the licensing problem of diagnostic genetics. United States and European perspectives', *Drug Discovery World*, Spring 2005, 87–91 www.rjcoms.com/data/pdfs/4patent%20pools.pdf

Krattiger, A., Kowalski, R., Eiss, R. & Taubam, A. 'Intellectual property management strategies to accelerate the development and access of vaccines and diagnostics: case studies on pandemic influenza, malaria and SARS', *2(2) Innovation Strategy Today*, 2006, 67–122. www.biodevelopments.org/innovation/index.htm

Simon, J. 'Patent pools in biotechnology setting a precedent with SARS', OECD workshop on management of IPR, 8 December 2005. Unpublished material supplied by the author

Simon, J., v Claassen E., Correa, C. & Osterhaus, A. 'Managing severe acute respiratory syndrome (SARS) intellectual property rights: the possible role of patent pooling', **83**(9) *Bulletin of the World Health Organization*, September 2005, 707–10

Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume

[28] Gaule, P. 'Towards patent pools in biotechnology?'

4 Critical analysis of patent pools

Jorge A. Goldstein[*]

4.1 Introduction: Are biotech patent thickets real?

As is well demonstrated by Verbeure,[1] Horn[2] and Correa,[3] the use of patent pools in biomedicine and biotechnology is in its infancy. The chapters by Verbeure and Horn especially, as well as publications of others,[4] sometimes appear to reflect more a premonition of problems to come than an existing paralysis of commerce caused by intractable patent thickets. These expositions at times seem less driven by a need to provide an immediate solution to frustrated marketing constituencies mired in stacked royalties and unavailable licenses, than an academic estimate of how time-proven solutions to thickets (learned primarily in the consumer electronics field) may be applied to the new world of genetics and molecular medicine.

Yet the problems of patent thickets in the field of commercial biotechnology are real. The Golden Rice problem, as pointed out by Verbeure,[5] was not imaginary or academic. Potrykus charged right ahead with the genetic engineering of rice so as to enrich it in ß-carotene, apparently oblivious to the existence of any IP rights – only to come to the end of his successful research and find out that there were seventy patents belonging to thirty-two companies that would potentially block commercialization! The fact that in this case an ingenious mixed humanitarian/mercantile solution was found is a testimony to

[*] The author wishes to thank Christine Formas Norris for her able assistance in the preparation of this chapter.

[1] Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', see Chapter 1 of this volume.

[2] Horn, A.H., 'Case 1. The MPEG LA® Licensing Model. What problem does it solve in biopharma and genetics', see Chapter 2 of this volume.

[3] Correa, C.E., 'Case 2. The SARS case. IP fragmentation and patent pools', see Chapter 3 of this volume.

[4] Ebersole, T. J., Guthrie, M., and Goldstein, J. A., 'Patent pools as a solution to the licensing problems of diagnostic genetics', **17** Intellectual Property & Technology Law Journal, Jan. 2005, 1–8.

[5] Verbeure, see Chapter 1 of this volume.

the creativity of the individuals involved. The inventors assigned their IP to one assignee, which acquired other needed IP from third parties, and then gave back to the inventors a humanitarian license with the right to sublicense public research institutions and low-income farmers in developing countries. The assignee retained commercial rights so as to produce Golden Rice as a nutraceutical in the developed world, although at the time of writing, it has no plans to commercialize.[6] It is not to be expected that such ingenious solutions will also be available or that the players involved will act in such smooth unison when we are dealing in other, more competitive, areas of modern biotechnology.

The SARS virus problem described by Correa[7] is particularly real – and has an additional twist to that of Golden Rice. The interested constituencies in this case carried out their IP due diligence ahead of completing the science[8] – apparently having learned from Potrykus not to wait until the last moment. They then found out how fragmented the IP would be once patents started issuing from the myriad of SARS patent applications on file.[9] Indeed the SARS example shows that the uncertainty of who would own what patent rights at the end of the day provided an additional impetus to think about and attempt to create a patent pool.[10] As Correa points out, the SARS pool seems to be composed primarily of pending patent applications, not issued patents – and she concludes that this fact 'seems irrelevant'.[11]

I cannot help, however, but warn that trying to use a patent pool to settle potential multi-party interferences in the US is a task to be approached with great care, lest the pool ends up containing patents that are not based on the first to invent principle, as is required under US patent law.[12] The danger of a collusive interference settlement would arise by deciding arbitrarily, i.e., not based on the facts of who was the first to invent, which patent applications (and eventual patents) will go into the pool and which ones will not. In order to prevent such a problem it would be advisable to establish a formal mechanism to elucidate who invented first, and then to pool the 'winners'. The 'losing' applications would then be abandoned and neither become patents nor become part of the pool. This would make it more likely that the actual settlement and consequent formation of the pool will survive a challenge in court by a third party who refuses to take a license from the pool and gets sued for patent infringement. If the pool contains an invalid patent – arising

[6] www.goldenrice.org/Content2-How/how9_IP.html.
[7] Correa, see Chapter 3 of this volume. [8] Ibid. [9] Ibid.
[10] Ibid. [11] Ibid. [12] 35 USC §102(g) (2007).

out of a commercially (not legally) driven decision to include it in the pool – the defendant could then demonstrate two things in court. First, that the invention was invented by one other than the patent holder and invalidate the patent. Second, that the interference was settled collusively, and that the resulting pool may – as a result – violate the antitrust laws.[13] By using a formal priority determination and including only the patent application winners, the pool can avoid such problems.

Finally, I agree with Correa that there may be numerous attempted projects involving fragmented IP rights that have never been publicized in that they were aborted at the due diligence stage. I have anecdotal evidence from commercial enterprises which, having determined that a thicket existed with multiple licenses needed, stopped further work towards the product stage. Such accounts abound in the field of gene microarrays, where the existence of one or more unlicensable gene patents have apparently prevented the production and commercialization of an array containing multiple genetic sequences useful for the diagnosis or evaluation of patients' gene profiles.

Thus I conclude that the thicket problems are real, not academic.

4.2 The case of polymutationally correlated genetic diagnostics

In 2005, Verbeure and I working independently, reached the identical conclusion – noted in her chapter – that the problems of thickets in biomedicine would be most acute in the area of genetic diagnostics of poly mutationally correlated diseases.[14, 15] These are diseases where the predisposition to disease is correlated to multiple genes and their mutations. (It should always be remembered that a correlation between gene mutation and disease is not the same as a cause and effect correlation. In other words, the diagnostic correlation – no matter how useful – is not always determinative of aetiology, i.e., of the origin of the disease.) If multiple patent owners hold patents over different mutational correlations, and all of them are necessary for a successful test, then a thicket may appear. Verbeure is correct that in situations like the diagnosis of breast cancer correlated to BRCA-1, where there is one main exclusively licensed patent on the gene and its correlation, a patent pool is of little if any aid.[16] If the patent holders (University of Utah and its

[13] *Medimmune, Inc.* v. *Genentech, Inc.*, 129 SCt 764 (2007) (which, although not in the context of a patent pool, is an example of an allegation by a third party that an antitrust violation had occurred during the settlement of an earlier interference).

[14] Ebersole, et al., 'Pools as a solution to licensing problems'.

[15] Verbeure, see Chapter 1 of this volume. [16] Ibid.

licensee Myriad Genetics) refuse to provide sublicenses to others who may want to enter the market, they are free to do so under the antitrust laws of the United States – pool or no pool.[17]

Verbeure's classification[18] into *vertically* oriented and *horizontally* oriented thickets is insightful, but does not shed more light on how to solve the ultimate problem of correlation between disease and multiple mutations – whether they are all around the same gene and its variations ('vertical'), or around multiple different genes ('horizontal'). If patent holders, each holding one of multiple mutational correlations, whether vertical or horizontal, go at it alone and refuse to deal with each other or a pool, there is little a potential market entrant can do to in order to crack the collective impasse.

4.3 Problem of patent owner holdouts

This brings me to the main focus of this chapter: the problem of patent owner holdouts in biotech pools. It is my belief, apparently shared by Horn,[19] that the holdout problem is uniquely acute to this field. I hope to demonstrate below, however, that medically driven standards[20] might be fruitfully used in the formation of valid biotech pools and that these may somewhat ameliorate the holdout problem. In addition, a recent decision from the United States Supreme Court, *eBay, Inc. v. MercExchange, LLC*[21] ('*eBay*'), may also have a positive impact on the problem. Thus, medically driven standards, when taken together with the *eBay* decision, may lead to a more collaborative rather than litigious environment in the patent thickets of biomedicine.

A holdout is a patent owner who by choice remains outside, or inadvertently gets left out, of a patent pool.[22] If the holdout is inadvertent, then once discovered, he may be invited to join the pool and will do so. His role is then the same as that of all others who have joined the same pool, i.e., he is entitled to a share of the royalties, as well as (if he wants to manufacture) cross licenses from other pool participants. If, however, the holdout is purposeful the situation is dramatically different. A holdout by choice may have decided to go at it alone, especially if he

[17] *Carborundum Co.* v. *Molten Metal Equipment Innovations, Inc.*, 72 F 3d 872 at 880 (Fed. Cir. 1995).

[18] Verbeure, see Chapter 1 of this volume.

[19] Horn, see Chapter 2 of this volume.

[20] Ebersole, T., Guthrie, M., and Goldstein, J. A., 'Patent pools and standard setting in diagnostic genetics', **23** *Nature Biotechnology,* Aug. 2005, 937–8.

[21] *eBay, Inc.* v. *MercExchange, LLC*, 126 SCt 1837 (2006).

[22] George, G. D., 'Note: what is hiding in the bushes? *eBay*'s effect on holdout behavior in patent thickets', **13** *Michigan Telecommunications and Technology Law Review,* 2007, 557–76, 559.

holds a patent that is judged to be essential to the functioning of the pool. Such a purposeful holdout has the ability to 'hold up' formation and/or implementation of the pool. He cannot normally be compelled by private parties to either join the pool or grant them or others an individual license.

In the US, one major exception to the rule of no compulsion is when the Government has jurisdiction to intervene. There are two US statutes which contemplate intervention by the US Government in compelling an involuntary license to a patent. The first one is related to Government procurement in which the Government would take the holdout's IP and force him to grant a compulsory license to the pool or to another private third party who would then manufacture the invention 'for the United States'.[23] The Government must then provide the holdout 'reasonable compensation' so as not to violate the 5th Amendment of the US Constitution.[24] A private party who wishes to obtain a license from the same patent holder cannot avail itself of this remedy – unless he becomes a Government contractor.

The second statute which gives the US Government the ability to force a license is related to the commercial development of Government-funded inventions made at universities or other recipients of US federal money – the so called Bayh-Dole Act.[25] The US Government may require the licensee of an invention made with federal funds to grant a sublicense if such 'action is necessary to alleviate health or safety needs which are not reasonably satisfied by the…[licensee]'.[26] A private party cannot avail itself of this remedy unless he petitions the Government to 'march in' and force a license or sublicense. Although parties have tried, this provision of the law has never been enforced.

Other than the intervention of the Government then, compulsory licenses – or 'forced cooperation' as called by Correa[27] – have not been historically available in the US until the *eBay* case (see below). The purposeful holdouts have remained free to ignore requests for licenses or requests that they join the pool. The optimistic calculation of a holdout – especially if the pool and its standards have already been established – is that he might be able to obtain direct royalties from the licensee that are higher than the secondary distribution royalties he would receive from the pool from the royalties paid to the pool by the licensee.[28] Faced with a holdout, a licensee of the pool might calculate

[23] 28 USC § 1498 (2007). [24] *US Const*. amendment V.
[25] The Bayh-Dole Act of 1980, 35 USC §§ 200 et seq. (2007).
[26] 35 USC § 203(a)(3) (2007). [27] Correa, see Chapter 3 of this volume.
[28] George, '*eBay*'s effect on holdout behavior', 560.

what are known as 'switch-over' costs – i.e. how much would it cost the licensee to switch over from the pool standard to another methodology or product? The holdout hopes to obtain directly from the licensee a royalty that is less than the switch-over cost, and yet will let the holdout do much better than his fellow patent holders who have joined the pool and are receiving only secondary distributions.

4.4 Different cultures of biotech and consumer electronics

Patent holders in the consumer electronics world generally have a hard time going at it alone and becoming holdouts. Patent pools in consumer electronics are combinations of essential and complementary IP held by interdependent players. The pools generally organize around industry standards. Such standards inform the universe of patent holders as to the essentiality and/or complementarity of patents to be added to the pools. The standards are, as Verbeure points out,[29] arbitrary and not functional, in the sense that, for example, there is nothing *a priori* functional about the diameter of a CD disk being 120 mm, or its standard sampling rate being 44.1 kHz. Consumer electronics manufacturers, however, truly need each other in order to create a market for their products (e.g. CD players that will play standard CDs). These manufacturers need to agree on a common language to avoid the Babel-like consequences of technical incompatibility. Any one such manufacturer is like a reluctant synchronized swimmer forced to perform within a team whose members are his fierce competitors, only because, were he to get out of the pool or perform a different routine he would be unable to compete at all, that is, to manufacture or sell products made to the agreed-upon standards. This acute interdependency of patent holders in consumer electronics makes holdout behaviour rare, although there are such examples.[30]

I believe that when it comes to collaborative behaviour the biotech industry is quite different than the consumer electronics industry. Manufacturers in the biotech industry do not operate in a market-driven environment that forces interdependency among them. Quite

[29] Verbeure, see Chapter 1 of this volume.

[30] www.ftc.gov/opa/1996/06/dell2.htm (From the 1996 Federal Trade Commission Consent Agreement with Dell Computer Corporation it appears that, during the standard-setting process, VESA [Video Electronics Standard Association] asked its members to certify whether they had any patents, trademarks or copyrights that conflicted with the proposed VL-bus standard; Dell certified that it had no such intellectual property rights. After VESA adopted the standard – based, in part, on Dell's certification – Dell sought to enforce its patent against firms planning to follow the standard.)

the contrary, as Horn points out[31] the value in biotech is driven not so much by market formation but by intellectual property and exclusivity. Especially in the biopharmaceutical sector, players are confronted by large costs and long regulatory times, and are not inclined to pool their IP with that of others who may not have invested the large sums required for drug or diagnostic approvals. The biopharma culture is much more like that of the solitary long-distance runner with one winner and multiple also-rans, than that of a team of synchronized swimmers.

4.5 Use of medically driven standards in genetic diagnostics

I have suggested that it is nevertheless possible to envision the use of medically driven standards in the formation of patent pools in genetic diagnostics.[32] Such standards might be established by respected health organizations such as WHO, PAHO, NIH, or the American College of Medical Genetics (ACMG) as a means to maximize the scientific efficiency and operability of genetic diagnostic tests across a wide pan ethnic population. For example, the ACMG has issued a policy statement recommending a 'standard' panel of twenty-five mutations for identifying carriers of Cystic Fibrosis (CF). The standard is that all CF-causing mutations with an allele frequency of $\geq 0.1\%$, should be included in the test so as to make it as widely pan-ethnic as possible.[33]

The medically driven standards I have proposed do not resolve thickets in the same manner as those of consumer electronics, where the arbitrary standards force interdependent manufacturers to 'speak' the same language. In contrast, a medical standard informs a 'best' medical practice. If a testing service or a test kit manufacturer wishes to offer the best diagnostic assay in the market it – no matter how reluctantly – may need to obtain licenses from its competitors in order to be able to do so. True, with such a best medical standard there is still an element of choice. Perhaps the diagnostic service lab is quite willing to offer an assay that has less than all of the patented mutations because, rather than being universally applicable, the test could apply only to a subpopulation. In spite of the cultural and commercial differences between

[31] Horn, see Chapter 2 of this volume.
[32] Ebersole, et al., 'Pools as a solution to licensing problems'.
[33] Grody, W. W., et al., 'Laboratory standards and guidelines for population-based cystic fibrosis carrier screening', **3** *Genetics in Medicine,* 2001, 149–54; *see also* Watson, M. S., et al., 'Cystic fibrosis population carrier population: 2004 revision of American College of Medical Genetics mutation panel', **6** *Genetics in Medicine,* 2004, 387–91.

the consumer electronics and biopharmaceutical industries, however, I do believe that establishment of a standard for diagnostic testing of polymutationally correlated diseases will decrease the propensity of the market leaders to want to go at it by themselves, i.e. to play holdout. I do believe that most if not all diagnostic labs will still want to offer the best test possible if it is recommended by respected medical authorities. The use of a medically driven standard, in addition to solving the holdout problem, may then also be used in determining essentiality of patents to a given pool and serve as the organizing principle around which a diagnostics pool would be formed.

4.6 Patent injunctions and the eBay decision of the US Supreme Court

Another reason for some guarded optimism that the biomedical holdout problem might be eased is the recent (2006) *eBay* decision of the Supreme Court. eBay is the well-known operator of an online auction service. MercExchange is a provider of online services and holds a patent on an online auction method.[34] MercExchange sued eBay, asking for a permanent injunction. The lower district Court denied the injunction – almost automatically. The Court of Appeals for the Federal Circuit reversed and granted the injunction – also almost automatically. The decision of the Court of Appeals was then appealed to the Supreme Court. The Supreme Court, *per* Justice Thomas, reversed the Appeals Court but disagreed with both it and the lower court, and remanded. In so doing, it stated that injunctions in patent law should neither be automatically granted nor automatically denied. Analyzing the need for an injunction in patent law should be done in accordance with the traditional four-factor test applied by the courts when considering whether to award permanent injunctive relief in other areas of the law. Under the four-factor test, a successful plaintiff must demonstrate: (1) that, absent an injunction, it will suffer irreparable injury; (2) that remedies available at law (e.g. money damages) are inadequate to compensate for that injury; (3) that considering the balance of hardships between the plaintiff and defendant, a permanent injunction is warranted; and (4) that the *public interest* would not be disserved by a permanent injunction.[35]

Public policy and fairness therefore now need to be regularly and carefully considered by a court before deciding on the entry of a

[34] http://mercexchange.com/index.html.
[35] *eBay, Inc.* v. *MercExchange, LLC*, 126 SCt 1837 at 1839 (2006).

permanent injunction. I conclude that, after the decision in *eBay,* permanent injunctions in patent law are no longer automatic, that in certain instances money remedies will be enough, and that patent holders who do not manufacture or license may not readily get injunctions. Since the public health is a major 'public interest' it would also follow that patent holders in the health sciences who do not work or actively license their inventions are now vulnerable to not getting injunctions.[36]

What does this mean to a passive patent holder who refuses to bring his patent into a formed biotech patent pool, i.e. what does this mean to our holdout? Given that our holdout can no longer count on a permanent injunction, his leverage has decreased. A licensee of the pool facing the holdout may now have more negotiating ability to reach a separate license with him, where the royalty – while perhaps higher than what the licensee is paying to the pool – might be substantially lower than the switch-over royalty. George, in evaluating holdout behaviour in the nanotechnology industry after *eBay* has concluded that *eBay* 'tends to discourage large numbers of holdouts and encourage more complete patent collections by suppressing the incentive for holdouts to litigate. A … likely outcome is that organizations charged with collecting patents, setting standards, and creating licensing regimes may become more numerous and more powerful.'[37] George actually speculates that without automatic injunctions available to holdouts, patent pools in areas like software or consumer electronics will become powerful cartels, and that such a result will not be beneficial.[38]

It is hard to conclude that in our field of biotechnology, where classic patent pools are still few, if any, the lack of automatic injunctions available to holdouts would end up creating a cartel like the ones feared by George in the software or electronics industries. What is clear, however,

[36] There has not yet been a post *eBay* decision of a lower court in the health sciences. In areas such as electronics, the lower court decisions have been mixed. For example, in *z4 Technologies* v. *Microsoft Corp* (434 F Supp 2d 437 (E.D. Texas 2006) and in *Paice LLC* v. *Toyota Motor Corp*, 2006 US Dist LEXIS 61600 (E.D. Texas, August 16, 2006) the lower courts denied permanent injunctions to the plaintiffs in that both z4 and Paice were primarily licensing entities and the inventions were not to the 'core functionality', but, rather, a small component. In contrast, in *CSIRO v. Buffalo Technology, Inc.*, E.D. Tex. (6:06-CV-324, June 15, 2007) where the patent sued upon dealt with wireless networks, the court did enter a permanent injunction, even though the plaintiff CSIRO is not a commercial entity but the principal scientific research organization of the Australian Federal Government, in a manner similar to the United States' National Science Foundation or National Institutes of Health. Among other factors analysed, the claimed invention in *CSIRO* was seen by the court as not merely a 'small component' of the system.

[37] George, '*eBay*'s effect on holdout behavior', 573. [38] Ibid., 576.

is that the absence of automatic injunctions is now part of the US legal scenario. Patent holders of essential or complementary patents – especially non-working patent holders – now need to carefully consider this uncertainty when planning whether to hold out from a pool or not.

4.7 Conclusions

Medically driven standards, set by international medical bodies, should be considered when creating a patent pool in genetic diagnostics. Such standards not only assure the legal acceptability of the pool but provide potential holdouts with a 'best practice' that would give them an incentive to join the pool rather than go at it alone. When coupled to the lack of automatic injunctions after *eBay*, a passive IP holder in genetic diagnostics may well decide that his best strategy for maximizing profits is not to hold out but to jump into the pool, and try – however reluctantly – to synchronize his swimming with those of his team members already in the water.

REFERENCES

Correa, C. E., 'Case 2. The SARS case. IP fragmentation and patent pools', Chapter 3 of this volume.

Ebersole, T., Guthrie, M., and Goldstein, J. A., 'Patent pools and standard setting in diagnostic genetics', **23** *Nature Biotechnology*, Aug. 2005, 937–8

'Patent pools as a solution to the licensing problems of diagnostic genetics', **17** *Intellectual Property & Technology Law Journal*, Jan. 2005, 1–8.

George, G. D., 'Note: what is hiding in the bushes? eBay's effect on holdout behaviour in patent thickets', **13** *Michigan Telecommunications and Technology Law Review*, 2007, 557–76, 559

Grody, W. W., et al., 'Laboratory standards and guidelines for population-based cystic fibrosis carrier screening', **3** *Genetics in Medicine*, 2001, 149–54

Horn, L. A., 'Case 1. The MPEG LA® Licensing Model. What problem does it solve in biopharma and genetics', Chapter 2 of this volume.

Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume.

Watson, M. S., et al., 'Cystic fibrosis population carrier population: 2004 revision of American College of Medical Genetics mutation panel', **6** *Genetics in Medicine*, 2004, 387–91

LEGISLATION

Bayh-Dole Act of 1980, 35 USC §§ 200 et seq. (2007)

35USC §102(g) (2007)

28USC § 1498 (2007)

35USC § 203(a)(3) (2007)
US Const. amendment V

CASE LAW

Carborundum Co. v. *Molten Metal Equipment Innovations, Inc*., 72 F 3d 872 at 880 (Fed. Cir. 1995)
eBay, Inc. v. *MercExchange, LLC*, 126 SCt 1837 (2006)
Medimmune, Inc. v. *Genentech, Inc*., 129 SCt 764 (2007)

WEBSITES

www.ftc.gov/opa/1996/06/dell2.htm
www.goldenrice.org/Content2-How/how9_IP.html
http://mercexchange.com/index.html

Part II

Clearinghouses

5 Clearinghouse mechanisms in genetic diagnostics

Conceptual framework

Esther van Zimmeren

5.1 Background

Both the *existence* and *exploitation* of human gene patents have gained wide attention. Although the controversy about the eligibility of patents in the field of human genetics remains, this primarily ethical debate has largely been 'outlawed' by the political international consensus to allow the registration of such patents as long as the general patentability requirements are fulfilled. Nevertheless, the voice of opponents of human gene patents is still regularly heard at various platforms and echoed in legislative proposals at both sides of the Atlantic.[1] It remains to be seen to what extent this will actually lead to a reopening of the patentability debate and ultimately amendments in the patent legislation and granting policies. Some people would probably even argue that the policy of the patent offices actually already became more restrictive with regard to gene patents. In this paper I do not explicitly deal with the desirability of gene patents, rigorous application of patentability standards and patent scope, although I do recognize that these issues are intrinsically connected with the subject of this paper. However, as these topics are not the principal focus of this book, we will start from the *status quo* where gene patents have been and are granted globally and we will focus on the problems that granted patents might create with respect to their *exploitation*.

Moreover, clearinghouses are part of a spectrum of solutions which may remedy the problems described below. Research exemptions, compulsory

[1] A recent example is a bill introduced in 2007 in the US House of Representatives by Congressmen Xavier Becerra and Dave Weldon. The Genomic Research and Diagnostic Accessibility Act would have added a new section to the US legal code: 'Notwithstanding any other provision of law, no patent may be obtained for a nucleotide sequence, or its functions or correlations, or the naturally occurring products it specifies.' Genomic Research and Accessibility Act, Washington, DC: Library of Congress, 2007, available at http://thomas.loc.gov/home/gpoxmlc110/h977_ih.xml.

licences and clearinghouses are just three of them. Research exemptions do not exist in all legal systems and if a research exemption exists, the scope of protection tends to vary from country to country. Compulsory licensing provisions exist in most national patent acts and compulsory licences might also be obtained in exceptional circumstances on the basis of competition law. However, the grant of a compulsory licence is a rather extreme measure. Its use is not common and the procedure generally long and time-consuming. Therefore, compulsory licences do not seem particularly useful to safeguard day-to-day freedom to operate. This paper examines a voluntary measure (clearinghouse)[2] while contemplating the need of some additional features which would guarantee serious reciprocal engagement in such collaborative endeavours.

The resistance against gene patents actually did not only concern the patentability as such, but equally concealed dissatisfaction at the level of *exploitation* with the incidence of royalty stacking and restrictive (exclusive) licensing practices of patent holders of (upstream) patents. These practices can be primarily accounted for by two phenomena: the (presumed) gradual emergence of patent thickets, on the one hand, and unilateral refusals to license or unbalanced licensing proposals amounting to clear-cut rejections, on the other hand.

The *first phenomenon* relates to the fear that the upsurge in patenting caused by the race on patents by private and public entities in the biomedical sector would lead to a growing omnipresence of patents in genetics which would inhibit research and access to health care. True, the essence of innovation in genetics is cumulative investigation: each invention builds on many previous findings. Public and private entities must thus gain permission of each person that previously contributed to the development of a certain product or process in order to exploit it and to pursue further research and development. If there are many patents in the hands of different owners this may ultimately lead to difficulties in bargaining licences to the patented inventions successfully. This phenomenon has been called a 'patent thicket'.[3] Every licensor will require the payment of royalties or upfront licence fees, which ultimately may lead to royalty stacking.

Patent thickets in genetics may disrupt further innovation, because in genetics substitutes for genetic inventions (such as patented genes) are

[2] For another voluntary measure which is part of the spectrum of remedies, the patent pool, see Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume.

[3] Shapiro, C., 'Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard-Setting', in Jaffe, A., Lerner, J., Stern, S. (eds.), *Innovation Policy and the Economy*, Cambridge, MIT Press, 2001, vol. I, 119–150, available at http://haas.berkeley.edu/~shapiro/thicket.pdf.

often lacking and competitors will therefore often not be able to invent around those patents. Heller and Eisenberg suggested that this increase in patents may result in a 'tragedy of the anticommons' in biomedical research.[4] The high costs involved in locating licensing partners ('search costs'), in negotiating licensing conditions ('bargaining costs') and the enforcement of the licensing agreement ('enforcements costs') – in other words the transaction costs, and the stacking of royalties – may stand in the way of an agreement.[5] This may lead to 'underuse' of the patents concerned.

However, one should note that the consequences of deoxyribonucleic acid (DNA) patenting may turn out to be more limited than some had feared. This may be due to the decline in the number of patent applications, more stringent examination procedures followed by the patent offices, and the apparent restriction of the scope of granted patents. Moreover, debates on the patenting in the area of genetics need to take into account the disparities between patent activity in the US and elsewhere.[6]

It was assumed that the emergence of patent thickets in the biomedical field would bar researchers from initiating new projects and companies from continuing R&D in particular areas where they could not ascertain freedom to operate. However, empirical studies have shown that as to now the patent thicket has not had the anticipated considerable impact, as far as genetics in general is concerned.[7, 8] Nevertheless,

[4] Heller, M.A., 'The Tragedy of the Anticommons: Property in the Transition from Marx to Markets', **111** *Harvard Law Review*, 1998, 621–688 and Heller, M.A., Eisenberg, R.S., 'Can Patents Deter Innovation? The Anticommons in Biomedical Research', 280 *Science*, 1998, 698–701.

[5] Coase, R.H., 'The Problem of Social Cost', **3** *The Journal of Law and Economics*, 1960, 1–44 and Cooter, R. and Ulen, T., *Law & Economics*, International Edition, Boston-San Francisco-New York, Pearson Addison Wesley, 2004, at 91–96.

[6] Hopkins, M.H., Mahdi, S., Patel, P., Thomas, S.M., *The Patenting of Human DNA: Global Trends in Public and Private Sector Activity*, Report for the European Commission, Brighton (UK), SPRU, 2006, available at www.sussex.ac.uk/spru/documents/patgen_finalreport.pdf, at ix and 14–35.

[7] National Research Council of the National Academies – Committee on Intellectual Property Rights in Genomic and Protein Research and Innovation, *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health*, Washington, DC, The National Academies Press, 2005, available at www.nap.edu/catalog/11487.html and Walsh, J.P., Arora, A., Cohen W.M., 'Effects of Research Tool Patents and Licensing on Biomedical Innovation', in Cohen, W.M., Merrel, S.A. (eds.), *Patents in the Knowledge-Based Economy*, Washington, DC, The National Academies Press, 2003, 285–340.

[8] Yet, these studies mainly focus on genetic research. Established companies may be reluctant to actively pursue licensing policies or even litigation against universities and research institutes, which might be different in more competitive relationships. Moreover, growing awareness amongst researchers, strategic enforcement behaviour

several studies have highlighted that in the field of genetic diagnostics patent holders are more active in asserting their patents. This appears to be having an inhibiting effect on research and clinical practice as some laboratories have ceased to perform tests or refrained from test development.[9] In addition, one might argue – even though the problem may still turn out to be less urgent also in genetic diagnostics after more empirical evidence on the existence of patent thickets will have been gathered[10] – that the establishment of patent clearing mechanisms is desirable for reasons of transparency and legal certainty, as still researchers in the field may be under the (false) impression that intellectual property (IP) rights keep them from research.[11] Therefore, genetic diagnostics may serve as a case study for examining different patent clearing models as an instrument to facilitate access to and use of patented genetic inventions. In this respect, in particular patent pools and clearinghouses have been suggested. This contribution will focus on clearinghouse mechanisms.

The *second phenomenon* concerns the situation where a single patent holder controls all patents/the major patent(s) relevant to for instance the genetic testing for a particular disease.[12] Such a patent owner holds a dominant position on the market for that particular test. If he would

by patent holders (including universities), and the proliferating complexity of biomedical research might lead to increased patent enforcement in genetics in the future. National Research Council of the National Academies, 'Reaping the Benefits', at 105–6.

[9] National Research Council of the National Academies, 'Reaping the Benefits', at 111; Walpole, I.R., Dawkins, H.J.S., Sinden, P.D., O'Leary, P.C., 'Human Gene Patents: the possible impacts on genetics services health care', **179** *Medical Journal of Australia*, 2003, 203–205; Matthijs, G., Halley, D., 'European-wide opposition against the breast cancer gene patents', **10** *European Journal of Human Genetics*, 2002, 783–4; Merz, J.F., Kriss, A.G., Leonard, D.G.B., Cho, M.K., 'Diagnostic testing fails the test', **415** *Nature*, 2003, 577–579; Cho, M.K., Illangasekare, S., Waever, M.A., Leonard, D.G.B., Merz, J.F., 'Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services', 5 *Journal of. Molecular Diagnostics*, 2003, 3–8 and Walsh et al., 'Effects of Research Tool Patents', 285–340.

[10] Our research group is carrying out empirical research concerning the existence of patent thickets in the field of genetic testing by closely analysing the scope of the relevant patents. For instance: Verbeure, B., Matthijs, G., Van Overwalle, G., 'Analysing DNA patents in relation with diagnostic genetic testing', **13** *European Journal of Human Genetics*, 2005, 1–8.

[11] This last concern may, however, also partially be solved by proper education of biomedical scientists on IP, and patents in particular.

[12] For example, one patent owner holds the different patents covering the diagnosis of hemochromatosis. Merz et al., 'Diagnostic testing fails the test', at 577–9. Bio-Rad acquired the patent on the Hereditary Hemochromatosis (HFE) gene after Mercator Genetics went out of business. The company offers to license laboratories to perform testing, but at a cost that makes Bio-Rads own, commercial test kit more economically attractive due to up-front payments and a per test fee of $20 (for two mutations).

decide not to grant licences neither for research[13] nor for development, and to exploit the patent autonomously, this might have serious consequences on both research and public health. It could impede further development of an existing test and research into complementary or alternative methods of diagnosis. Furthermore, testing will be quantitatively limited to the capacity of the patent owner, which will not necessarily meet the demands of the number of patients. Additionally, there would be no price competition which might lead to a substantial increase in genetic testing costs and thus a serious drain on funds of public health services. The medical practice could be dictated by the single provider without procedures for ensuring quality control and peer review. And the close link between testing, clinical and counselling services could be disrupted. Even in the case where the patent owner would be rather 'cooperative' and would issue exclusive licences for a specific territory and/or a specific type of testing, further research and the provision of clinical testing services could be seriously hampered. The situation may be even more urgent, if the patent owner uses his rights for defensive purposes without even actively exploiting the patents himself. Competition law on abuse of a dominant position and the 'essential facilities doctrine', as well as compulsory licensing mechanisms established in patent law, might play a role in remedying such restrictive licensing practices. However, for now these remedies do not seem very effective in solving this phenomenon as part of short-term day-to-day licensing strategies. Though, a more detailed examination of these instruments is outside the scope of this paper, some reference will be made now and then to competition law and compulsory licensing in the framework of the analysis of the clearinghouse model.

For releasing the market from the burden of patent thickets and problems related to restrictive licensing practices, the current state of the patent and competition law lack legal remedies effective and sufficiently flexible to be used by practitioners. Experts have been discussing various solutions. Different national and international advisory organs[14]

[13] In some countries research is exempted from patent infringement. In principle, researchers would not be obliged to negotiate a license to allow them to carry out their research. However, the scope of those statutory/non-statutory exemptions varies considerably. See, for instance: Dent, C., Jensen, P., Waller, S., and Webster, B., *Research Use of Patented Knowledge: A Review*, Paris, OECD Directorate for Science, Technology and Industry, STI Working Paper No. 2006/2, 2006, available at www.oecd.org/dataoecd/15/16/36311146.pdf.

[14] Organisation for Economic Co-operation and Development (OECD), *Genetic Inventions, Intellectual Property Rights and Licensing Practices, Evidence and Policies*, Paris, OECD, 2002, available at www.oecd.org/dataoecd/42/21/2491084.pdf; OECD, *Guidelines for the Licensing of Genetic Inventions*, Paris, OECD, 2006, available at

and experts[15] have suggested that a clearinghouse should be set up in the field of patents related to genetic inventions in order to solve both the problem of patent thickets and unilateral blocking licensing practices. However, none of these organizations has precisely defined what type of clearinghouse would be optimal and how it should function in practice. In view of the broad interpretation of the clearinghouse concept and the wide variety of existing clearinghouses, it is important to be more precise and to define different types of clearinghouses, the desirable functions, the organization and the features of a clearinghouse. A typology of five types of clearinghouses will be distinguished in Section 5.2,[16] based on real-life case studies and the excellent papers of Krattiger,[17] who focused on collaborative and technology transfer mechanisms for biotechnology in general, and Graff et al.,[18] who explored an IP clearinghouse for agricultural biotechnology. The other chapters focus on one particular type of clearinghouse, the royalty collection clearinghouse. Section 5.3 deals with copyright collection societies often referred to as the major example of collective administration and a source of inspiration for a clearinghouse for patent licensing in genetics. The major characteristics of copyright collection societies (CCS), some justifications, the legal framework and the relevant competition law jurisprudence will be provided. This will give some insights

www.oecd.org/dataoecd/39/38/36198812.pdf, para. 41; Human Genome Organisation (HUGO), *Statement on the Scope of Gene Patents, Research Exemption and Licensing of Patented Gene Sequences for Diagnostics*, 2003, available at www.hugo-international.org/PDFs/Statement%20on%20the%20Scope%20of%20Gene%20Patents,%20Research%20Exemption.pdf; Nuffield Council on Bioethics, *The Ethics of Patenting DNA*, London, Nuffield Council on Bioethics, Discussion Paper No. 932002, 2002, available at www.nuffieldbioethics.org, and the Australian Law Reform Commission (ALRC), *Gene Patenting and Human Health*, Sydney, Australian Law Reform Commission, Discussion Paper No. 68, 2004, available at www.alrc.gov.au.

[15] Krattiger, A.F., 'Financing the Bioindustry and Facilitating Biotechnology Transfer', **1** *IP Strategy Today* 8, 2004, 1–45, at 19–23; Graff, G.D., Cullen, S.E., Bradford, K.J., Zilberman, D., Bennett, A.B., 'The Public-Private Structure of Intellectual Property Ownership in Agricultural Biotechnology', **21** *Nature Biotechnology*, 2003, 989–95, at 994–5; Gold, E.R., 'Biotechnology patents: strategies for meeting economic and ethical concerns', **30** *Nature Genetics*, 2002, 359, at 359; Graff, G.D., Zilberman, D., 'Towards an Intellectual Property Clearinghouse for Ag-Biotechnology. An Issues Paper', **1** *IP Strategy Today* 3, 2001, 1–38, at 10–14; and Van Overwalle, G., van Zimmeren, E., Verbeure, B., Matthijs, G., 'Models for facilitating access to patents on genetic inventions', **7** *Nature Reviews Genetics*, 2006, 143–148, at 145–147.

[16] See also: van Zimmeren, E., Verbeure, B., Matthijs, G., Van Overwalle, G., 'A Clearinghouse for diagnostic testing: the solution to ensure access to and use of patented genetic inventions?', 84 *Bulletin of the World Health Organization*, 2006, 352–359 and Van Overwalle et al., 'Models for facilitating access', at 145–147.

[17] Krattiger, 'Financing the Bioindustry', at 1–45.

[18] Graff et al., 'The Public-Private Structure', at 989–95 and Graff et al., 'Towards an Intellectual Property Clearinghouse', at 1–38.

in the viability and compliance with competition law principles of a clearinghouse for genetic diagnostics. In the present chapter, not the similarities but the differences between copyright collection societies and patent royalty collection clearinghouses will be underlined. Sections 5.4 and 5.5 set out the building blocks of the royalty collection clearinghouse in a patent context and the potential pitfalls in this process. I conclude with some final remarks and suggestions in Section 5.6.

5.2 Clearinghouses: concept and typology

The term clearinghouse is derived from banking institutions and refers to the mechanism by which cheques and bills are exchanged amongst member banks in order to transfer only the net balances in cash. Nowadays the concept has acquired a much broader meaning. It is used in relation to almost any mechanism whereby providers and users of goods, services and information are matched.[19]

Five types of clearinghouses can be distinguished. The first two models merely provide access to (protected) information. This can be 'simple' information related to technology, patents, claims etc. (information clearinghouse). In addition, lists of technologies available through licensing can be furnished. On the basis of this information, technology owners and users may enter into licensing negotiations (technology exchange clearinghouse). Hence, these clearinghouses do not guarantee the authorized use of the patented inventions and still require time-consuming licensing negotiations. The remaining three more advanced clearinghouse types aim at catering for both access to *and* (standardized) use of the inventions. Access and use can be offered by a clearinghouse on a royalty-free, open access basis (open access clearinghouse), or via standard licences (standard licences clearinghouse and royalty collection clearinghouse). The royalty collection clearinghouse might offer various services, such as information exchange, standard licences, collection and distribution of royalties, monitoring and enforcement, and dispute resolution.

This typology is arbitrary to the extent that the distinction into clearinghouses could be based on other criteria. For instance, whether the clearinghouse is a collaboration between patent holders or an independent mechanism.[20] The distinctive criterion used in the present paper is

[19] Krattiger, 'Financing the Bioindustry', at 20.

[20] Aoki, R., Schiff, A., *Intellectual Property Access Systems*, Tokyo, Institute of Economic Research Hitotsubashi University, Discussion Paper Series A, No. 491, March 2007, available at www.ier.hit-u.ac.jp/Common/publication/DP/DP491.pdf.

the kind of services related to patent licensing provided by the clearinghouse. The typology is dynamic to the extent that in practice a clearinghouse may develop from one end of the spectrum to the other end: from an information clearinghouse to a more advanced type of clearinghouse. I acknowledge that in some case studies the clearinghouse provides services complementary to the services described in this paper. However, in line with the chosen typology these will not be highlighted in this paper.

The different types of clearinghouses will be evaluated in view of their potential to remedy three practical impediments practitioners may face as a result of patent thickets and unilateral restrictive licensing practices, which may ultimately hamper access to diagnostic testing services for patients; first, the rising level of *transactions costs*, especially the bargaining costs due to the high number of licensing negotiations necessary to guarantee freedom to operate; second, the subsequent accumulation of royalties – *royalty stacking*; and, third, the impossibility to obtain a licence from a *non-cooperative patent holder* leading to a blocking position.

A clearinghouse could be administered either as a *voluntary* scheme or as a statutory framework on a *compulsory* basis. In the framework of this paper the compulsory regime is regarded as the last resort. In principle, the establishment of a clearinghouse is regarded as a voluntary process.[21] This starting point yields some pros and cons and a need to consider additional incentives that trigger the voluntary participation of the stakeholders in the clearinghouses (especially in light of the third impediment, see above).

Clearinghouses facilitating access

Information clearinghouse

The information clearinghouse provides a mechanism for exchanging (technical) information, and/or information related to the IP status of said information. Information mechanisms are relatively easy to set up but require constant maintenance and updating.[22]

Examples vary from general search engines such as Google or PubMed, to global biodiversity information networks, such as the

[21] Cf.: Merges, R.P., 'Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations', **84** *California Law Review*, 1996, 1293–1386 and Merges, R.P., 'Of Property Rules, Coase and Intellectual Property', **94** *Columbia law Review*, 1994, 2655–2673.

[22] Krattiger, 'Financing the Bioindustry', at 20 and Graff et al., 'Towards an Intellectual Property Clearinghouse', at 1–6.

Global Biodiversity Information Facility (GBIF)[23] and the Convention on Biological Diversity Clearinghouse.[24] Well-known examples of information clearinghouses in the field of patents are Espacenet from the European Patent Office (EPO)[25] and Google Patent Search[26] which are freely accessible, and fee-based databases, like Delphion,[27] STN International,[28] Dialog[29] or Micropatent.[30] There are specific patent biotech search platforms as well, such as Patent Lens.[31] Patent Lens is established in the framework of the Biological Innovation for an Open Society (BiOS) initiative[32] launched by Cambia[33] and offers a free, fully text-searchable database of US, European and Australian agricultural and life science patents, complemented with advisory and educational services.

For this chapter especially the information clearinghouses in the field of patents are relevant. These information clearinghouses facilitate searches by patent experts to assess an organization's freedom to operate with regard to a specific product or process. Researchers may use them as a source of detailed, technical information for further innovation. Despite the facilitation of access to information on the patented inventions, these clearinghouses do not contribute directly to the solution of the above-mentioned impediments[34] except for the search costs for locating the licensing partners. The name of the applicant or proprietor mentioned on the patent may be helpful. However, one should be aware that this person will not necessarily be the competent licensing partner due to assignment, mergers, strategic IP management, research collaborations, complicated ownership arrangements within universities etc.

Technology exchange clearinghouse

The technology exchange clearinghouse is based on the concept of Internet business-to-business (B2B). Technology exchange clearinghouses offer information services listing the available inventions related

[23] GBIF offers free digital access to primary scientific data on biodiversity to everyone in the global community. See: www.gbif.org/. See the contribution of Edwards, J., 'Case 3. The Global Biodiversity Information Facility. An example of an information clearinghouse', Chapter 6 of this volume.

[24] The Convention on Biological Diversity Clearinghouse aims at promoting technical and scientific cooperation, and facilitating the exchange of scientific, technical, and legal information related to biodiversity. See: www.biodiv.org/chm/.

[25] www.ep.espacenet.com. [26] www.google.com/patents. [27] www.dephion.com.

[28] www.stn-international.de. [29] http://dialog.com.

[30] www.micropatent.com/static/index.htm. [31] www.patentlens.net.

[32] www.bios.net.

[33] www.cambia.net. See the contribution of Berthels, N. 'Case 8. CAMBIA's Biological Open Source Initiative (BiOS)', Chapter 13 of this volume.

[34] See above, at 10.

to a specific technology. On the basis of this information technology users will then initiate negotiations with the patent proprietor for a licence. Some clearinghouses allow licensees to opt for additional partnering, mediating and managing services.[35]

BirchBob[36] and yet2.com[37] are examples of global technology exchange clearinghouses. Specific healthcare technology exchange platforms include Pharmalicensing[38] or TechEx,[39] which provide online partnering support enabling companies in the biopharmaceutical and biomedical industry to find licensing partners and conclude licensing contracts. Specific biotechnology clearinghouses include PIPRA (Public Intellectual Property Resource for Agriculture).[40] PIPRA is an organization committed to strategic management of patents owned by universities, foundations and non-profit research institutions encouraging the broadest application of existing emerging agricultural technologies to develop and distribute improved staple crops and improved specialty crops for the public benefit. The PIPRA Agricultural IP Database[41] is established to monitor and advertise, on an ongoing basis, the status information of PIPRA member institutions' agricultural biotechnology patents and allows member institutions to effectively contract out some of their technology through increasing exposure of their availability. PIPRA's European counterpart, inspired by the model of PIPRA, is the European collective management of Public Intellectual Property for Agricultural Biotechnologies (EPIPAGRI).[42] The EPIPAGRI initiative is a European project established with support from the European Commission and aiming to encourage public sector research organizations to collaborate in the management and promotion of their intellectual property assets in the field of agricultural science.

The technology exchange clearinghouse model will in general be cheap to maintain and will require only relatively low operating costs. However, the clearinghouse is dependent on the cooperation of patent holders in providing the necessary information. It might be difficult to bring together a critical mass of genetic patents in order to turn the

[35] Krattiger, 'Financing the Bioindustry', at 21–22 and Graff et al., 'Towards an Intellectual Property Clearinghouse', at 6–8.

[36] www.birchbob.com. For a more profound insight into this clearinghouse, see the contribution of van Zimmeren, E. and Avau, D., 'Case 4. BirchBob: An example of a technology exchange clearinghouse', Chapter 7 of this volume.

[37] www.yet2.com. [38] www.pharmalicensing.com. [39] www.techex.com.

[40] www.pipra.org. For a more detailed analysis of this clearinghouse see the contribution of Bennet, B. and Boettiger, S., 'Case 5. The Public Intellectual Property Resource for Agriculture. A standard license public sector clearinghouse for agricultural IP', Chapter 8 of this volume.

[41] http://pipra.m-cam.com/. [42] www.epipagri.org/.

clearinghouse into a tool ensuring effective access to patented inventions. Public organizations and small- and medium-sized companies may have a rather large interest in transferring information on their inventions to foster their 'visibility' as a patent holder (provided they pursue an active out-licensing strategy). Big pharma and biotech multinationals with their IP and licensing departments might not have this visibility incentive. Anyway, they might appreciate technology exchange clearinghouses more from the in-licensing perspective, than for out-licensing purposes. This might lead to a rather one-sided technology portfolio of the clearinghouse.

At present, most of the clearinghouses only offer a small (pro)portion of the market and a low density of patents, and hence one has to search various websites (sometimes paying considerable registration fees). Some may argue that this model is only suitable for technologies that can be easily defined and valued. It would only be a useful model for general purpose research methods, such as Polymerase Chain Reaction (PCR), and for patents protecting very specific and well defined improvements to familiar upstream products or processes.[43] Well-trained and experienced staff and a cooperative attitude of right owners and users may partially solve this issue.

It is essential to remember that effective access to the patented inventions is not granted by the technology exchange clearinghouse but by the individual patent holder after one-to-one licensing negotiations have taken place with the licensee. These negotiations are, nevertheless, based on the information provided by the clearinghouse. The clearinghouse provides access to the technical information described in the patent and contact information on the patent holder/licensor involved, but does not provide a one-stop licensing access. The transaction costs may be lower than without the interference of the clearinghouse as the information on available technologies is nicely organized and at hand. Hence, the search costs will be lower than without the technology exchange clearinghouse. Different from what its name may suggest, the technology exchange clearinghouse does not guard the whole exchange process but merely serves as a 'dating service' without guarantee of a prosperous relationship. The user still has to enter into negotiations with the patent holder and develop a relation of trust and understanding.

On the one hand, this gives opportunities to bargain a well-tailored licence fitting the desires of both parties. On the other hand, such an

[43] Krattiger, 'Financing the Bioindustry', at 22 and Graff et al., 'Towards an Intellectual Property Clearinghouse', at 6–7.

optimal result will generally only be achieved when a legal counsel is involved and after a period of intense discussions. So, if for instance the licensee would expect the occurrence of royalty stacking in view of the 'thicket' of licences that has to be settled before bringing the product to the market, he will need good negotiation skills to persuade all patent holders to insert a reasonable 'anti-royalty stacking clause' in the licence.[44] A typical anti-stacking provision states that the royalty rate payable to the licensor will be reduced if the licensee is obliged to enter into licences with third parties in relation to the product. It is not difficult to see how such a provision can lead to a disparity between the expectations of the licensor as to the royalty it will receive from the licensee and the actual royalty the licensee is contractually obliged to pay. These expectations may be tempered by information and negotiation obligations on the licensee. Or one may consider putting a floor on the extent to which the royalty rate can be reduced in response to stacking.

This example shows that despite the economies yielded for the search costs by the interference of the technology exchange clearinghouse, in the end, the need of complex licensing negotiations may still lead to high bargaining costs. The licensing partners will not be indebted for the royalty stacking remedy to the clearinghouse but to the negotiation skills of their representatives. Nor would there be any safeguard to drag a non-cooperative patent holder into negotiations.

Clearinghouses facilitating access and use

Open access clearinghouse

A rather unique type of a clearinghouse is the open access clearinghouse.[45] This type of clearinghouse does not only foster free access to information as its name may suggest, but also free use of inventions. A recent example of an open access clearinghouse is the Eco-Patent Commons initiative.[46] The World Business Council for Sustainable Development (WBCSD) and IBM are initiating this effort in partnership with Nokia, Pitney Bowes and Sony. Its purpose is to foster innovation and establish new collaborative efforts by making patented

[44] For more information, see for instance Liberman, A., *Royalty stacking: tips for licensors and licensees*, 25 November 2005, available at www.freehills.com.au/publications/publications_5332.asp regarding *Cambridge Antibody Technology* v. *Abbott Biotechnology Ltd,* [2004] EWHC 2974 (Pat) and Clark, V., *Pitfalls in drafting royalty provisions in patent licences*, available at http://pharmalicensing.com/articles/disp/1087832097_40d70021d738c.

[45] Krattiger, 'Financing the Bioindustry', at 22–3.

[46] www.wbcsd.org.

technology that provides environmental benefit (e.g. energy conservation or efficiency, pollution prevention, use of environmentally preferable materials or substances, materials reduction, increased recycling ability) easily available.

The Eco-Patent Commons is open to all companies from a wide diversity of industry sectors. It is fed with initial and subsequent 'patent pledges' by companies that become members. Which patents are contributed to the Commons and whether maintenance fees on pledged patents are being paid[47] is left to the discretion of each patent holder. Probably, companies will want to retain their exclusive rights to patents that may represent a significant business advantage.

The patents can be identified in a searchable website hosted by the WBCSD. Through the Eco-Patent Commons, the patents will be made available for free use by all, subject to defensive termination. This means that a patent holder may terminate a specific party's rights on the occurrence of an offensive use of patents by that party. The Eco-Patent Commons has a minimal structure sufficient to handle some administrative work, manage the website, and provide a point of contact for prospective members. Membership fees are initially set to zero, but eventually there may be a membership fee to cover costs associated with the management of the Eco-Patent Commons.

In the life sciences, a well-known example is the SNP Consortium. The goal of the SNP Consortium,[48] a non-profit entity, is to identify and collect single nucleotide polymorphisms (SNPs) and to create and make freely publicly available the SNP map of the human genome at the earliest possible date, without any proprietary rights maintained by the members of the Consortium, in order to enable further drug discovery. It is interesting to note that a variety of organizations cooperate in the consortium ranging from academic research institutes to large pharmaceutical companies. The IP strategy pursued to safeguard these goals included the filing of provisional patent applications upon the discovery of new SNPs and prior to release into the public domain, thereby maintaining the priority date of discovery of the SNP for use as prior art. These provisional applications were later converted into US utility patent applications and instead of prosecuting the grant of the patents, the applications were converted into statutory invention registrations.[49] The identified SNPs were only released to the public when

[47] However, if a patent holder decides to let a pledged patent lapse or it otherwise becomes unenforceable, the patent holder shall provide written notice to the Commons.

[48] http://snp.cshl.org.

[49] 35 U.S.C. 157 Statutory invention registration: '(a) Notwithstanding any other provision of this title, the Director is authorized to publish a statutory invention registration

mapping had been achieved to prevent the patenting of these SNPs by third parties.[50]

Open access clearinghouses may especially be a well-tailored model for sharing and exchanging unpatented inventions. As access is free and the inventions available without further need for bargaining, in principle transaction costs are zero. Royalty stacking will be out of order as the inventions are accessible free of charge.

However, most of the genetic inventions are the outcome of long-lasting research initiatives requiring high investments. Both private enterprises and universities wish to recover those investments and therefore apply for patent protection. For this reason, apart from situations where the patent rights are extremely fragmented, as illustrated by the SNP Consortium, or cases where one may seriously doubt whether the patentability requirements can be met, holders of patents related to genetics will probably not have a strong incentive to *voluntarily* cooperate in a scheme where the patented inventions will end up in the public domain without any compensation. Or either they will want to use their discretion and retain exclusive rights to patents that represent significant business advantages (judging the example of the Eco-Patent Commons). Therefore, the scope of application for this type of clearinghouse in order to safeguard broad access and use in genetic diagnostics is expected to be rather limited, at least in the near future.

Standard licences clearinghouse

An upcoming and celebrated model is – what I term – the 'standard licences clearinghouse' providing access to and standard licences for the use of protected inventions. Standard licences will need to reflect the complexity of the market, the product and the variety of users. Therefore, 'standard' would not mean a one-size-fits-all licence but a preset licence with options that have been established in negotiations between the right holder and the clearinghouse. This could be operated by a portal through

containing the specification and drawings of a regularly filed application for a patent without examination if the applicant – (1) meets the requirements of section 112 of this title; (2) has complied with the requirements for printing, as set forth in regulations of the Director; (3) waives the right to receive a patent on the invention within such period as may be prescribed by the Director; and (4) pays application, publication, and other processing fees established by the Director. If an interference is declared with respect to such an application, a statutory invention registration may not be published unless the issue of priority of invention is finally determined in favor of the applicant.'

[50] Holden, A.L., 'The SNP Consortium: Summary of a Private Consortium Effort to Develop an Applied Map of the Human Genome', **32** *BioTechniques*, 2002, S22-S26. See also the contribution of Verbeure, 'Patent pooling for gene-based diagnostic testing. Conceptual Framework', Chapter 1 of this volume.

which licensors and licensees can use a simple interface, with drop-down menus and standard questions, to choose a patent licence. By answering simple questions, they will be offered a choice between specific standard licences or the ability to choose from a standard set of options that can be mixed and matched to create a customized agreement, tailored to fit the large variety of circumstances in patent licensing.

An example of a standard agreement scheme is offered by Science Commons.[51] Science Commons examines, in cooperation with the stakeholders concerned, standard licensing models to facilitate wider access to scientific subject matter. Science Commons works in three project areas: scholarly publishing, licensing policies and the realization of the 'semantic web' for science. It aims at broadening access to scholarly communications in a range of disciplines (Scholar's Copyright Project)[52] and at encouraging intellectual property licensing, technology transfer (Biological Material Transfer Agreement Project)[53] and data sharing (Neurocommons Project).[54] The Biological Materials Transfer Agreement Project develops and deploys standard, modular contracts to lower the costs of transferring physical biological materials, e.g. DNA, cell lines, model animals, antibodies. The project covers transfers among non-profit institutions as well as between non-profit and for profit institutions. It integrates existing standard agreements (Uniform Biological Materials Transfer Agreement and the Simple Letter Agreement) with new Science Commons' contracts, and allows for the emergence of a transaction system along the lines of Amazon or eBay.

Its 'mother/sister-organization' Creative Commons[55] has already been in operation for a couple of years facilitating the use of *copyrighted* material by way of standardized, simplified licences.[56] The criteria decisive for the applicable copyright licence are whether the work would be used commercially, whether it would be modified, what would be the appropriate jurisdiction, and the format of the work. In addition to these 'general' copyright licences, over the years some more specific copyright licences have been developed, amongst which are the so-called 'developing nations licence', the 'music sharing licence' and the Creative Commons GNU GPL.[57] The most comprehensive licence is the 'public

[51] http://sciencecommons.org/. [52] http://sciencecommons.org/projects/publishing/.
[53] http://sciencecommons.org/projects/licensing/.
[54] http://sciencecommons.org/projects/data/. [55] http://creativecommons.org/.
[56] Creative Commons offers its standard licences in three versions: the official licence including all the legally correct terms and detailed licensing conditions, the versions readable for the general public and the machine-readable version.
[57] This licence adds the Creative Commons metadata and the Commons deed (human-readable version of the licence) to the Free Software Foundation GNU General Public License.

domain dedication' by which the right holder promises not to enforce his copyright. This approach aligns with the goals of the open access clearinghouse. The Science Commons Licensing Project aims at extending such practices beyond copyright into the realms of patents, technology transfer and intellectual property licensing. Besides the development of the standard licences, Creative Commons and Science Commons do not provide other legal services. Monitoring and enforcement of the licences is in principle the responsibility of the right owners.

Standard licences for patented genetic inventions could be differentiated as to the nature of the user, the objective of the use and the profile of the eventual product to be developed by the licensee. Whereas the existing Creative Commons licences not requiring licence fees may do in the area of copyright, it will most likely be more difficult to persuade patent holders into such a licensing scheme. Deciding upon the royalty will probably be the most sensitive and controversial subject. Fixing a certain percentage and/or upfront payment in a standard licence will meet with strong opposition. Innovation is also a dynamic process which should be reflected in the licence. Moreover, drafting the clauses of licences necessitates a careful balancing of the interests of the licensor and licensee, which will be reflected in the licensing conditions. To function as an effective alternative, standard licences should at least offer enough variety and the system should allow for different options that can be mixed to create a customized agreement.

In principle replacing the tailored licence by a (customized) standard licence agreement would – once the standard licences have been developed in consultation with the stakeholders – diminish the bargaining costs for individual licences. In principle licencees would have but one choice if the licencees is generated through the transaction system of the clearinghouse: 'take it or leave it'. It appears desirable that only in exceptional circumstances the licensee would be permitted to notify the clearinghouse of a reasoned request to enter into further negotiations for an adapted version of the standard licence. Otherwise, the decrease of transaction costs would yet be undone. In order to prevent the accumulation of royalties in the interest of the licensees, licences should contain an anti-royalty stacking clause.

A patent holder who is not willing to step into the clearinghouse, remains in principle free to stay out of it. Assuming the standard licences clearinghouse is not embedded in a compulsory scheme where the patent holder can no longer decide for himself whether a licence will be granted or not to a specific user (be it on an exclusive or non-exclusive basis), the owner will remain in control on who will have access to his inventions. Therefore, access to and use of the patented

inventions cannot be guaranteed for all inventions nor for all users. A non-cooperative patent holder will, unless competition law would in exceptional circumstances provide ground for action, not be prevented from refusing the grant of a licence or imposing restrictive licensing conditions.

Royalty collection clearinghouse

The royalty collection clearinghouse comprises all the functions of the information clearinghouse, the technology exchange clearinghouse and the standard licences scheme (see Figure 5.1).

On top of this, the royalty collection clearinghouse sets up a mechanism to cash licence fees from users on behalf of the patent holders in return for the access to and use of the inventions. The patent holders will be reimbursed by the clearinghouse pursuant to a pre-established allocation formula or according to the reported real use of the respective patented inventions by the licensees. Classical examples of collection schemes include copyright collection societies. Nevertheless, from the detailed analysis provided below it will become clear that there are also quite some differences between the royalty collection model as defined for patents, and the copyright collection societies.

For the national copyright collection societies one may think of the American Society of Composers, Authors and Publishers (ASCAP),[58] the Dutch association BUMA for performance rights and the foundation STEMRA for mechanical reproduction rights (BUMA/STEMRA),[59] the German *Gesellschaft für musikalische Aufführungs – und mechanische Vervielfältigungsrechte* (GEMA),[60] the Japanese Society for Rights of Authors, Composers and Publishers (JASRAC),[61] the *Société Belge des Auteurs, Compositeurs et Éditeurs* (SABAM),[62] and the French *Société des Auteurs, Compositeurs et Éditeurs de Musique* (SACEM).[63] These copyright collection societies may vary from country to country as to their legal basis, legal structure, decision-making procedures, price-setting procedures, licensing conditions, etc.

At present no clear-cut examples of a royalty collection clearinghouse seem to exist (yet) for the management of patents.[64] However, Drahos

[58] www.ascap.com/. [59] www.bumastemra.nl/InterXtranet/bsinterxtranet/home.
[60] www.gema.de/. [61] www.jasrac.or.jp/ejhp/index.htm.
[62] www.sabam.be/. [63] www.sacem.fr/.
[64] Some business models closely resemble the patent royalty collection clearinghouse as to the services they provide. Often they differ to the extent that those entities require the assignment of the rights and take up responsibilities that exclude the role of an independent agent (see below) that takes both the interests of the right owner and the users into account. Example: BTG (www.btgplc.com).

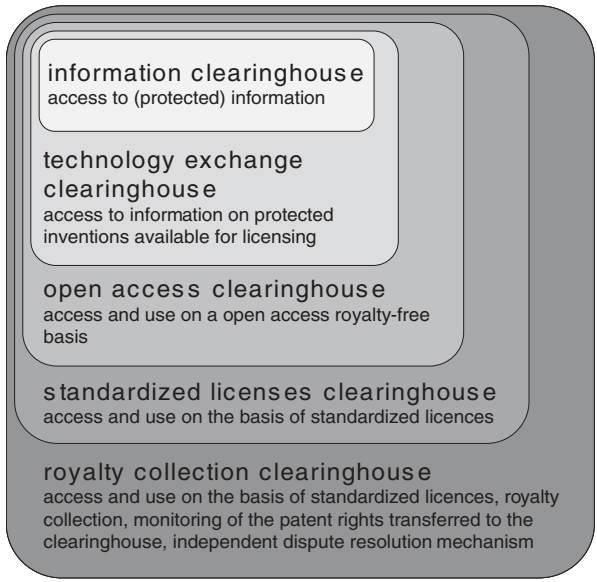

Figure 5.1 Five types of clearinghouses can be distinguished: The first two models merely provide access to (protected) information. The remaining three types aim at providing both access to and (standardized) use of the patented genetic inventions. A royalty collection clearinghouse may offer monitoring and independent dispute resolution on top.

proposed the establishment of the so-called Global Bio-Collecting Society (GBS).[65] The GBS was designed as an efficient, fair and equitable exchange model of indigenous knowledge between knowledge holders, merely non-IP holders (indigenous groups) on the one hand and knowledge users, IP holders (life science industry) on the other hand. The GBS model has not been realized, probably because the necessary political support was missing and protection of traditional knowledge as such is already a highly sensitive and hotly debated issue.

The royalty collection clearinghouse would act as an *independent intermediary* (a kind of 'broker') fulfilling various services for both patent right holders and technology users. The royalty collection clearinghouse

[65] Drahos, P., 'Indigenous Knowledge, Intellectual Property and Biopiracy: Is a Global Bio-Collecting Society the Answer?', **20** *European Intellectual Property Review*, 2000, 245–50.

would facilitate access to the information on the patented and 'licensable' inventions by providing a one-stop information platform. Also the use of the patented inventions by the licensee would be enabled as the clearinghouse would ease the bargaining process: the clearinghouse would match the licensee with the patent holder and offer the appropriate standard licence. Comparable to the standard licences clearinghouses, licensees will generally only be able to choose either to take or leave the standard licence as it is, due to the transaction costs involved in renegotiating the specific clauses of the standard licence. In order to prevent the accumulation of royalties in the interest of the licensees, the clearinghouse might apply anti-royalty stacking rules requiring reduced royalties or a cap on royalties in the event of stacking.

If a patent holder decides to transfer his patent rights to the royalty collection clearinghouse this would increase the visibility of those rights. Former infringers will have an easy access to the clearinghouse database and can contact clearinghouse staff members for more detailed information on patented inventions. Moreover, the transfer would simplify the collection of royalties by the patent proprietor and infringement monitoring. Assuming that users that infringe upon the patents at present would be willing to pay royalties if determined by an independent intermediary (the clearinghouse) at a reasonable level, this would most likely lead to a rise in licensing and thus licensing revenue for the patent holder. The clearinghouse could promote awareness and respect for IP rights amongst researchers[66] and their public and private institutions, which might result in a decline in enforcement costs. Hence, there would be an incentive for patent holders to cooperate with the clearinghouse. Moreover, a reasonable price for both licensees and licensors would be achieved. The use of essential patented technology for a reasonable royalty would be safeguarded for licensees without the need to undertake complex searches, and without costly negotiations and high litigation risks. Licensors will make their technology available under flexible conditions in line with their business strategy for which they will receive a reasonable royalty without the necessity to negotiate licences with all partners interested and with the advantage of more consistent monitoring of infringements.

An important prerequisite for the royalty collection clearinghouse to be effective is that there should be a recurring need to transact in

[66] It is acknowledged that although until now patent holders do not actively assert their rights against academics, this may change in the future and for specific technology areas. Moreover, differences regarding the existence and scope of research exemptions lead to legal uncertainty. Zero sum royalty licences for researchers may clear this uncertainty.

patents included in the clearinghouse.[67] As diagnostic tests are carried out on a regular basis on a worldwide level (although there might be differences between states regarding the diseases for which patients are regularly tested), and both public and private entities are performing research on existing tests and developing complementary and alternative tests, in genetic diagnostics this requirement will most probably be fulfilled. This is further strengthened by the developments in chip technology and pharmacogenomics.

Nevertheless, it is only worthwhile to establish such a clearinghouse if many patent holders or an entire branch of industry participates.[68] It remains to be seen, whether the benefits of the royalty collection clearinghouse could persuade patent proprietors with a strong portfolio and a well-established in-house IP and licensing department to voluntarily participate in the clearinghouse. Similarly, one may doubt whether the third obstacle concerning the non-cooperative patent holder might be overcome by a voluntary royalty collection clearinghouse. A patent holder who does not wish to grant licences at all or on conditions that conflict with the clearinghouse's objectives in principle cannot be compelled to join the clearinghouse. A back-door mechanism to bring the unwilling patent holder within the clearinghouse scheme could be to impose a 'reciprocal positive comity clause' or a 'grant-back clause' in the standard licences. The idea of a 'positive comity clause' is derived from international law and constitutes an obligation to cooperate with the clearinghouse; it articulates a socially responsible approach in the light of access to medicines and treatment. The obligation to cooperate is mutual. Licensees of patented inventions licensed by the clearinghouse should transfer essential patent rights to the clearinghouse (and thus become licensors in this respect), or agree to adopt a (fair), reasonable and non-discriminatory unilateral licensing strategy (in Europe called FRAND-terms and in the US described as RAND-terms)[69] outside the clearinghouse. A broad 'grant-back clause' would oblige the patent holder to 'license back' his (essential) patents non-exclusively to the clearinghouse if he applies for licences from the clearinghouse. However, patent and competition law require cautiousness in imposing such broad, invading measures.

[67] See also: Merges, 'Contracting into Liability Rules', at 1293–1386.
[68] Krattiger, 'Financing the Bioindustry', at 19.
[69] See also the debate with regard to patent pools and industry standards for the interpretation of (F)RAND-terms.

5.3 Copyright collection societies

The following analysis will examine the major characteristics of CCS, highlight some justifications for the establishment of CCS, provide an overview of the relevant international and European legal framework, describe a number of recent developments related to the European collection societies, summarize the relevant US and European Union (EU) competition law jurisprudence and will conclude by pointing to some concerns regarding the copyright collection societies. In order to distinguish the royalty collection clearinghouse for *patent licensing* from the *copyright* collection societies, from now on I will use the term '*patent* royalty collection clearinghouse' (PRCCH) for the former.

The rationale for analyzing CCS is twofold. First, highlighting the special characteristics of copyright collection societies in comparison with the concept of a patent royalty collection clearinghouse as used in this paper. At several instances commentators have put PRCCHs on a level with CCS in order to explain the concept of PRCCHs. In my opinion this link failed to appreciate the considerable differences between patents and copyright, between licensors and licencees of patents on the one hand and licensors and licencees of copyright on the other hand, and the institutional framework of the CCS and the PRCCH. The failure to articulate these differences actually obscured the idea of a PRCCH. Moreover, criticism with regard to CCS does not automatically apply to patent royalty collection clearinghouses. Second, the analysis aims at providing some valuable basic principles for the assessment of the viability and competition law compliance of a patent royalty collection clearinghouse for genetic diagnostics.

This review is far from exhaustive, but may function as a starting point and source of inspiration for further debate.

Characteristics of CCS

Already in the eighteenth century composers and authors themselves initiated the collective management and protection of their copyrights by setting up the first collection societies. Right holders founded these societies to engage in joint licensing, exploit their remuneration rights, and monitor and enforce their rights at a reasonable cost. Individual right holders benefited because they faced difficulties in exercising these activities on an individual basis in view of the potentially high numbers of uses and users. Similarly, users were expected to benefit from a single point of reference when seeking a licence both in terms of authorization and payment of royalties.

Despite benefits for both right owners and users, copyright collection societies' major task is to represent their members' interests vis-à-vis users. In doing so, copyright collection societies are not acting as independent intermediaries,[70] whereas one of the major features of a patent royalty collection clearinghouse in genetic diagnostics is its independence. The PRCCH would act as an agent without representing solely the interests of the patent owners/licensors or of the technology users/licensees.

In a copyright collection scheme the author or performer transfers his economic rights (excluding his moral right) to the copyright collection society by assignment or a licence.[71] Copyright collection societies may be corporate, charitable, for profit or not-for-profit entities. According to the European Commission, the legal status as such does not necessarily have an impact on a society's efficiency.[72]

Many states have regulated the management of rights by copyright collection societies to a greater or lesser extent. Regulation includes for instance statutory requirements for obtaining an authorization to exercise collective management, government supervision, distribution of royalties, establishment of a specialized dispute settlement body, the obligation to appropriate part of the royalties for cultural or other public interests and the requirement to set up welfare and assistance schemes.[73] In view of the perceived advantages of collective management of remuneration rights, several states have set up compulsory schemes for collective management. This means that remuneration rights may only be administered by the designated collection societies.[74]

[70] Cf.: Graff et al., 'Towards an Intellectual Property Clearinghouse', at 9.

[71] Assignment is a transfer of rights in an exclusive and definitive manner. Licenses authorize the performance of a specific act, which without the authorization would be an infringement of the right concerned. Licenses may be exclusive, non-exclusive or sole licenses.

[72] European Commission, Communication from the Commission to the Council, the European Parliament and the European Economic and Social Committee, *The Management of Copyright and Related Rights in the Internal Market*, Brussels, 16 April 2004, COM(2004) 261 final, at 18 (hereinafter 'Communication Management of Copyright').

[73] Tuma, P., 'Pitfalls and Challenges of the EC Directive on the Collective Management of Copyright and Related Rights', **17** *European Intellectual Property Review*, 2006, 220–9.

[74] See for instance Germany, *Wahrnemungszwang*, § 6 Abs1UrhWg (Gesetz über die Wahrnemung von Ürheberrechten und verwandten Schutzrechten). See: Kretschmer, M., 'The Failure of Property Rules in Collective Administration: Rethinking Copyright Societies as Regulatory Instruments', **13** *European Intellectual Property Review*, 2002, 126–136; and Liholm, J., 'GEMA and IFPI', **13** *European Intellectual Property Review*, 2002, 112–125.

Usually, the collection societies manage the rights for a specific category of copyright or neighbouring right holders.[75] In this paper I will not distinguish between the different categories of rights and refer to copyright collection societies in general. Nevertheless, the examples and case law will primarily concern music and in particular performers' rights.

CCS grant licences, determine tariffs, administer, collect, distribute the payment of royalties and monitor the use of the protected material and enforce their members' rights on the basis of national law with respect to their respective territories. The royalties collected will be distributed by the collection societies to their members and other collection societies[76] after deduction of the administration costs on the basis of set distribution rules. These rules should reflect the delicate balance between the interests of the different groups of rights holders.

Many CCS offer so-called 'blanket licences', the centerpiece of collective administration of rights in music. By a single licence and for a fixed royalty, users acquire unlimited access to the repertoire of the members of the society. An important aspect of this system is that licencees do not pay for each use and for each individual work used, but pay a flat-royalty rate. Hence, the rate is not related to the actual use of the music, but in many countries calculated on the basis of a sample of an 'average user' in a specific sector. Users have criticized this method, as it lacks flexibility and generally would not reflect the commercial value of the use. To increase the flexibility, it has been proposed to introduce subcategories of works for which a licence could be granted. Also in the relationship between the collection society and its members, there are generally no individual arrangements compensating each use of each of their individual works.

Most CCS are part of a global network of bilateral, reciprocal agreements, by which rights are cross-licensed between societies in different countries. The network of agreements guarantees access to a global catalogue of rights.[77] This way, societies can provide a one-stop licens-

[75] Copyright collection societies administer rights in the area of music, literary and dramatic works as well as audiovisual works, productions and performances for activities such as communication to the public and cable retransmission of broadcasting programs, mechanical reproductions, reprography, public lending, artist's resale right, private copying or certain educational uses. See: European Commission, 'Communication Management of Copyright', at 14.

[76] For which they have gathered royalties on the basis of so-called reciprocal licensing agreements. See below.

[77] In this regard the activities of the Confédération Internationale des Sociétés d'Auteurs et Compositeurs (CISAC) (established in 1926)) and Bureau International des Sociétés Gérant les Droits d'Enregistrement et de Reproduction Mécanique (BIEM)

ing mechanism to the world repertoire, including their own members' repertoire and the works of the members of the societies with which reciprocal agreements exist. However, the one-stop (blanket) licence will generally only affect use of the world repertoire within the territory of operation of the society concerned.[78]

Justifications for the establishment of CCS

Advocates of copyright collection societies refer to both economic and social reasons to justify the establishment of collection societies. The major economic justification relates to the fact that collective administration has the characteristics of a natural monopoly. The concept 'natural monopoly' implies that a single entity can provide services at a lower per-unit cost than can two or more entities; efficiency would thus be better served if a single entity supplies the entire market.[79] In the area of copyright this single entity would be the national copyright collection society.

Several features of copyright management explain the characterization as a natural monopoly. First, natural monopolies have a high barrier for new market entrants. Building a new catalogue of copyrights requires time and enormous investments. Furthermore, fixed costs of administration, distribution of royalties, monitoring and enforcement are high. Hence, new market entrants representing a limited number of right holders and thus collecting only relatively modest royalty revenue, will probably not be able to attain a healthy equilibrium between costs and benefits.

Second, an existing collection society would enjoy economies of scale. Individually licensing rights for millions of works between thousands of right holders and users would engender enormous transaction costs.[80] These costs would be generated by the identification and location of the right holders, the exchange of the relevant information and the

(established in 1929)) developing model agreements are crucial. For more information, see: www.cisac.com/ and www.biem.org/.

[78] See, however, Section 'EU and US competition law framework for CCS'.

[79] Depoorter, B., 'Regulation of a Natural Monopoly', in Bouckaert, B., and De Geest, G. (eds.), *Encyclopedia of Law and Economics*, Cheltenham, Edward Elgar, vol. III, 2000, 498–532.

[80] Kretschmer, 'The Failure of Property Rules', at 127 and 133–6. Kretschmer argues that the transaction costs justification for collective administration may support not a *universal* rights administration system (to which all, right holders have access on similar terms), but a system where the major right holders selectively decide, supported by sophisticated information technology, whether collecting license fees is worthwhile.

negotiation of separate licences. The transaction costs would probably even be higher than the actual licence fees received in such transactions. To avoid wasting money or effort, users might refrain from using the works altogether, or might resort to doing so illegally. CCS enable both right holders and users to save transaction costs by allowing right holders to become a member of the society on the basis of just one agreement, while users obtain a single blanket licence granting them unlimited access to the world repertoire for a flat royalty-rate. Apart from reducing the bargaining costs associated with individual licensing negotiations, the blanket licence may substantially reduce the enforcement costs of protecting the right holder from copyright infringement. In addition, contracting for arm's length transactions (between right holder and user) might be hindered by information deficits or asymmetric information.[81] The collection society appears to be in a better position to efficiently deal with transaction costs, information deficits and asymmetric information.

Third, the network effects of the bilateral reciprocal agreements between the individual collection societies would increase the economic value of a world repertoire exploited through blanket licences.

A vivid debate has emerged to what extent these economic justifications are valid and in their own right point to the collective administration of copyright by monopolistic copyright collection societies instead of the need for collective administration by intermediaries.[82] Some commentators deem rent seeking the primary reason for right owners to support the collective management of copyrights instead of a decrease in transaction costs and facilitation of monitoring and enforcement. They fear that the system has turned into a 'rent-seeking orgy'.[83] This did not prevent others from proposing the creation of new forms of collection societies. In fact, for instance in Canada it is still generally believed that the advent of digital technologies requires a greater role for collective management of copyright. Consequently, some thirty-six

[81] One party may possess information about the potential agreement that the other party does not possess but values highly, for instance detailed information on the use.

[82] Kretchmer, 'The Failure of Property Rules'; Katz, A., 'The Potential Demise of another Natural Monopoly: Rethinking the Collective Administration of Performing Rights', **1** *Journal for Comp. Law & Economics*, 2005, 541–593. See also: Katz, A., *Copyright Collectives: Good Solution but for Which Problem?* NY University, Engelberg Center, Working Within the Boundaries of Intellectual Property, La Pietra Conference, June 5–6, 2007, available at www.law.nyu.edu/engelbergcenter/conferences/LaPietra/Katz.pdf; and Gervais, D., 'The Changing Role of Copyright Collectives', in Gervais, D. (ed.), *Collective Management of Copyright and Related Rights*, The Hague, Kluwer Law International, 2006, at 3.

[83] Lemley, M.A., Weiser, P.J., 'Should Property or Liability Rules Govern Information', **85** *Tex. L. Rev.* 2007, at 829–830 and Katz, 'Copyright Collectives', at 32.

copyright collection societies – a majority of which are new – have emerged.[84]

And yet one might argue that the Internet and new digital technologies further undermine the economic justifications for copyright collection societies as they may lower many of the transaction costs[85] which previously were a major justification for collective administration.[86] However, this development does not imply that all right owners would indulge in administering their rights individually, but that various intermediaries of different sizes may do so. For now, especially large right holders, such as music publishers, seem to benefit from these technologies and shift to individual rights management instead of collective administration.[87]

In some countries collection societies also have an important socio-cultural function. A certain amount of the collected royalties are intended to be used to foster culturally significant works and performances and set up social welfare and assistance schemes for the holders of the rights they administer. The collection societies will also represent their members in political debates by which their members' interests are concerned. Germany is often cited as an example of a country where

[84] Katz, 'Copyright Collectives', at 1.

[85] Internet and digital rights management may facilitate the identification, licensing and distribution of music. Technologies that enable computerized automatic screening and tracking of songs, jingles, movies, videoclips, etc. may guarantee easy monitoring and enforcement.

[86] Digital rights management refers to technologies which allow owners of digital content to control access to this content, to restrict its usage in a way specified by the owner for instance in accordance with respect for copyright law (but also beyond). It may also be used for accounting and payment purposes.

[87] Katz, A., 'The Potential Demise'; Jenny, F., EC *Competition Law Enforcement and Collecting Societies for Music Rights: What Are We Aiming for?* European University Institute, Robert Schuman Centre for Advanced Studies, 2005 EU Competition Law and Policy Workshop/Proceedings, available at www.iue.it/RSCAS/Research/Competition/2005/200510-CompJenny.pdf. See also: Kretschmer 'The Failure of Property Rules', at 132: In 1996 Polygram already reported that it had identified potential savings of $2.5 million per annum if royalties payable from Polygram Records to Polygram Publishing were processed directly. In South Asia, multinational music publishers have signed a Memorandum of Understanding, which allows the major players to collect mechanical royalties themselves without having to support a system of copyright societies along European lines. Cf.: 'The Department is continuing to investigate the extent to which the growth of [Digital Rights Management (DRM)] technologies warrants additional changes to the antitrust decrees against ASCAP and [Broadcast Music, Inc.] BMI, including the possibility that the [collecting societies] should be prohibited from collectively licensing certain types of users or performances' (Department of Justice, Memorandum of the United States in Support of the Joint Motion to Enter Second Amended Final Judgment, *United States* v. *ASCAP*, No. 41–1395 (S.D.N.Y. 2000), at fn. 10, available at www.usdoj.gov/atr/cases/f6300/6395.pdf).

this function is highly valued. However, one may doubt whether these socio-cultural activities are necessarily performed under the umbrella of collective rights administration.[88]

Finally, it is often submitted that collection societies exist for the purpose of manifesting a counterforce to the market power of major exploiters and distributors of musical material, such as broadcasting bodies and record manufacturers.[89]

International and European copyright framework for CCS

International treaties do not provide clear guidance regarding the management of rights. Article 5(2) of the Berne Convention stipulates that the exploitation of rights is subject to the law of the place of exploitation.[90] Articles 11bis(2) and 13(1) of the Berne Convention and Article 12 of the Rome Convention[91] state that Member States may determine the conditions under which certain rights may be exercised. Article 2(6) of the Berne Convention adds that 'protection shall operate for the benefit of the author and successors in title'. Such an approach leaves considerable freedom to individual states and hence at the national level significant differences exist in legislation and practice on rights management.

Initially, at the European level the management of copyright and related rights gained little interest from the European Commission and had only been addressed to a limited extent in some directives,[92]

[88] Kretschmer, 'The Failure of Property Rules', at 127, and 133–6.

[89] Case 127/73, *Belgische Radio- en Televisieomroep (BRT)* v. *SABAM and NV Fonior* [1974] ECR 313 (hereinafter 'BRT II'), at para. 9 and Fujitani, J.M., 'Controlling the Market Power of Performing Rights Societies: An Administrative Substitute for Antitrust Regulation', **72** *California Law Review*, 1984, 103–137, at 111–113.

[90] Berne Convention for the Protection of Literary and Artistic Works of September 9, 1886 (Paris Act as amended on 28 September 1979).

[91] International Convention for the Protection Performers, Producers Phonograms and Broadcasting Organisation of October 26, 1961

[92] For instance in Articles 4(3) and (4) of Council Directive 92/100/EEC of 19 November 1992 on rental right and lending rights and on certain rights related to copyright in the field of intellectual property, [1992] *OJ* L290/09 addresses collective management as a model for the management of the right of equitable remuneration; Article 9 of Council Directive 93/83/EEC of 27 September 1993 on the coordination of certain rules concerning copyright and rights related to copyright applicable to satellite broadcasting and cable retransmission, [1993] *OJ* L248/15 defines 'collecting society' ('any organization which manages or administers copyright or rights related to copyright as its sole purpose or as one of its main purposes' (Article 1(4)) and obliges collective management for cable distribution rights, but expressly leaves the regulation of the activities of collecting societies to Member States; Recitals 18, 26 and 17 of Directive 2001/29/EC of the European Parliament and of the Council of 22 May 2001 on the harmonization of certain aspects of copyright and related

without addressing the conditions of rights management as such. However, between 1995[93] and 2002, the Commission widely consulted stakeholders on the question of management of rights. This resulted in a communication from the Commission concluding that there is a 'need for complementary action on those aspects of collective management which affect cross-border trade and have been identified as impeding the full potential of the Internal Market'.[94] Especially with the emergence of the digital environment, cross-border trade and goods based on copyright and related rights has become common practice. Often the exploitation will extend to more than one state. The lack of common rules may be detrimental to both users and right holders, as it may lead to legal uncertainty and rules may even be conflicting.

During the consultation process the Commission established a call for EU-wide licensing[95] to overcome the legal hurdles that stand in the way of efficient online licensing. EU-wide licensing would allow the grant of a licence by a single collection society in a single transaction for exploitation throughout the Community. Stakeholders already had been seeking contractual and technological solutions to ensure European or worldwide access to copyrighted works. For instance, the BIEM/IFPI standard contract between authors' collection societies and the association of phonogram producers concerns community-wide licensing for mechanical reproduction rights.[96] Collection societies have notified several agreements intended to facilitate the grant of multi-repertoire, multi-territorial licences for the transmission by electronic means, like webcasting, to the Directorate General (DG) Competition for an assessment in the light of Article 81 of the European Communities (EC) Treaty.[97] In addition, both the European Commission and the

rights in the information society, [2001] *OJ* L167/10 respectively respect and stimulate collective licensing arrangements, and require a higher level of rationalization and transparency with regard to compliance with competition rules; and Article 4(c) of Directive 2004/48/EC of the European Parliament and the Council of 29 April 2004 on the enforcement of intellectual property rights, [2004] *OJ* L195/16 recognizes collective rights-management organizations as 'persons' to seek application of the enforcement measures, procedures and remedies.

[93] European Commission, Green Paper, *Copyright and Related Rights in the Information Society*, Brussels, 19 July 1995, COM(1995) 382 final.

[94] European Commission, 'Communication Management of Copyright', at 9.

[95] *Ibid.*, at 8.

[96] The standard contract forms the basis for reciprocal agreements between collecting societies. The most recent contract expired on 30 June 2000, but has not been renewed yet and societies and record producers are still operating under the provisions of the latest standard contract, available at: www.biem.org/downloads/MenuItems/109/BIEM/Standard%20Contract%20English.pdf (Doc. No. 98/1490, 30 June 1998).

[97] Three major agreements have been notified. (1) The Santiago Agreement: nearly all the major authors' collection societies concluded a reciprocal agreement for music

European Court of Justice (ECJ) have examined statutes and licensing practices of several European collection societies on their compliance with competition law.[98]

In July 2005 the European Commission issued a staff working document on the cross-border collective management of legitimate online music services.[99] It proposed a rather radical model allowing right holders across the EU to adhere to any collection society of their choice for the EU-wide licensing of the use made of their works. This system would introduce choice and competition at the level of right holders and collection societies.[100] However, there is no consensus as to whether this model would actually remove the legal hurdles that stand in the way

performance rights, which allows them to issue multi-territorial licenses of public performance rights to be used on-line. BUMA and SABAM submitted undertakings. The Commission invited parties for comments (Notice published pursuant to Article 27(4) of Council Regulation (EC) No. 1/2003 in Cases COMP/C2/39152-BUMA and COMP/C2/39151-SABAM (Santiago Agreement-COMP/C2/38126), but has never issued a formal decision. (2) The Barcelona Agreement: a standard bilateral agreement to be entered into between all the collection societies member of BIEM to allow for the licensing of mechanical reproduction rights for exploitation of the musical compositions in their repertoire by electronic means, including the Internet (Notification of cooperation agreements, case COMP/C-2/38.377-BIEM Barcelona Agreements, [2002] *OJ* C132/18. (3) The Simulcasting Agreement: users may obtain a European Economic Area (EEA)-wide license from any society within the EEA clearing the remuneration rights of phonogram producers for the simultaneous on-line transmission by radio and TV stations of sound recordings included in their broadcasts of radio and TV signals. This agreement combines freedom of choice with increased transparency obligations for collection societies. On 31 January 2006, the European Commission sent a statement of objections to CISAC and its members concerning parts of the CISAC model contract and its implementation at bilateral level by CISAC members containing membership and territorial restrictions and the network effects of the agreements. See: Press Release, Brussels, 7 February 2006, MEMO/06/03, available at http://europa.eu.int/rapid/ and for CISAC's reaction: Press Release, 14 April 2006, available at www.cisac.com. No formal decision had been issued at the time of writing.

[98] This case-law will be discussed below in Section 'EU and US competition law framework for CCS'.

[99] European Commission, Commission Staff Working Document, *Study on a Community Initiative on the Cross-border Management of Copyright*, Brussels, 7 July 2005. This document has been reviewed and re-issued: European Commission, Commission Staff Working Document, *Impact Assessment Reforming Cross-border Management of Copyright and Related Rights for Legitimate Online Music Services*, Brussels, 11 October 2005, SEC(2005) 1254.

[100] See also: Lueder, T., *Working toward the next generation of copyright licenses*, 14th Fordham Conference on International Intellectual Property Law & Policy, 20–21 April 2006 (on file with the author). Lueder is Head of the Copyright Unit, DG Internal Market and Services of the European Commission. And: Vinje, T. and Niiranen, O., *The Application of Competition Law to Collecting Societies in a Borderless Digital Environment*, European University Institute, Robert Schuman Centre for Advanced Studies, 2005 EU Competition Law and Policy Workshop/Proceedings, available at www.iue.it/RSCAS/Research/Competition/2005/200510-CompVinje.pdf.

of efficient online licensing and on how it would work in practice.[101] Following the staff working document, the Commission adopted a Recommendation on 12 October 2005,[102] which proposes a less radical approach. It recommends the elimination of territorial restrictions and customer allocation provisions in existing bilateral reciprocal agreements while leaving right holders who do not wish to make use of those agreements the possibility to entrust the management of their online rights for EU-wide licensing to a collective rights manager of their choice.[103] The definition of a collective rights manager is rather broad, meaning 'any person [my italics] providing the services set out in point (a) [the grant of licences to commercial users, the auditing and monitoring of rights, the enforcement of copyright and related rights, the collection of royalties and the distribution of royalties] to several right-holders'. Hence, in principle collective rights management could also be carried out by other organizations that the existing national copyright collection societies.

The recommendation also includes some basic provisions on governance, transparency, dispute settlement and accountability of collective rights managers. Contrary to the Commission's expectation, first experiences seemed to indicate that instead of stimulating existing societies to compete to be elected by right holders as their EU-wide licensor of choice for online rights, the recommendation triggered stakeholders to create new licensing platforms that pooled several publishers' or societies' repertoires.[104]

At the time of writing the Commission is monitoring the development of Europe's online music sector in the light of the 'Recommendation on collective cross-border management'. The Commission has invited all interested stakeholders to submit views and comments on their initial experience with the Recommendation and, in general, on their views on how the online music sector has developed since its adoption. More specifically, questions are asked regarding the set up of EU-wide licensing arrangements and initiatives of national CCS to improve transparency

[101] Tuma, 'Pitfalls and Challenges', at 227–8.

[102] European Commission, *Commission Recommendation of 18 May 2005 on collective cross-border management of copyright and related rights for legitimate online music services* [2005] *OJ* L276/54 and Press Release, Brussels, 12 October 2005, IP/05/1261, available at http://europa.eu.int/rapid/ (hereinafter 'Recommendation on collective cross-border management').

[103] European Commission, 'Recommendation on collective cross-border management', at point 1(e).

[104] Lueder, 'Working Toward', at 17–18.

and good governance.[105] At the moment of finalizing this chapter, we were still awaiting the outcome of the consultation.

EU and US competition law framework for CCS

Introduction

Under EU law, copyright collection societies have to respect Article 81 and 82 of the EC Treaty. Article 81(1) of the EC Treaty prohibits agreements between undertakings which restrict competition and affect trade between Member States. CCS are subject to compliance with Article 82 of the EC Treaty, where a society is constituted as a legal monopoly or under 86(1) of the EC Treaty where it is granted special rights by national legislation.[106] Collection societies are 'undertakings' within the meaning of Article 81(1) and 82 of the EC Treaty, because they participate in the commercial exchange of services and are therefore engaged in the exercise of economic activities.[107] National CCS enjoy a dominant and in most cases even monopolistic position in their respective markets. Collection societies in the EU have a virtual 100% share of the market in their respective territories, as nearly all individual holders entrust their rights in each Member State to one collection society. The ECJ has acknowledged this dominant position resulting from their (legal or) *de facto* monopoly position.[108] In this respect, they are the 'usual suspects'[109] and have a special responsibility in the way they exploit this position.

[105] European Commission, *Call for comments on Commission Recommendation of 18 October 2005 (2005/737/EC) on collective cross-border management of copyright and related rights for legitimate online music services*, January 17, 2007, available at http://ec.europa.eu/internal_market/copyright/docs/management/monitoring_en.pdf.

[106] The ECJ interprets Article 86(2) of the EC Treaty restrictively, as it permits – in certain circumstances – derogation from the competition rules. 'Private undertakings may come under that provision, but they must be entrusted with the operation of services of general economic interest by an act of public authority . . . That is not the position in the case of an undertaking to which the state has not assigned any tasks and which manages private interests, including intellectual property rights protected by law.' BRT II, at paras. 20–3. Mestmäcker, E-J., *Collecting Societies*, European University Institute, Robert Schuman Centre for Advanced Studies, 2005 EU Competition Law and Policy Workshop/Proceedings, available at www.iue.it/RSCAS/Research/Competition/2005/200510-CompMestmaecker.pdf, at 3–4.

[107] Case 7/82, *Gesellschaft für müsikalische Aufführungs- und mechanische Vervielfältigungsrechte (GVL)* v. *Commission* [1983] ECR 483 and BRT II.

[108] *GVL* v. *Commission*, at paras. 44–45 and BRT II, at para. 5.

[109] Allendesalazar, R., Vallina, R., *Collecting Societies: The Usual Suspects*, European University Institute, Robert Schuman Centre for Advanced Studies, 2005 EU Competition Law and Policy Workshop/Proceedings, available at www.iue.it/RSCAS/Research/Competition/2005/200510-CompAllendesalazar.pdf.

The US has two major *competing* performing rights organizations, the American Society of Composers Authors and Publishers (ASCAP), established in 1914 and Broadcast Music, Inc. (BMI), dating from 1939.[110] A failure of negotiations on a substantial increase of ASCAP's licence fees between ASCAP and its licensees prompted the formation of BMI: some broadcasters boycotted ASCAP and created BMI, which became (surprisingly) successful.[111] ASCAP is an unincorporated non-profit association. BMI is a non-profit corporation owned entirely by broadcasters. The ASCAP and BMI operate on the basis of consent decrees:[112] settlements between the Antitrust Division of the US Department of Justice (DOJ) and the collection societies.

The anti-competitive concerns which might occur with regard to CCS will be described under the following three headings: (i) the relationship between the CCS and their members, the right owners; (ii) the relationship between CCS and the users of the works, the licensees; (iii) and the reciprocal agreements between different CCS.

Relationship between CCS and members

The collection societies generally act as trustee for their members, the right owners, managing their rights and representing their economic, social and cultural interests. This does not mean that copyright collection societies in the EU can oblige a right holder to assign *all* present and *future* rights. This would amount to an abuse of the collection society's dominant position within the meaning of Article 82(a) of the EC Treaty, as it imposes an unfair trading restriction.[113] Moreover, a

[110] The Society of European Stage Authors & Composers (SESAC) (1930) is the smallest of three performing rights organizations in the United States. Whereas ASCAP and BMI operate on a not-for-profit basis and distribute all performance royalty income to their composer and publisher affiliates (minus an administrative fee), SESAC retains a certain amount of royalty income as profit. See: www.sesac.com/.

[111] Though some authors seem to suggest that broadcasters wanted an alternative source of music licenses, even if the immediate dispute over ASCAP's license fee could have been resolved. See: Besen, S.M., Kirby, S.N., and Salop, S.C., 'An Economic Analysis of Copyright Collectives', **78** *Virginia Law Review* 1992, 383–411, at 401–2.

[112] For an overview of the official sources of the former consent decrees, see for instance: Einhorn, M.A., *Intellectual property and Antitrust: Music Performing Rights in Broadcasting*, 2002, available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=336045, at 1, at fn. 1–7.

[113] European Commission, Decision of 6 August 2002, case COMP/C2/37.219, *Banghalter & Honem Christo* v. *SACEM* ('Daftpunk'-decision), available at http://europa.eu.int/comm/competition/antitrust/cases/decisions/37219/fr.pdf. Furthermore: BRT II, paras. 11–12; European Commission, Decision 71/224/EEC of 20 June 1971, case IV/26.760, GEMA I [1971] *OJ* L134/15; European Commission, Decision 72/268/EEC of 6 July 1972, case IV/226.760, GEMA II [1972] *OJ* L166/22 and European Commission, Decision 82/204/EEC of 4 December 1981, case IV/29.971, GEMA III [1981] *OJ* L94/12. The decisive criterion is whether the conditions imposed on the

collection society with a dominant position on the relevant market is not allowed to exclude right holders from other EU Member States from becoming a member, or to impose discriminatory terms.[114]

The European authorities have, however, left considerable freedom to the CCS in determining the rules on the distribution of royalties. In contrast, the US consent decrees initially constrained the weights used to divide the royalties collected (by ASCAP) amongst their members for different uses of music. On top of that, rules for voting, performance surveys and mechanisms for resolving disputes among members were prescribed. These rules were considerably liberalized in 2001, when the consent decree was amended, allowing ASCAP to decide on the weighting method, as long as the selected method would be applied consistently and would be fully and clearly disclosed.[115]

Relationship between CCS and users

As has been stated above, blanket licences for copyright users are the centerpiece of copyright collection. In *Tournier*, the ECJ stated that blanket licences charging flat royalty-rates from users in principle do not violate Article 82 of the EC Treaty, as long as no other method might be capable of protecting the interests of the members of the copyright collection society, without thereby increasing the costs of managing contracts and monitoring the use of protected creative works.[116] Moreover, European collection societies may not engage in a concerted practice leading to systematic refusals to grant direct access to their repertoires by users located in foreign territories. Despite the fact that reciprocal agreements as such may be lawful,[117] European collection societies may not retain any restrictive practices that strengthen anti-competitive effects. This can be explained by the fact that also dominant or monopolistic undertakings cannot merely refuse to license a user

members exceed the limits absolutely necessary for effective protection or whether they unnecessarily limit the individual copyright holder's freedom to dispose of his or her work. Allendesalazar &Vallina, 'Collecting Societies: The Usual Suspects', at 13–21.

[114] *GVL* v. *Commission*, at paras. 54–56; European Commission, Decision of 29 October 1981, case IV/29.839, GVL [1981] *OJ* L370/49 and European Commission, Decision 71/224/EEC of 20 June 1971, case IV/26.760, GEMA I [1971] *OJ* L134/15. The requirement for foreign nationals to have their fiscal domicile in Germany and restricting membership of the supervisory council to German nationals constitute discriminatory terms.

[115] *United States of America* v. *ASCAP*, Second Amended Final Judgment, June 11, 2001, Civ. Action No. 41–1395 (S.D.N.Y. 2001), Section XI(B) (hereinafter 'AFJ2'). See also: Einhorn, 'Intellectual Property and Antitrust', at 18.

[116] Case 395/87, *Ministère public* v. *Jean-Louis Tournier* [1989] ECR 2521, at para. 44.

[117] See below, section 'Reciprocal agrrements between CCS'.

in their own territory without a legitimate reason either. Nevertheless, a refusal to license directly to foreign users could be justified by the impracticability of setting up a collective administration system in another country.[118]

Similarly, under the US consent decrees and a number of judgments, the practice of blanket licensing has been preserved. In 1979 the US Supreme Court held that the issuance of blanket licences by ASCAP and BMI at fees negotiated by them is not price fixing *per se* unlawful under the antitrust laws, but should be considered under the rule of reason.[119] It is argued that the use of blanket licences does not exclude price competition, because the blanket licences are non-exclusive and cannot prevent right holders from individually administering their rights.[120] Users may still directly approach individual right holders, who would thus remain independent in setting a competitive price for individual licensees willing to deal with them directly. Hence, the blanket licence would not result in a restraint of trade.[121] This view is remarkable because in theory price competition may be available, but in practice obtaining the licence directly from the right owner will not be a viable alternative for most users.[122]

CCS in Europe and the US have regularly refused special authorizations for sub-groups of rights, or several sub-groups corresponding to a specific repertoire, such as the UK and US repertoire, and stick to the blanket licences. According to the ECJ this refusal does not have the object or effect of restricting competition. It could only be criticized if the differentiation in sub-groups might be capable of attaining the legitimate aim of safeguarding the rights and interests of the members of the collection societies, without thereby increasing the costs of managing contracts and monitoring the use of protected works.[123] In the US, however, ASCAP and BMI have been obliged to issue the blanket licences to selected groups of music users, such as radio and television broadcasters. To these groups ASCAP shall offer a 'per-programme licence' or 'mini-blanket' that makes the full catalogue of rights available on an

[118] *Ministère public* v. *Tournier,* at para. 24 and cases 110/88, 241/88 and 242/88, *François Lucazeau et al.* v. *Société des Auteurs*, Compositeurs et Éditeurs de Musique (SACEM) et al. [1989] ECR 2811, at para. 18.

[119] *Broadcast Music, Inc.* v. *Columbia Broadcast System, Inc.*, 441 US 1, at 4 (1979).

[120] See, for instance: AFJ2, Section VI.

[121] *Buffalo Broadcasting Co.* v. *ASCAP,* 744 F.2d. 917 (2d Cir. 1984) and *Columbia Broadcast System, Inc.* v. *ASCAP*, 620 F.2d 930, 936 (2d Cir. 1980), cert. denied, 450 US 970 1981. See also: Einhorn, 'Intellectual Property and Antitrust', at 10–11, 18 and Fujitani, 'Controlling the Market Power', 103–37.

[122] Fujitani, 'Controlling the Market Power', at 123–9.

[123] *Ministère public* v. *Tournier,* at paras. 28–33 and 45.

individual programme basis. According to an amendment to the existing consent decrees (the so-called 'Second Amended Final Judgment' or 'AFJ2') ASCAP should grant genuine licence alternatives to more user groups, such as background music providers and online transmitters ('per-segment licences').[124]

Furthermore, as a general rule, ASCAP and BMI are not allowed to discriminate in prices or terms charged to similar users.[125]

Another important issue in the relationship between copyright collection societies and users that has been subject to review in the EU and the US is the (reasonable) level of tariffs charged to the licensees. The ECJ observed that one of the most marked differences between copyright collection societies lies in the level of operating expenses. It held that it cannot be ruled out that it is the lack of competition in the market that accounts for high administrative costs and hence the high level of royalties.[126] If a collection society establishes unfair conditions by imposing appreciably higher tariffs than those applicable in other European Member States, the collection society abuses its dominant position in violation of Article 82 of the EC Treaty, unless the differences are justified by objective reasons.[127] This appears to be a rather unreliable criterion, because all CCS in the EU have a dominant position and hence a comparison of the tariffs in the different Member States will not disclose information on the level of fees that is generally commensurate with the value that a competitive market would place on collective rights administration. In spite of that, the ECJ held in another case that whether the remuneration is equitable is to be assessed, in particular, in the light of the value of the use in trade.[128]

In the US 'rate courts' have been appointed to decide what fees should be paid for the commercial use of music when users and ASCAP or BMI are unable to agree on the royalty rate.[129] The US District Court

[124] AFJ2, Section VII(A). Cf.: Fels, A., Walke, J., *Australian Intellectual Property Law, Competition and Collecting Societies: Efficiency, Monopoly, Competition and Regulation*, European University Institute, Robert Schuman Centre for Advanced Studies, 2005 EU Competition Law and Policy Workshop/Proceedings, available at www.iue.it/RSCAS/Research/Competition/2005/200510-CompFels.pdf.

[125] Einhorn, 'Intellectual Property and Antitrust', at 7–8 and AFJ2, Section VIII(A).

[126] *Ministère public* v. *Tournier,* at para. 42 and *Lucazeau* v. *SACEM*, at para. 29.

[127] *Ministère public* v. *Tournier*, at paras. 37–8 and *Lucazeau* v. *SACEM*, at paras. 24–25. Allendesalazar & Vallina, 'Collecting Societies: The Usual Suspects', at 3–11.

[128] Case C-245/00, *Stichting ter Exploitatie van Naburige Rechten (SENA)* v. *Nederlandse Omroep Stichting (NOS)* [2003] ECR I-1251, at para. 37.

[129] Already under the US Copyright Act of 1976 another specialized institution was established, the Copyright Royalty Tribunal, to set royalty rates for compulsory licensing fees to be paid to copyright owners for mechanical rights, and for blanket performance rights for jukeboxes and secondary cable transmission.

for the Southern District of New York[130] found that the appropriate benchmark for setting the ASCAP's rate at a reasonable, competitive level was the fee set by BMI, ASCAP's 'competitor'.[131] This view is controversial as well.[132] The case law and criticism on both the approach of the ECJ and the US District Court for the Southern District of New York confirm once more that royalty setting is a highly complicated and sensitive area.

Reciprocal agreements between CCS

Reciprocal representation agreements between CCS are not in themselves restricting competition in the sense of Article 81(1) of the EC Treaty. This might be different if the agreements would explicitly stipulate that copyright management societies decide not to allow direct access by users established in another territory. As has been stated above, even if such clauses are removed from the agreements, copyright collection societies may not retain such exclusivity conditions by means of a concerted practice.[133] The agreements appear economically justified in a context where the collection societies would otherwise be obliged to organize their own management and monitoring system in other countries.[134]

In the *Simulcasting*-decision, the European Commission adapted these principles to the on-line environment. The absence of territorial boundaries in this environment enables users to choose any collection society in the EEA which is a member of the one-stop licensing mechanism that is established for the delivery of EEA-wide licences. To increase transparency, the tariff which covers the royalty was separated from the fee related to the administrative costs. This should enable users to recognize the more efficient societies and allow them to apply for a licence from the societies that grant licences at the lowest cost.[135]

[130] The US District Court for the Southern District of New York is ASCAP's fee-setting Rate Court for license disputes.

[131] *American Society of Composers Authors and Publishers* v. *Showtime/The Movie Channel*, 912 F.2d 563 at 569–70 and 577–8 (F.2d 1990).

[132] Besen et al., 'An Economic Analysis', at 405–7 and Einhorn, 'Intellectual Property and Antitrust', at 15.

[133] *Ministère public* v. *Tournier,* at paras. 20–21.

[134] *Ibid.*, at paras. 20–6 and *Lucazeau* v. *SACEM*, at paras. 14–18.

[135] European Commission, IFPI Simulcasting, Decision of 8 October 2002, case COMP/C2/38.014 [2003] *OJ* L107/58, at para. 71–107.

Criticisms and concerns regarding CCS

During the consultation process initiated by the European Commission, both users and right holders criticized the operation and accountability of the copyright collection societies.[136] Criticisms from users focused on the tariffs, the administrative fees charged by the societies, the length of the negotiations, the alleged shortcomings in the internal decision-making process, the apparent lack of transparency regarding the pricing policy, the supervision of collection societies[137] and the limited access to courts or arbitration.[138] Most right owners, on the other hand, favour a greater influence on the distribution of royalties and more flexibility on the part of the CCS regarding the acquisition of rights. Moreover, right holders with sufficient bargaining power, like major phonogram producers argue that digitization, in facilitating watermarking, identification and tracking of the use of works, has empowered them to individually control the licensing and royalty payment process and question the role of collective rights management as such.[139]

In response to these concerns, the European Commission in its Communication of 2004 envisaged greater common ground on a number of issues in order to achieve a level playing field at Community level.[140] More in general, the Commission was concerned about the establishment and legal status of copyright collection societies, the persons that may establish a society, the minimum number of represented right owners, and the necessary proof of efficiency, operability

[136] On May 11, 2002, the US Subcommittee on Courts, the Internet, and Intellectual Property of the Committee on the Judiciary House of Representatives also organized a Hearing on Public Performance Rights Organizations. This Hearing especially mirrored the concerns on accountability, transparency and reasonable tariffs. The appointment of separate 'rate courts' to decide on the licensing fees in case of disputes was considered effective. See: US Subcommittee on Courts, the Internet, and Intellectual Property of the Committee on the Judiciary House of Representatives, *Hearing on Public Performance Rights Organizations*, 109th Congress, First Session, 11 May 2005, Serial No. 109–25, available at www.house.gov/judiciary/. Nevertheless, several US authors have suggested the establishment of a system of administrative regulation, comparable to for example Germany or the UK, as a safeguard against potential monopolistic abuses by the US collection societies. See, for instance: Fujitani, 'Controlling the Market Power', at 129–37.

[137] Rochelandet suggested on the basis of an empirical study that when more external supervision is exercised CCS appear to manage the rights more efficiently. Rochelandet, F., *Are copyright collecting societies efficient? An evaluation of collective administration of copyright in Europe*, The Society for Economic Research on Copyright Issues, Madrid: Inaugural Annual Congress 2002, available at www.serci.org/2002/rochelandet.pdf.

[138] European Commission, 'Communication Management of Copyright', at 16.

[139] *Ibid*. [140] *Ibid*, at 4, 18–19.

and accountability.[141] These issues should be subject to rules of good governance.

In the interest of users, collection societies should respect transparency with regard to tariffs and licensing conditions, adopt reasonable conditions, and options for internal control, including internal dispute settlement mechanisms, should be available. On top of this, adequate external control mechanisms concerning the behaviour and functioning of the societies, their tariffs and licensing conditions and internal dispute settlement mechanisms should exist. This role could be played by specialized tribunals, administrative authorities or arbitration boards.

The societies, often the only gatekeeper of the market for collective management of rights, should also observe principles of good governance, non-discrimination, transparency and accountability vis-à-vis their right owners. These principles should apply to the acquisition of rights, the conditions of membership (including termination of membership) and representation, access to internal documents and financial records concerning the licensing revenue, distribution of licensing revenue and administrative deductions, (genuine) influence of right holders on the decision-making process and on the social and cultural policy. In addition, right holders should have a certain degree of flexibility regarding the duration and scope of the mandate and in principle, unless the law provides otherwise, have the possibility – if they so desire – to manage some of their rights on an individual basis. The Commission intended to propose a legislative instrument on these elements of collective management and good governance of the collection societies. Except for some minor suggestions in the above-mentioned recommendation of October 2005, the Commission has not realized this yet.

Lessons from CCS for the PRCCH

The analysis shows that even though CCS have a long history, their role in copyright management is not uncontroversial. Hence, extensive discussions are necessary to examine the actual value and legitimacy of a PRCCH and its costs and benefits before actually proposing the establishment of PRCHHS for reasons of economies of scale and transaction

[141] The Commission recognizes that some Member States have already adopted or initiated new legislation aiming at rendering the management of rights by copyright collection societies more transparent and improving their accountability. The Communication of the European Commission of 2004 refers to France, Belgium, the Netherlands, Luxembourg and Portugal (European Commission, 'Communication Management of Copyright', at 15).

cost savings. Prior to promotion of PRCCHs, its superiority as a solution over other solutions such as bilateral licences, cross-licences, research exemptions and patent pools should be evaluated. Obviously, the evaluation may differ according to the actual circumstances, such as the patenting and licensing strategy in a specific field of technology, geographical region, market conditions etc.

In this section, I would like to provide some general principles on how a PRCCH can be organized and function, based on the case law and the academic and political debate in the US and the EU on copyright collection societies.

Good governance

Like CCS, PRCCH should observe principles of good governance, non-discrimination, transparency and accountability vis-à-vis patent owners and licensees. To guarantee respect for these principles, internal and external supervision mechanisms should be established.

Adequate functioning of collective administration mechanisms in a patent context requires effective external regulatory oversight and access to (specialized) courts or arbitration. Competition authorities should regularly review (both *ex ante* and *ex post*) the justification for the establishment of collective administration mechanisms, their eligibility in the light of changing circumstances (new technologies, economic theories, previous experiences with the performance of the clearinghouse, changing market conditions etc.) and whether the royalties and licensing terms comply with market conditions.

Competition

In order to safeguard quality and price competition there is preferably more than one patent royalty collection clearinghouse within a specific territory that delivers search, licensing, collection and distribution, monitoring and enforcement services. In this scenario, right owners are not forced to assign or licence their patent rights exclusively to one clearinghouse, but remain free to license their rights non-exclusively themselves or to other clearinghouses for further sub-licensing. This dynamic allows quality and price competition in the interest of both patent owners and users. In the case of competing PRCCHS rational market players will turn to the most efficient PRCCH. However, if for reasons of economies of scale for licensing, monitoring and enforcement and transaction costs savings it will turn out to be more efficient to have only one PRCCH, the free market will inevitably move into that direction. Moreover, equally important is that licensees may encounter difficulties if they will have to approach several PRCCHs in order to

clear access to all the relevant patents. This would plead for the establishment of only one PRCCH or a limited number of clearinghouses per country or for a particular technology.

Furthermore, the European experience with national monopolistic copyright collection societies teaches us that despite the fact that patents are granted for a specific national territory, a patent royalty collection clearinghouse had better not define its territory too narrow. PRCCHs should consider at least EU-wide or worldwide multi-territorial licences. Patent owners and users will be free to make use of the services of a clearinghouse in another country as well. As long as the geographical scope of the licence and the patents involved are clearly stated and described in the licence, it may cover several jurisdictions. Indeed, this is also a common practice in bilateral licences. Search, licensing, monitoring and enforcement services are in principle not disturbed by geographical boundaries. I acknowledge that this will require a highly educated and experienced, international legal staff. A solution would be to form an exchange network with clearinghouses in other countries to swap experience and knowledge. Patent royalty collection clearinghouses would thus compete on the provision of cross-border services.

Licensing practices

The centerpiece of collective administration of rights in music, the 'blanket licence', is definitely not a desirable feature for a PRCCH. Already in copyright there is no consensus on the effectiveness of this instrument. In the US, the amended consent decrees explicitly state that the CCS should grant genuine licence alternatives to user groups. If royalties would have to be paid without considering the actual inventions used and the number of times they are being used, but on the basis of a flat-royalty rate covering unlimited access and use to the 'repertoire' of all patent right holders, it is highly unlikely that many licensees and patent owners would be interested in the clearinghouse. For licensees, a blanket licence arrangement would only be beneficial if the flat-royalty rate would be set at such a low level that – in all likelihood – it would not be acceptable to patent owners. In other words, it is hard to reach a fair balance between the interests of the right owners and the interests of the technology users in setting rates for a blanket licence. This is further complicated by the fact that right owners in genetics at one occasion may well be technology users applying for a licence with the PRCCH the next time. In such circumstances, ultimately a blanket licence might even entail right owners paying for access to their own patented technology. This is less likely in the area of copyright.

On top of this, the interests of the highly diverse community of rights owners should be balanced. Patent owners want a reward for their investments and not a social security system for inventors with minor, less valuable patents. Moreover, generally, people tend to value their own property rights higher than their competitors'. A blanket licences system would create a risk of the royalty collection clearinghouse becoming a 'market for lemons'[142] where 'masterpieces' are not compensated appropriately and inventors of 'mediocre' advances would receive excessive remunerations.[143]

Clearinghouses are not allowed to discriminate in prices or licensing terms charged to similar users. This will not withhold the PRCCH from distinguishing between different kinds of users, uses and product profiles through flexible standard licences. Such standard licences may be appropriate 'to protect the interests of the right owners and different types of users without thereby disproportionally increasing the costs of managing contracts and monitoring the use of protected inventions'.[144] Due to the complexity of patents, of genetic diagnostics, and the variety of actors performing diagnostic testing, patent monitoring and enforcement is a costly endeavour anyway. Here economies of scale, network effects and visibility arguments maybe a more viable argument than for copyright.

Royalties

Royalties charged should be fair, reasonable and non-discriminatory. But what is fair and reasonable and who decides what is fair and reasonable? Balancing all the interests involved is not an easy task. However, to start with, transparency can be improved by separating the tariff which covers the royalty from the fee related to the administrative costs. For copyright, the ECJ held that whether the remuneration is equitable is to be assessed, in particular, in the light of the value of the use in trade. For patents, this will be a very complex task which requires the input of independent experts. In the US, to decide what fees should be paid for the use of music if the parties involved are unable to agree on a royalty rate, rate courts have been appointed. Within the scope of the PRCCH, such conflicts may be solved by way of internal dispute-resolution mechanisms, e.g. mediation or arbitration, or one may consider external review by way of patent tariff courts.

[142] Akerlof, G.A., 'The Market for "Lemons": Quality Uncertainty and the Market Mechanism', **84** *Quarterly Journal of Economics*, 1970, 488–500.
[143] Cf. Katz, 'Copyright Collectives', at 30–1.
[144] For this criterion, see also: *Ministère public* v. *Tournier*, at paras. 28–33, 44–45.

With regard to the royalty distribution to the right owners, the clearinghouse should design a reasonable weighing method. The copyright case law does not provide detailed criteria, but as long as the selected method would be applied consistently and would be fully and clearly disclosed, the PRCCH will probably be in line with competition law. The best way will probably be to compensate right owners on the basis of an auditing mechanisms managed by the clearinghouse.[145]

5.4 Building a PRCCH in genetic diagnostics

The typology for clearinghouses and the principles described above inspired by the CCS leave quite some leeway for the final set up of a PRCCH in genetic diagnostics. Some key building blocks will be described below.

Legal status and infrastructure

The PRCCH in genetic diagnostics would act as an independent intermediary or agent. It would not be a society representing the interests of its members, as copyright collection societies do, but would treat the interests of the various right owners and users of the patented technology on an equal footing. It could be set up as a neutral public agency by a national or international organization, as a public-private partnership, or as a private initiative on a non-profit or profit basis. The clearinghouse could in principle be implemented as a voluntary scheme or as a statutory framework on a mandatory basis. For copyright collection societies, the European Commission considered the legal status not very relevant.[146] Still further research is necessary to decide on the most appropriate legal model for the PRCCH in view of the various legal traditions and taking into account the interests of the patent holders, the licensees and the clearinghouse in an effective management of the patent rights.

For the moment, I prefer voluntary private initiatives or public-private partnerships over a public, statutory, compulsory regime. Also private organizations can be charged with public duties, like the promotion and distribution of innovation through licensing management and access to health care services. Prices and other licensing terms are best determined on the basis of market conditions and government agencies generally tend to have limited knowledge and experience in this regard.

[145] See also Section 'Access, use, reporting, royalty collection and disbursement'.
[146] European Commission, 'Communication Management of Copyright', at 18.

Nevertheless, external supervision on the price-setting procedure is a prerequisite.

Various competing national or regional clearinghouses (European, North American, Asian, African etc.) could be set up to perform the services with respect to identification, matching, standardized licensing, royalty collection and distribution, monitoring and enforcement. Even a kind of network of decentralized clearinghouses could be established and coordinated by a worldwide, overreaching 'umbrella' organization. Such a global approach would, on the one hand, be cost-effective and could, on the other hand, feed the incentive of patent holders to voluntarily participate in a model limiting the points of registration with good visibility for technology users. Certainly, due to the global character of the genetics marketplace, potential licensees would be better served with a global checkpoint for the existing patent rights and cross-border licences.

Licensing practices

Patent holders in favour of collective administration select the patent rights they wish to manage through the licensing scheme of the clearinghouse. Patents in the clearinghouse can be substitutes or complements. In principle, the patent licence may take many legal forms. In any case, patent owners would remain free to license directly to licensees outside the scope of the clearinghouse. The licence to the clearinghouse could refer to all, or part of the exploitation rights (manufacturing, distribution etc.).

If the PRCCH would operate on the basis of standard licences, this would diminish the transaction costs. However, in all likelihood, reaching agreement on the licensing terms will be one of the most complicated and burdensome hurdles to be taken by the initiators of a clearinghouse. Blanket licences used in copyright, praised (but also criticized) for their simplicity and easy enforcement, will probably not be accepted by patent proprietors. Bilateral patent licences are very complex and require a subtle consideration of all the interests involved. For instance, licensee's indulgence with regard to the basis for royalty calculation may be compensated by flexible minimum manufacturing quantities and a sliding scale of royalties; the obligation for the licensee to grant back improvements to the licensor may be confined to a narrow definition of improvements in accordance with the type of invention; and so on. Here, one may draw on the experience of Science Commons in its Biological Material Transfer Project[147] in developing

[147] See above, at 20.

differentiated material transfer agreements together with the stakeholders concerned.

The basic criteria for differentiation of the standard licences could be the nature of the user, the objective of the use and the profile of the eventual product to be developed by the licensee. In practice, this would mean that the standard licence agreements are linked to electronic forms with specific parameters. Such forms would include tick-off boxes related to the nature of the user, the specific goal of the intended use (research, product development (improvement/new product), diagnostic testing etc.), geographical scope of application, followed by a list of the various patented genetic inventions (DNA sequences, mutations, proteins, technical applications etc.). Users from developing and developed countries could all use the clearinghouse services, but it would be opportune to bargain for special standard licences for humanitarian use at low or zero cost.

Industry standards could be employed as an administering tool for managing the royalty collection clearinghouse. Industry standards are technical specifications relating to a product or an operation, which are recognized by a large number of manufacturers and users.[148] In genetic diagnostics, a standard should not necessarily be looked at in terms of a technical specification, but could present itself as a set of mutations, recognized by the international scientific community, or reflecting national or international best practice guidelines for genetic testing for a particular disease.[149] Good examples are the standards and guidelines issued by the American College of Medical Genetics for Cystic Fibrosis.[150] Whereas such best practice guidelines may serve as an important incentive for the establishment of patent pools in consumer electronics and telecommunications,[151] in a royalty collection

[148] European Commission, *Communication of 27 October 1992 on Intellectual Property Rights and Standardisation*, COM(92) 445 final. See also: Verbruggen, J., and Lôrinz, A., 'Patents and Technical Standards', **33** *International Review of Intellectual Property and Competition Law*, 2002, 125–54, at 132 and Mueller, J.M., 'Patenting Industry Standards', **34** *Int'll Prop. L. Rev.*, 2002, 201–50, at 209.

[149] Van Overwalle et al., 'Models facilitating access', at 145; Verbeure, B., van Zimmeren, E., Matthijs, G., Van Overwalle, G., 'Patent Pools and diagnostic testing', **24** *Trends in Biotechnology*, 2006, 115–20, at 118 and Ebersole, T.J., Guthrie, M.C., Goldstein, J.A., 'Patent pools and standard setting in diagnostic genetics', **23** *Nature Biotechnology*, 2005, 937–938.

[150] Richards, C.S., Bradley, L.A., Amos, J., Allitto, B., Grody, W.W., Maddalena, A. et al., 'Standards and Guidelines for CFTR Mutation Testing', **4** *Genetic Medicine*, 2002, 379–91.

[151] OECD, 'Genetic Inventions'; Van Overwalle et al., 'Models for facilitating access', at 143–8; Verbeure et al., 'Patent pools', at 115–20 and Ebersole et al., 'Patent pools', at 937–8.

clearinghouse for genetic diagnostics, those guidelines could be transformed into an administering tool for the identification and grouping of the patent rights into one licence to increase the clearinghouse's transparency and effectiveness. All the patented products and technologies which – according to the guidelines – are essential for genetic testing for a particular disease, could be made available as a 'set' on the basis of a standard licence with a non-stacked, fair, reasonable and non-discriminatory royalty rate.[152]

Next to offering sets of patented inventions, the royalty collection clearinghouse should also allow to shop around and pick and choose only those inventions a specific scientist, clinical geneticist, laboratory or clinic needs to carry out or develop upon the diagnostic tests concerned. If the pick-and-choose option would be excluded and only packages of pre-specified licences would be available, this might amount to tying and have anti-competitive effects.

As the best practice guidelines for genetics are subject to regular review following new developments in this discipline, the sets of patented inventions and the related standard licences should thus be dynamic as well.

Access, use, reporting, royalty collection and disbursement

The clearinghouse database provides information on inventions, the related patents and the respective claims relevant for a specific application in genetic diagnostics (cf. information clearinghouse). The patent owner(s) and licensee are 'matched', either with or without intervention of a patent expert (cf. technology exchange clearinghouse). The licensee ticks boxes according to his needs, on the basis of which a standard licence will be generated and the appropriate royalty will be calculated. Depending on the specific parameters (nature of the user, intended use, geographical scope of application, relevant inventions etc.) a particular standard licence will be offered. By paying the royalty fees, the licensee acquires the right to exploit the selected patents/patent claims. Only in exceptional circumstances would it be opportune to allow licensees to request complementary negotiations on additional clauses or requirements. Otherwise, the transaction costs savings will be wiped out.

To facilitate the monitoring and enforcement of the licence agreements, a reporting system would be set up. Unlike a system administered by blanket licences, the standard licences stipulate that licensees

[152] Cf. Graff et al., 'Towards an Intellectual Property Clearinghouse', at 9–10.

should report their use of the patented invention to the auditing department of the clearinghouse without having to submit confidential information to the patent owners. Currently, users in genetic diagnostics appear to be quite reluctant to provide details on their testing activities both vis-à-vis patent owners and the general public. Partially, this can be explained by the fact that at present, so-called 'home-brew' methods infringe patents. Moreover, restitutions by public insurance schemes require complex calculations that involve some creative book-keeping, or track records are simply incomplete. If the figures would only have to be submitted to an independent auditor within the licensing and collection clearinghouse for the sole reason of calculating the appropriate royalties (with a guarantee of confidentiality), users might be more willing to cooperate.

An electronic royalty collection and disbursement accounting system is indispensable in the framework of a PRCCH. The clearinghouse would collect the royalties from the licensees on a yearly or half-yearly basis and compensate the patent holders, either pursuant to a set allocation formula or based on the figures reported by the licensees after deduction of the administration costs. Depending on the actual number of patent holders and licensees, the administrative burden of both the collection and the reallocation of the royalties may be substantial. However, appropriate software tools and decentralized settlement of these duties of the clearinghouse will deduce this Herculean task to manageable proportions.

Monitoring and enforcement

In case the clearinghouse auditor notices some irregularities in the reports, he would be allowed access to the licensee's records. Monitoring, notification and enforcement against infringement by non-licensees will, however, be more complicated to carry out. The patent holder will generally be best-placed to ascertain such facts. Nevertheless, it could be one of the basic services provided by the clearinghouse, or it might be optional and patent holders interested in such services would pay complimentary fees to the clearinghouse.

It would also be convenient to accommodate an in-house dispute resolution mechanism. Many disputes might be tackled before adversaries end up before court. Especially because in genetic diagnostics, the same companies and institutions are dealing with one another in different projects subject to a continuous metamorphosis (at one time as an IP holder, at another occasion – or even in the same transaction in case of a cross-licence – as a user of the IP); the maintenance of

sound, long-lasting business relationships is of vital importance. As the clearinghouse employs experts in the area of patents and licensing and in practice has ample contacts with external experts as well, mediation and arbitration services can be offered in-house.

5.5 Pitfalls of the PRCCH in genetic diagnostics

Royalty collection clearinghouses offer an interesting opportunity for remedying the practical impediments relative to the emergence of patent thickets. Clearinghouses could function as a platform for information, partnering, standardized licensing, royalty collection and distribution, monitoring and enforcement. As independent intermediaries, they are beneficial for right owners, users and patients by lowering transaction costs, preventing the stacking of royalties and safeguarding access to the patented technology. The second problem identified above regarding the non-cooperative patent holder will be more difficult to overcome through the voluntary mechanisms of a PRCCH. However, this problem might be remedied by tools complementary to the clearinghouse instead of the use of drastic measures such as compulsory licensing. Examples of such tools might be reciprocal positive comity or grant-back clauses, which should be tested on their conformity with competition law.

A PRCCH will clearly have some disadvantages as well. First, the analysis of the copyright collection societies has shown that attention should be paid to any anti-competitive effects caused by the licences offered by the clearinghouse, and to the risk of the clearinghouse abusing its strong market position. This risk is relieved in case several competing royalty collection clearinghouses would exist. Also the voluntary nature of the clearinghouse, fair, non-exclusive and non-discriminatory licences, the auditing role of independent experts and external supervision may act as safeguards to prevent abuse.

Second, copyright holders initially had a clear interest in collective management, as it was almost impossible for them to monitor and track every single copyright infringement. This incentive for setting up a royalty collection clearinghouse might be absent amongst a major part of the right owners in genetic diagnostics where – contrary to the situation in copyright – the number of users is not nearly infinite, but limited to the public and private entities involved in carrying out research and testing and pursuing the further development of products. Patent holders with their own IP and licensing departments may not be particularly interested in participating in a royalty collection clearinghouse, as they dispose of monitoring tools in house. Small and medium enterprises

without the means to set up such a division will gain more from the services of a clearinghouse. This bears the risk that only small players will join the clearinghouse which, in turn, will represent an asymmetric patent portfolio.

Moreover, as long as the clearinghouse does not constitute a critical mass of patented technology, it might not be a viable and effective alternative, nor prevent the emergence of an anticommons effect. If major patent holders would not be willing to participate in a clearinghouse, the clearinghouse would only be one out of several licensing partners. Licensees would be obliged to enter into separate negotiations with the clearinghouse and the patent owners that do not want to collaborate with the clearinghouse. Hence, the anticommons effect will only partially be remedied and the transaction costs will not be substantially diminished. If these concerns would appear realistic, a cost–benefit analysis of the establishment of the clearinghouse will most probably not result in a positive evaluation. Heller and Eisenberg already expressed hesitation as to whether companies in the biomedical sphere would be willing to cooperate at all in private arrangements in order to reduce transaction costs of bundling multiple licences. "Because patents matter more to the pharmaceutical and biotechnology industries than to other industries, firms in these industries might be less willing to participate in such [collective rights organizations[153]] that undermine the gains from exclusivity".[154] Third, current bilateral licensing practices leave a lot of leeway for creative solutions.[155] The negotiated terms reflect numerous circumstances, e.g. the nature of the product, the strength of the parties, the strength of the IP, the stage of development of the product and the number of competitors. Standard licences might hardly be able to meet those demands. Furthermore, some common business practices, such as due diligence and networking, highly appreciated in the patent licensing business might be thwarted. The use of extensive in-house due diligence procedures is extremely helpful in evaluating the validity, strength and scope of patents. Building and nurturing long-term business relationships based on trust and understanding with major patent holders is of vital importance especially for small- and medium-sized

[153] At this instance Heller and Eisenberg were explicitly considering patent pools, but their concerns apply to collective rights organizations in general and as such to clearinghouses as well.

[154] Heller & Eisenberg, 'Can Patents Deter Innovation?', at 700.

[155] Licensing practices are rather creative with regard to the royalty calculation schemes, minimum amounts of royalties, field of use, setting milestones, quality standards, transfer of materials, reporting duties, warranties, infringement procedures by third parties, improvements regarding the patented inventions, technical assistance, product liability, termination of the license agreement, etc.

enterprises. In this respect, contacts between research departments, management and licensing agents are indispensable. The options for flexibility and 'business-relationship maintenance' in the clearinghouse and its standard licences are inherently restricted. It is, therefore, vital for the success of the clearinghouse that the standard licences will meet at least the most common expectations for alternatives for licensing clauses.

Fourth, also the exchange of complementary know-how is generally fundamental for the smooth operation and further development of the patented inventions. Know-how is confidential in nature and generally protected as a business secret. The clearinghouse may not be able to guarantee the exchange of know-how to all its non-exclusive licensees and maintain secrecy. Thus, with respect to complex technologies, direct negotiations between the licensor and the licensee on the know-how may still be required which might do away with part of the advantages of the PRCCH. This might be a reason to advocate the establishment of a royalty collection clearinghouse limited to patented DNA sequences and mutations, and a handful of commonly used diagnostic tools. Such inventions, indeed, do not normally necessitate the exchange of complementary know-how.

Fifth, royalty collection clearinghouses will be more complicated and costly to set up in comparison to the other clearinghouse models. The information and technology exchange clearinghouse will only require a small team of experts who continuously evaluate and manage the information, and information technology experts for the management of the database. A royalty collection clearinghouse will not function adequately without highly educated scientists, experienced patent attorneys and lawyers for evaluating the patents, developing standard licence agreements, matching licensees with the relevant patented inventions, monitoring, auditing and organizing enforcement and dispute resolution. It is difficult to predict in general to what extent these costs will outweigh the benefits related to a decrease of transaction costs and prevention of royalty stacking. Probably, this is to be evaluated on a case-by-case basis and with respect to a particular technology and use.

5.6 Concluding remarks

The foregoing analysis explains why at present a patent royalty collection clearinghouse is probably too big a leap forward.

Case law and literature on copyright collection societies have taught us that we should not favour 'collectivization' as such, but carefully

examine the justifications and added value on a case-by-case basis. Historical justifications such as economies of scale for licensing, monitoring and enforcement may not be valid. Advantages detected for the role of intermediaries for rights management do not imply collective administration by one clearinghouse but may allow several competing collective mechanisms. Collective administration in copyright does not inevitably show an urgent need and effective role for collectives in the patent sphere. In some areas, the establishment of a PRCCH may be appropriate, in other cases bilateral licences, cross-licences or patent pools may be better, more efficient remedies to safeguard freedom to operate.

Just as for copyright collective administration, collective administration of patent rights is not 'the magic bullet that bridges the unfortunate trade off between incentive and access'.[156] This is even more so in view of the complexity and importance of patents and the characteristics of the biotech industry. Moreover, pharmaceutical and biotechnology companies rely heavily on their patent portfolio and exclusive licences and favour a rather protective approach. However, a successful and fair operation of a patent royalty collection clearinghouse presupposes a willingness to employ non-exclusive licences or exclusive licences for only limited fields of use and a certain release of control once the patented technology is licensed to the clearinghouse. This might not be so obvious in the biotech sector.

Is there a future for broad application of the patent royalty collection clearinghouses in genetic diagnostics? At present, the concept has to mature and be subjected to more thorough review and debate with the stakeholders. In order to seriously engage in the ideas for a royalty collection clearinghouse for patents in genetic diagnostics, the work on copyright collection societies, including the judgments and decisions on competition law, and the present debate within the European Union on the cross-border collective management of copyright and related rights for online music services, should be followed up closely. In particular, economists should be invited to analyse to what extent royalty collection, monitoring and enforcement by a clearinghouse for patented genetic inventions might be more efficient than bilateral licences or other remedies that have been proposed. This will hopefully provide the necessary guidance in this highly challenging and extremely complicated area.

For now, it may be more realistic to promote a global technology exchange clearinghouse and/or standard licences clearinghouse as an

[156] Katz, 'Copyright Collectives', at 1.

intermediary solution for genetic diagnostics. These types of clearinghouses are not a new phenomenon in the patent field; they will raise awareness, remedy some of the problems, and will meet with less opposition. Ultimately, if it would be demonstrated that a more advanced mechanism is desirable, those technology exchange and standard licences clearinghouses could be expanded by offering a wider spectrum of services and gradually develop into a patent royalty collection clearinghouse over time.

REFERENCES

LITERATURE

Akerlof, G.A., 'The Market for "Lemons": Quality Uncertainty and the Market Mechanism', **84** *Quarterly Journal of Economics*, 1970, 488–500

Allendesalazar, R. and Vallina, R., *Collecting Societies: The Usual Suspects,* European University Institute, Robert Schuman Centre for Advanced Studies, 2005 EU Competition Law and Policy Workshop/Proceedings, available at www.iue.it/RSCAS/Research/Competition/2005/200510-CompAllendesalazar.pdf

Aoki, R. and Schiff, A., *Intellectual Property Access Systems*, Tokyo, Institute of Economic Research Hitotsubashi University, Discussion Paper Series A, No. 491, March 2007, available at www.ier.hit-u.ac.jp/Common/publication/DP/DP491.pdf

Australian Law Reform Commission (ALRC), *Gene Patenting and Human Health*, Sydney, Australian Law Reform Commission, Discussion Paper No. 68, 2004, available at www.alrc.gov.au

Bennet, B. and Boettiger, S., 'Case 5. The Public Intellectual Property Resource for Agriculture. A Standard License Public Sector Clearinghouse for Agricultural IP', Chapter 8 of this volume

Berthels, N. and Jefferson, R., 'Case 8. CAMBIA's Biological Open Source Initiative (BiOS)', Chapter 13 of this volume

Besen, S.M., Kirby, S.N., and Salop, S.C., 'An Economic Analysis of Copyright Collectives', **78** *Virginia Law Review* 1992, 383–411

Cho, M.K., Illangasekare, S., Waever, M.A., Leonard, D.G.B. and Merz, J.F., 'Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services', **5** *Journal of. Molecular Diagnostics*, 2003, 3–8

Clark, V., 'Pitfalls in drafting royalty provisions in patent licences', available at http://pharmalicensing.com/articles/disp/1087832097_40d70021d738c

Coase, R.H., 'The Problem of Social Cost', **3** *The Journal of Law and Economics*, 1960, 1–44

Cooter, R. and Ulen, T., *Law & Economics*, International Edition, Boston-San Francisco-New York, Pearson Addison Wesley, 2004

Dent, C., Jensen, P., Waller, S., and Webster, B., *Research Use of Patented Knowledge: A Review*, Paris, OECD Directorate for Science, Technology

and Industry, STI Working Paper No. 2006/2, 2006, available at www.oecd.org/dataoecd/15/16/36311146.pdf

Depoorter, B., 'Regulation of a Natural Monopoly', in Bouckaert, B., and De Geest, G. (eds.), *Encyclopedia of Law and Economics*, Cheltenham, Edward Elgar, vol. III, 2000, 498–532

Drahos, P., 'Indigenous Knowledge, Intellectual Property and Biopiracy: Is a Global Bio-Collecting Society the Answer?', **20** *European Intellectual Property Review*, 2000, 245–250

Ebersole, T.J., Guthrie, M.C. and Goldstein, J.A., 'Patent pools and standard setting in diagnostic genetics', **23** *Nature Biotechnology*, 2005, 937–8

Edwards, J., 'Case 3. The Global Biodiversity Information Facility. An Example of an Information Clearinghouse', Chapter 6 of this volume

Einhorn, M.A., *Intellectual property and Antitrust: Music Performing Rights in Broadcasting*, 2002, available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=336045

Fels, A. and Walke, J., *Australian Intellectual property Law, Competition and Collecting Societies: Efficiency, Monopoly, Competition and Regulation*, European University Institute, Robert Schuman Centre for Advanced Studies, 2005 EU Competition Law and Policy Workshop/Proceedings, available at www.iue.it/RSCAS/Research/Competition/2005/200510-CompFels.pdf

Fujitani, J.M., 'Controlling the Market Power of Performing Rights Societies: An Administrative Substitute for Antitrust Regulation', **72** *California Law Review*, 1984, 103–37

Gervais, D., 'The Changing Role of Copyright Collectives', in Gervais, D. (ed.), *Collective Management of Copyright and Related Rights*, The Hague, Kluwer Law International, 2006

Gold, E.R., 'Biotechnology Patents: Strategies for Meeting Economic and Ethical Concerns', **30** *Nature Genetics*, 2002, 359

Graff, G.D., Cullen, S.E., Bradford, K.J., Zilberman, D. and Bennett, A.B., 'The Public-Private Structure of Intellectual Property Ownership in Agricultural Biotechnology', **21** *Nature Biotechnology*, 2003, 989–95

Graff, G.D. and Zilberman, D., 'Towards an Intellectual Property Clearinghouse for Ag-Biotechnology. An Issues Paper', **1** *IP Strategy Today* 3, 2001, 1–38

Heller, M.A., 'The Tragedy of the Anticommons: Property in the Transition from Marx to Markets', **111** *Harvard Law Review*, 1998, 621–88

Heller, M.A. and Eisenberg, R.S., 'Can Patents Deter Innovation? The Anticommons in Biomedical Research', **280** *Science*, 1998, 698–701

Holden, A.L., 'The SNP Consortium: Summary of a Private Consortium Effort to Develop an Applied Map of the Human Genome', **32** *BioTechniques*, 2002, S22-S26

Hopkins, M.H., Mahdi, S., Patel, P. and Thomas, S.M., *The Patenting of Human DNA: Global Trends in Public and Private Sector Activity*, Report for the European Commission, Brighton (UK), SPRU, 2006, available at www.sussex.ac.uk/spru/documents/patgen_finalreport.pdf

Human Genome Organisation (HUGO), *Statement on the Scope of Gene Patents, Research Exemption and Licensing of Patented Gene Sequences for Diagnostics*, 2003, available at www.hugo-international.org/PDFs/Statement%20on%20the%20Scope%20of%20Gene%20Patents,%20Research%20Exemption.pdf

Jenny, F., EC *Competition Law Enforcement and Collecting Societies for Music Rights: What Are We Aiming for?* European University Institute, Robert Schuman Centre for Advanced Studies, 2005 EU Competition Law and Policy Workshop/Proceedings, available at www.iue.it/RSCAS/Research/Competition/2005/200510-CompJenny.pdf

Katz, A., 'The Potential Demise of another Natural Monopoly: Rethinking the Collective Administration of Performing Rights', **1** *Journal for Comp. Law & Economics*, 2005, 541–93

Copyright Collectives: Good Solution but for Which Problem? NY University, Engelberg Center, Working Within the Boundaries of Intellectual Property, La Pietra Conference, 5–6 June 2007, available at www.law.nyu.edu/engelbergcenter/conferences/LaPietra/Katz.pdf

Krattiger, A. F., 'Financing the Bioindustry and Facilitating Biotechnology Transfer', **1** *IP Strategy Today* 8, 2004, 1–45

Kretschmer, M., 'The Failure of Property Rules in Collective Administration: Rethinking Copyright Societies as Regulatory Instruments', **13** *European Intellectual Property Review*, 2002, 126–136

Lemley, M. A. and Weiser, P. J., 'Should Property or Liability Rules Govern Information', **85** *Tex. L. Rev.* 2007, 783–841

Liberman, A., *Royalty stacking: tips for licensors and licensees*, 25 November 2005, available at www.freehills.com.au/publications/publications_5332.asp

Liholm, J., 'GEMA and IFPI', **13** *European Intellectual Property Review*, 2002, 112–25

Lueder, T., *Working toward the next generation of copyright licenses*, 14th Fordham Conference on International Intellectual Property Law & Policy, 20–21 April 2006 (on file with the author)

Matthijs, G. and Halley, D., 'European-wide opposition against the breast cancer gene patents', **10** *European Journal of Human Genetics*, 2002, 783–4

Merges, R. P., 'Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations', **84** *California Law Review*, 1996, 1293–1386

'Of Property Rules, Coase and Intellectual Property', **94** *Columbia law Review*, 1994, 2655–73

Merz, J. F., Kriss, A. G., Leonard, D. G. B. and Cho, M. K., 'Diagnostic testing fails the test', **415** *Nature*, 2003, 577–9

Mestmäcker, E-J., *Collecting Societies*, European University Institute, Robert Schuman Centre for Advanced Studies, 2005 EU Competition Law and Policy Workshop/Proceedings, available at www.iue.it/RSCAS/Research/Competition/2005/200510-CompMestmaecker.pdf

Mueller, J. M., 'Patenting Industry Standards', **34** *Int'll Prop. L. Rev.*, 2002, 201–50

National Research Council of the National Academies – Committee on Intellectual Property Rights in Genomic and Protein Research and Innovation, *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health*, Washington, DC, The National Academies Press, 2005, available at www.nap.edu/catalog/11487.html

Nuffield Council on Bioethics, *The Ethics of Patenting DNA*, London, Nuffield Council on Bioethics, Discussion Paper No. 932002, 2002, available at www.nuffieldbioethics.org

OECD, *Guidelines for the Licensing of Genetic Inventions*, Paris, OECD, 2006, available at www.oecd.org/dataoecd/39/38/36198812.pdf

OECD, *Genetic Inventions, Intellectual Property Rights and Licensing Practices, Evidence and Policies*, Paris, OECD, 2002, available at www.oecd.org/dataoecd/42/21/2491084.pdf

Richards, C. S., Bradley, L. A., Amos, J., Allitto, B., Grody, W. W., Maddalena, A. et al., 'Standards and Guidelines for CFTR Mutation Testing', **4** *Genetic Medicine*, 2002, 379–391

Rochelandet, F., *Are copyright collecting societies efficient? An evaluation of collective administration of copyright in Europe*, The Society for Economic Research on Copyright Issues, Madrid: Inaugural Annual Congress 2002, available at www.serci.org/2002/rochelandet.pdf

Shapiro, C., 'Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard-Setting', in Jaffe, A., Lerner, J., Stern, S. (eds.), *Innovation Policy and the Economy*, Cambridge, MIT Press, 2001, vol. I, 119–50, available at http://haas.berkeley.edu/~shapiro/thicket.pdf

Tuma, P., 'Pitfalls and Challenges of the EC Directive on the Collective Management of Copyright and Related Rights', **17** *European Intellectual Property Review*, 2006, 220–9

US Subcommittee on Courts, the Internet, and Intellectual Property of the Committee on the Judiciary House of Representatives, *Hearing on Public Performance Rights Organizations*, 109th Congress, First Session, 11 May 2005, Serial No. 109–25, available at www.house.gov/judiciary/

Van Overwalle, G., van Zimmeren, E., Verbeure, B., Matthijs, G., 'Models for facilitating access to patents on genetic inventions', **7** *Nature Reviews Genetics*, 2006, 143–148

van Zimmeren, E. and Avau, D., 'Case 4. BirchBob: An Example of a Technology Exchange Clearinghouse', Chapter 7 of this volume

van Zimmeren, E., Verbeure, B., Matthijs, G. and Van Overwalle, G., 'A Clearinghouse for Diagnostic Testing: the Solution to Ensure Access to and Use of Patented Genetic Inventions?', **84** *Bulletin of the World Health Organization*, 2006, 352–9

Verbeure, B., 'Patent Pooling for Gene-Based Diagnostic Testing: Conceptual Framework', Chapter 1 of this volume

Verbeure, B., van Zimmeren, E., Matthijs, G. and Van Overwalle, G., 'Patent Pools and diagnostic testing', **24** *Trends in Biotechnology*, 2006, 115–120

Verbeure, B., Matthijs, G. and Van Overwalle, G., 'Analysing DNA patents in relation with diagnostic genetic testing', **13** *European Journal of Human Genetics*, 2005, 1–8

Verbruggen, J.,and Lôrinz, A., 'Patents and Technical Standards', **33** *International Review of Intellectual Property and Competition Law*, 2002, 125–54

Vinje, T. and Niiranen, O., *The Application of Competition Law to Collecting Societies in a Borderless Digital Environment*, European University Institute, Robert Schuman Centre for Advanced Studies, 2005 EU Competition Law and Policy Workshop/Proceedings, available at www.iue.it/RSCAS/Research/Competition/2005/200510-CompVinje.pdf

Walpole, I.R., Dawkins, H.J.S., Sinden, P.D. and O'Leary, P.C., 'Human Gene Patents: the possible impacts on genetics services health care', **179** *Medical Journal of Australia*, 2003, 203–5

Walsh, J.P., Arora, A. and Cohen W.M., 'Effects of Research Tool Patents and Licensing on Biomedical Innovation', in Cohen, W.M., Merrel, S.A. (eds.), *Patents in the Knowledge-Based Economy*, Washington, DC, The National Academies Press, 2003, 285–340

LEGISLATION AND SOFT LAW

Eu

European Commission, Commission Staff Working Document, *Impact Assessment Reforming Cross-border Management of Copyright and Related Rights for Legitimate Online Music Services*, Brussels, 11 October 2005, SEC(2005) 1254

European Commission, Commission Staff Working Document, *Study on a Community Initiative on the Cross-border Management of Copyright*, Brussels, 7 July 2005, available at http://ec.europa.eu/internal_market/copyright/docs/management/study-collectivemgmt_en.pdf

European Commission, *Commission Recommendation of 18 May 2005 on collective cross-border management of copyright and related rights for legitimate online music services* [2005] *OJ* L276/54

European Commission, Communication from the Commission to the Council, the European Parliament and the European Economic and Social Committee, *The Management of Copyright and Related Rights in the Internal Market*, Brussels, 16 April 2004, COM(2004) 261 final

European Commission, Decision of 8 October 2002, case COMP/C2/38.014-IFPI Simulcasting [2003] *OJ* L107/58

European Commission, Notice published pursuant to Article 27(4) of Council Regulation (EC) No 1/2003 of 17 August 2005, cases COMP/C2/39152-BUMA and COMP/C2/39151-SABAM [2005] *OJ* C200/11

European Commission, Notification of cooperation agreements of 28 February 2002, case COMP/C2/38377-BIEM Barcelona Agreements [2002] *OJ* C132/18

European Commission, Decision of 6 August 2002, case COMP/C2/37.219, *Banghalter & Honem Christo* v. *SACEM* ('Daftpunk'-decision), available at http://europa.eu.int/comm/competition/antitrust/cases/decisions/37219/fr.pdf

European Commission, Notification of cooperation agreements of 17 April 2001, case COMP/C2/38126-Santiago Agreement [2001] *OJ* C145/2
European Commission, Green Paper, *Copyright and Related Rights in the Information Society*, Brussels, 19 July 1995, COM(1995) 382 final
European Commission, *Communication of 27 October 1992 on Intellectual Property Rights and Standardisation*, COM(92) 445 final
European Commission, Decision 82/204/EEC of 4 December 1981, case IV/29.971-GEMA III [1981] *OJ* L94/12
European Commission, Decision of 29 October 1981, case IV/29.839-GVL [1981] *OJ* L370/49
European Commission, Decision 72/268/EEC of 6 July 1972, case IV/226.760-GEMA II [1972] *OJ* L166/22
European Commission, Decision 71/224/EEC of 20 June 1971, case IV/26.760-GEMA I [1971] *OJ* L134/15

Directive 2004/48/EC of the European Parliament and the Council of 29 April 2004 on the enforcement of intellectual property rights [2004] *OJ* L195/16
Directive 2001/29/EC of the European Parliament and of the Council of 22 May 2001 on the harmonization of certain aspects of copyright and related rights in the information society [2001] *OJ* L167/10

Council Directive 93/83/EEC of 27 September 1993 on the coordination of certain rules concerning copyright and rights related to copyright applicable to satellite broadcasting and cable retransmission [1993] *OJ* L248/15
Council Directive 92/100/EEC of 19 November 1992 on rental right and lending rights and on certain rights related to copyright in the field of intellectual property [1992] *OJ* L290/09

US

Genomic Research and Accessibility Act, Washington, DC: Library of Congress, 2007, H.R. 977, 110th Congress, 1st Session, available at http://thomas.loc.gov/home/gpoxmlc110/h977_ih.xml

TREATIES

Berne Convention for the Protection of Literary and Artistic Works of September 9, 1886 (Paris Act as amended on September 28, 1979)
International Convention for the Protection of Performers, Producers of Phonograms and Broadcasting Organisations of October 26, 1961

CASE LAW

EU

Case C-245/00, *Stichting ter Exploitatie van Naburige Rechten (SENA)* v. *Nederlandse Omroep Stichting* (NOS) [2003] ECR I-1251

Cases 110/88, 241/88 and 242/88, *François Lucazeau et al. v. Société des Auteurs, Compositeurs et Éditeurs de Musique (SACEM) et al.* [1989] ECR 2811
Case 395/87, *Ministère public v. Jean-Louis Tournier* [1989] ECR 2521
Case 7/82, *Gesellschaft für müsikalische Aufführungs- und mechanische Vervielfältigungsrechte (GVL)* v. *Commission* [1983] ECR 483 Case 127/73, *Belgische Radio- en Televisieomroep (BRT)* v. *SABAM and NV Fonior* [1974] ECR 313

US

United States of America v. *ASCAP*, Second Amended Final Judgment, 11 June 2001, Civ. Action No. 41–1395 (S.D.N.Y. 2001)
United States v. *ASCAP,* No. 41–1395 (S.D.N.Y. 2000), Department of Justice, Memorandum of the United States in Support of the Joint Motion to Enter Second Amended Final Judgment, available at www.usdoj.gov/atr/cases/f6300/6395.pdf
American Society of Composers Authors and Publishers v. Showtime/The Movie Channel, 912 F.2d 563 (F.2d 1990)
Buffalo Broadcasting Co. v. *ASCAP*, 744 F.2d. 917 (2d Cir. 1984)
Columbia Broadcast System, Inc. v. *ASCAP*, 620 F.2d 930 (2d Cir. 1980), cert. denied, 450 US 970 (1981)
Broadcast Music, Inc. v. *Columbia Broadcast System, Inc.*, 441 US 1 (1979)

6 Case 3. The Global Biodiversity Information Facility (GBIF)

An example of an information clearinghouse

James L. Edwards

6.1 Introduction

The Global Biodiversity Information Facility (GBIF) is an example of an *information clearinghouse* that focuses on biological diversity, primarily at the species and specimen levels. Although GBIF does contain some genetic information (especially about cultivars or varieties archived in living stock centres), it does not provide access to any patent data and all the information it provides is freely and openly available to all users. Therefore, GBIF does not provide a very apt model for gene patents. However, GBIF does provide some interesting lessons for how to assemble a distributed network of information.

6.2 Background

GBIF[1] is an international organisation designed to make the world's biodiversity data freely and universally available via the Internet, for the benefit of science, society and a sustainable future. It was established in 2001 as a result of deliberations and discussions in the OECD's Global Science Forum.[2]

However, GBIF is a free-standing organisation, not directly linked to the OECD or United Nations. It is based upon a unique Memorandum of Understanding, but has no formal standing in international law.

Inspirational models for the formation of GBIF included the International nucleotide sequence databases (GenBank, EMBL and DDBJ);[3] Mexico's CONABIO (Comisión nacional para el conocimiento y uso de la biodiversidad);[4] Costa Rica's INBio (Instituto Nacional de Biodiversidad);[5] and Australia's ERIN (Environmental Resources

[1] www.gbif.org/. [2] See www.gbif.org/GBIF_org/facility/OECD_Endorsement.
[3] www.insdc.org/page.php?page=home. [4] www.conabio.gob.mx/.
[5] www.inbio.ac.cr/en/default.html.

Information Network).[6] GBIF was able to build upon these pioneering national activities to develop its international approach.

The Convention on Biological Diversity[7] defines biodiversity as 'the variability among living organisms from all sources including, inter alia, terrestrial, marine and other aquatic ecosystems and the ecological complexes of which they are part; this includes diversity within species, between species and of ecosystems'. GBIF focuses on what it calls 'primary scientific biodiversity data', or species-occurrence data, which it defines as information about where, in time and space, plants, animals and microorganisms have been found. This kind of information is valuable for policymakers (land-use planning, management of invasive species, control of disease vectors) and scientists, and is also of great interest to the general public.

The data served by GBIF come from three kinds of sources: (1) specimens that are now held in natural history museums, herbaria, botanical gardens and living organism stock centres, (2) observations of organisms where no specimens are collected (e.g. bird banding projects, bioblitzes), and (3) information on the current and past scientific names of species (these name data largely come from the Catalogue of Life partnership)[8]. These data have been amassed over the last 300 years, allowing users to follow the changes in where species are found over much of this time period.[9]

The primary biodiversity data served by GBIF come from a worldwide network of data providers.[10] The data themselves remain with the data providers; GBIF indexes the information and allows users to search all it at once, instead of having to go individually to each data provider's site. GBIF is thus what Reichman and Uhlir call a *federated data repository*.[11]

But GBIF is much more than just a data repository. It also engages in a wide range of education activities about biodiversity informatics; provides funding to help data owners to digitise their information and serve it to the world; and plays an increasingly important role in developing data protocols and standards for sharing, exposing and searching data. In addition, it has commissioned several well-cited reports on a diverse

[6] www.environment.gov.au/erin/about.html. [7] www.cbd.int/.

[8] See www.catalogueoflife.org/info_about_col.php.

[9] A tutorial on using the information in the GBIF data portal is available at www.gbif.org/Stories/STORY1183131151/documents/english.

[10] As of mid-August 2007, GBIF was serving 134 million data records made available by more than 200 data providers.

[11] Reichman J, Uhlir P, 2003, 'A contractually reconstructed research commons for scientific data in a highly protectionist intellectual property environment', *Law and Contemporary Problems*, Winter-Spring, 315–462.

range of topics including the uses of primary species-occurrence data and principles and methods of data cleaning. All these activities are undertaken in collaboration with GBIF's membership, consisting of forty-seven countries and forty international organisations[12] and with non-member partners and user groups.

Most of the data being served by GBIF were derived from public funding, and GBIF complies with the *OECD Principles and Guidelines for Access to Research Data from Public Funding*.[13] In an analysis of the application of these principles, Arzberger et al.[14] cite GBIF as a model for implementing these principles.

GBIF's intellectual property (IP) principles are simple:

- Open access to data.
- All IP stays with the data providers; GBIF itself asserts no rights to the data it serves.
- Data providers can restrict access to sensitive information, such as geographic coordinates of endangered species.
- Users must sign an agreement that they will adhere to any use restrictions required by the data providers and that they will acknowledge the sources of any data they use from the GBIF network.

6.3 Why does GBIF work as an information clearinghouse?

A confluence of interests and information technologies has allowed GBIF to become a successful information clearinghouse.

First, there is political and scientific interest in freely sharing biodiversity data. The establishment of the Convention on Biological Diversity in 1992 gave a strong political incentive to countries to understand and manage the biodiversity within their borders. At the same time, the scientific community began to recognise that researchers gained more by sharing their information than by locking it up.

Second, primary biodiversity data are in themselves of relatively little commercial value. Some exceptions do exist, such as in preparing environmental impact studies. Ultimately, however, it is the biological molecules and the genes found within the organisms that hold the most commercial value, not the species-occurrence data per se.

[12] The most up to date list of members is at www.gbif.org/GBIF_org/participation.
[13] Available at www.oecd.org/dataoecd/9/61/38500813.pdf.
[14] Arzberger PW, Schroeder P, Beaulieu A, Bowker GC, Casey K, Laaksonen L, Moorman D, Uhlir P, Wouters P., 2004, 'Promoting Access to Public Research Data for Scientific, Economic, and Social Development', *Data Science Journal* 3, 135–52.

Third, developed countries have begun to recognise the need to help erase the digital content divide. Although the greatest diversity of species lies in the tropical, developing world, most of the information about those species lies in the natural history collections and literature of the developed world.

Fourth, at the beginning of the twenty-first century information technology had matured to the point where it was relatively easy to link together distributed databases into a federated network without requiring that all of them use the same underlying data architecture. In addition, the rapid expansion and increase in speed of the Internet made it feasible to access those databases in real time. And the invention of the open-source software movement made it easy for people around the world to contribute to the common software pool and to build value-added components.

Finally, GBIF's independence from other international bodies has meant that it has escaped much of the political wrangling so common in the international sphere. For an organisation that is just a few years old, it has moved quite quickly in developing and implementing its international work programme.

6.4 Is the GBIF model applicable to gene patents?

The innovative aspects of GBIF that could be appealing in the gene patent arena are (1) its international character, (2) its provision of free information to all users, and (3) its basis in a flexible Memorandum of Understanding among its participants.

Although the GBIF approach of providing free and open access works well with primary scientific biodiversity data, it may not be as applicable for gene patents for the following reasons.

First, GBIF does not provide any brokerage services. It does allow users to directly contact data providers if they wish further information than what is served through the GBIF data portal, but otherwise it does not explicitly try to link users and providers.

Second, GBIF has no mechanism, other than the moral suasion common to scientific endeavours, to enforce its data-use and data-provider agreements. To date, this has proved sufficient, as there are no known cases of abuse. But such amity may not prevail in the genetic arena.

Third, GBIF's Memorandum of Understanding is not legally binding. This has provided great flexibility in developing and implementing its activities, but might not be sufficient in the highly charged area of gene patents.

6.5 Conclusions

The Global Biodiversity Information Facility is a relatively successful information clearinghouse. A major part of its success is the 'primary', scientific nature of the data that it serves. Still, it may offer some interesting ideas for a clearinghouse for human gene patents.

REFERENCES

Arzberger PW, Schroeder P, Beaulieu A, Bowker GC, Casey K, Laaksonen L, Moorman D, Uhlir P and Wouters P, 'Promoting Access to Public Research Data for Scientific, Economic, and Social Development', *Data Science Journal* **3,** 2004, 135–52

Reichman J, and Uhlir P, 'A contractually reconstructed research commons for scientific data in a highly protectionist intellectual property environment', *Law and Contemporary Problems*, Winter-Spring, 2003, 315–462

7 Case 4. BirchBob

An example of a technology exchange clearinghouse*

Esther van Zimmeren and Dirk Avau

7.1 Introduction

BirchBob is a private company offering services to both technology holders (patent owners) and technology users in order to allow them to perform better in the global technology marketplace. These services are not limited to any particular technology sector or discipline. BirchBob assists universities, research institutes and industry and has clients with different profiles, varying from laboratories to manufacturers.

The BirchBob platform was launched in 1999 in the US. The name 'BirchBob' is a tribute to Senators Birch Bayh of Indiana and Robert Dole of Kansas, who co-sponsored the so-called Bayh-Dole Act.[1] Enacted on 12 December 1980, the Bayh-Dole Act created a uniform patent policy among the many federal US agencies that fund research by enabling small businesses and non-profit organizations, including universities, to retain title to inventions made under federally funded research programs, and encouraging universities to collaborate, to file patents on inventions and to promote the commercial use of those inventions through technology transfer activities.

Since its inception in 1999 BirchBob has been cooperating with key US universities such as the University of Harvard, John Hopkins and the University of California and from 2003 onwards BirchBob has gradually been expanding its network of technology providers to five continents.

BirchBob's business model involves various services which ultimately facilitate access to patented technology and in some cases also the use of the technology by setting the scene for licensing negotiations.

* This paper is based on Dirk Avau's presentation on the two-day international workshop organized by the Centre for Intellectual Property Rights of the K.U.Leuven on 'Gene Patents and Clearing Models. From Concepts to Cases' on 8 and 9 June 2006, and on BirchBob's website www.birchbob.com/.

[1] US, enacted December 12 1980 (P.L. 96–517, Patent and Trademark Act Amendments of 1980), codified in 35 U.S.C. §200–212, and implemented by 37 C.F.R. 401.

In doing so, BirchBob could be classified as a "technology exchange clearinghouse".

In the following Section 7.2, BirchBob's business model will be described and attention will be paid to its major objectives, its geographical coverage, the services provided and the search tool employed. Section 7.3 will then analyze to what extent BirchBob fits into the categorization put forward by van Zimmeren in her conceptual framework, and what the pros and cons are of this kind of business model. The final Section 7.4 contains some concluding remarks.

7.2 BirchBob business model

Objectives of BirchBob

The major objective of BirchBob is to centralize offers for licensing and sale of technologies, and research and development (R&D) collaborative projects from academia, government and industry around the globe, by way of a single Internet search. As a follow-up to the Internet search, BirchBob can be contacted and can be requested to put its networking experience at work, acting as an international gateway for technology exchange and providing assistance to companies, universities and research institutes in identifying the technology and technology partners they need to safeguard future growth.

Geographical coverage

With representations in Europe, Asia, and in the United States, the BirchBob network covers fifty-two countries on five continents. On-going efforts are made to consolidate the network, and to further extend it to new organizations in other countries and regions which are expected to soon generate greater interest from the technology marketplace, such as Ukraine.

BirchBob services

The services provided by BirchBob can roughly be distinguished in services related to licensing and sale of technology, R&D collaborations and a patent option market.

Licensing and sale of technology

BirchBob assists organizations in promoting their own technologies, on the one hand, and, identifying technologies which are available in

the market and relevant to their business, on the other hand. For this purpose, it has developed a licensing repository and a search tool for screening technologies available for licensing within the repository. In the repository one finds technologies from a rich variety of sectors and disciplines. The repository provides information on particular technologies, their availability for licensing or R&D collaboration, the organization holding the technology, the field of expertise, a brief description of the technology, the field of use and a reference to a web address where you can find the full description of the technology.

In order to facilitate the operation of the repository, BirchBob created a cross-industry Extensible Markup Language (XML) standard.[2] This XML standard relates to the core of the BirchBob activities, which is mining sites that have been XML-tagged. As the BirchBob system is dependent on XML tagged forms, websites to be screened by the search tool need to be XML tagged. Most corporations have been using XML tagging, but for small non-commercially oriented government/university research labs XML tagging has not been general practice thus far. Therefore, it has been essential for the development and effectiveness of BirchBob's search engine that US technology transfer professionals participated in this project. In 2003, BirchBob, along with government and academic technology transfer professionals, developed an XML-tagging standard that joins technology transfer offices from academia, government and industry to create a one-stop search engine for technologies available for licensing. The creation of the BirchBob Open XML standard included input from the National Institutes of Health (NIH), the National Technology Transfer Center (NTTC), the National Aeronautics and Space Administration (NASA), the Federal Laboratory Consortium for Transfer of Technology (FLC), the US Department of Energy (DOE), the University of California, the University of Rochester and Harvard University. BirchBob also made use of many personal contributions from people attending the Special Interest Group at the Association of University Technology Managers (AUTM) Annual meeting in Orlando and the comments received through the BirchBob web site. The standard represents XML tags that are placed on webpages describing an organization's technologies. The BirchBob search engine uses its XML standard in combination with keywords and concept-relations searching methods.

[2] XML is a general-purpose specification for creating custom markup languages. It is classified as an extensible language because it allows its users to define their own elements. Its primary purpose is to facilitate the sharing of structured data across different information systems, particularly via the Internet, and it is used both to encode documents and to serialize data and designed to be relatively human-legible. For more information, see: www.w3.org/TR/xml/.

BirchBob also uses the free placement of its search box on third parties' websites – acting as relays – to ensure wide national and international access.

Technology holders can report their technology to BirchBob by sending the web address where the licensable technology is described or by providing BirchBob access to a database. The advantages of this system for technology holders are that it is free, that it is open to input from all kinds of organizations and partners and that the technology will be available on a worldwide level. BirchBob will offer to add XML tags, or post the technology in the repository by way of the web address. If necessary, BirchBob can provide some additional services in this part of the process, such as developing a commercially attractive description for publication on the Internet, web hosting services or help in XML tagging.[3]

For the *technology seeker/user*, BirchBob can offer several services complementary to the repository. Basic searches are free, but more advanced search features require taking a subscription (e.g. "gold plan", "corporate plan"). Such a subscription will bring more flexibility in the searching process with features such as sorting results, customizing lists, creating filters, indexing categories and exporting lists into the client's databases. Through its corporate plan BirchBob can also assist by evaluating the most pertinent options for buying or licensing technology and know-how within a particular budget. In this evaluation lifetime costs, intellectual property (IP), scientific value, financing methods and implementation will be taken into consideration.

When the licensing opportunities are identified via the repository one may request additional information on a particular technology with the service called "handshake". The information provided will concern the technology itself, the IP and a profile of the organization, including its track record in technology transfer, and the transfer of technology opportunities. In this framework a non-disclosure agreement will be signed, which will enable parties to exchange confidential information. If the technology which the technology seeker is missing is not available through the repository, BirchBob will use its worldwide network of technology holders to identify potential sources and terms. Moreover, it could build a proprietary database of relevant technologies for the technology seeker, searching and benchmarking capacities. Ultimately, BirchBob can try to match technology holders with the technology seekers, and if the parties wish so, assist in negotiating technology transfer agreements.

[3] Avau, D., 'Creatieve kenniseconomie: België in de spits van wereldwijde technologie marketing met BirchBob, *Incrowd* May, 2005, 13, at 13.

R&D collaborations

BirchBob also helps organizations in setting up early stage collaborations. A valorization strategy produces better results when partnerships with business are made early, while research is still on-going, rather than when research is far advanced, or when research is completed and patent applications are already filed.

The resulting collaborations may be scientific, financial and/or commercial. The objective is to involve potential licensees already in the research process, enabling the parties to set common goals, assessing together the relevance of potential patent filings and persuading licensees to bear the filing costs. In many cases, the partnerships translate into production and commercial agreements. This way, research organizations will not need to search for licensees once they hold patent applications/patents and they do not have to put their limited resources into patent filings. Many of these collaborations generate long-term commitments with perspectives such as further research, production and distribution.

Patent option market

Another instrument provided by BirchBob in an aim to transfer technology early in the innovation process is the patent option market. The patent option market enables technology users to take out an option for buying or licensing a patent. This patent option market focuses on early stage inventions. This has the advantage that both parties will have some time to decide on the final deal. The price of the option will often cover the investment for obtaining international patent protection.

All transactions are listed at conditions pre-approved by the technology holders. Final closings of the transaction may, however, take place on conditions resulting from negotiations between the parties. BirchBob works closely together with the inventors. The fee that will be collected through the option will contribute to ensure maximum coverage of the corresponding inventions (in some cases this will for instance mean extending a national patent application into a PCT application).

7.3 BirchBob a 'technology exchange clearinghouse'?

BirchBob is a private company offering services that fit well into the technology exchange clearinghouse model.[4] A technology exchange clearinghouse has been described as a platform designed to "offer

[4] van Zimmeren, E., 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', see Chapter 5 of this volume.

information services listing the available inventions related to a specific technology. On the basis of this information technology users will then initiate negotiations with the patent holder for a license. Some clearinghouses allow licensees to opt for additional partnering, mediating and managing services."[5] BirchBob indeed supplies basic information services and additional partnering, consultancy (economics and informatics), managing, and negotiation services.

A key element of the technology exchange clearinghouse is that legitimate access to the patented inventions is not granted by the technology exchange clearinghouse, but by the individual technology holder after one-to-one licensing negotiations have taken place with the potential licensee (technology user). These negotiations are, nevertheless, based on the information provided by the clearinghouse. The technology exchange clearinghouse provides access to the technical information and contact information on the technology holder/licensor involved, but does not provide a one-stop licensing access in terms of open access, standard licenses or customized licenses.

Through its licensing repository BirchBob provides information on the licensable technology or opportunities for R&D collaboration. To identify the relevant technology holders, some basic information is given on the technology and the organization, but more detailed information can be obtained through the handshake service. As BirchBob is closely following the market developments it can also give more exclusive information on technology holders, such as track records on technology transfer, customized according to the profile and needs of the technology seeker. This will enable clients to better evaluate the chances of success and the opportunities for long-term collaboration. The technology holder and technology user will be matched and brought together in order for the negotiations to take place. If the partners consider it necessary, these negotiations can take place on the basis of confidentiality agreement processed by BirchBob. BirchBob could also assist in the negotiation process itself.

Making use of BirchBob's services has some pros and cons. By way of the search engine BirchBob creates more transparency in the market.

[5] Ibid. See also: van Zimmeren, E., Verbeure, B., Matthijs, G., Van Overwalle, G., 'A Clearinghouse for Diagnostic Testing: the Solution to Ensure Access to and Use of Patented Genetic Inventions?', **84** *Bulletin of the World Health Organization*, 2006, 352–9, at 353–4; Van Overwalle, G., van Zimmeren, E., Verbeure, B., Matthijs, G., 'Models for Facilitating Access to Patents on Genetic Inventions', **7** *Nature Reviews Genetics*, 2006, 143–8, at 145; Krattiger, A.F., 'Financing the Bioindustry and Facilitating Biotechnology Transfer', **1** *IP Strategy Today* 8, 2004, 1–45, at 21–2 and Graff, G.D., Zilberman, D., 'Towards an Intellectual Property Clearinghouse for Ag-Biotechnology. An Issues Paper', **1** *IP Strategy Today* 3, 2001, 1–38, at 6–8.

If a technology holder decides to report its technology to BirchBob, the worldwide scope of the system will increase the visibility of the licensable technology. When scrolling through the licensing opportunities offered through BirchBob, it appears that most technology providers are universities and research institutes. Public organizations and small- and medium-sized companies seem to have a rather large interest in transferring information on their technology to foster their visibility as a technology holder by using BirchBob's free information service. Big multinationals with their own IP and licensing departments might not have this "visibility incentive". However, BirchBob might be attractive to them in order to exploit their sleeping IP. Anyway, big companies might appreciate technology exchange clearinghouses more from the in-licensing and buying perspective, rather than for out-licensing purposes.

In general, technology exchange clearinghouses are said to be cheap to maintain and to require only relatively low operating costs. On the other hand, all the services complimentary to the search tool offered by BirchBob appear to be quite labour-intensive and therefore costly. As it is difficult to offer those more advanced services from one centralized office, BirchBob collaborates with a worldwide network of technology transfer experts.

Furthermore, technology exchange clearinghouses are dependent on the cooperation of technology holders in reporting technology. Therefore, BirchBob is actively marketing and promoting its services on a worldwide scale. Still it might be difficult to bring together a critical mass of technology in order to turn the clearinghouse into an effective tool. At the time of writing, BirchBob's licensing repository includes over 40,000 technology licensing offers, which makes it a suitable tool. It should, however, be noted that BirchBob is not restricted to the medical sector. Hence, the high number of licensable technologies is no indicator for the effective access BirchBob is safeguarding with respect to the health care sector as such. At the same time, the cross-sectoral approach is advantageous as it allows for cross-selling to other sectors.

BirchBob is becoming quite well known but it is neither the sole actor in this field, nor the single point of reference. At present, most of the existing clearinghouses only offer a small (pro)portion of the market and a low density of patents. For technology seekers, it is therefore advisable to search also other websites besides BirchBob even though this may amount to paying several registration fees. For technology holders, it is advisable to approach several technology exchange clearinghouses to make information widely available in order to fully exploit the potential of their technology.

Some have argued that the technology exchange clearinghouse is only suitable for technologies that can be easily defined and valued.[6] At first sight, the BirchBob repository seems indeed particularly useful for general-purpose research methods and for very specific and well-defined improvements to familiar upstream products or processes. However, well-trained, specialized, experienced and pro-active staff with a good scientific background may create more opportunities for more complicated technologies in performing customized analyses under the heading of the BirchBob "corporate plan".

As to whether a profit or non-profit organization is preferred for taking the lead in a technology exchange, it should be underlined that it is important that some external supervision is carried out in order to safeguard the quality of the services both when the organization is driven by profits and when it is not. As to the private or public nature of the clearinghouse, most probably, the importance of networking and IP management skills, and the strong focus on the needs of the market will be better guaranteed by a private than a public entity.

Does the BirchBob construction comply with other, more advanced types of clearinghouses? The use of standard licenses as in the standard licenses clearinghouse or customized standard licenses in the patent royalty collection clearinghouse does not seem to fit BirchBob's business model. First, as for now technology holders and users are still in charge of their negotiation process and the determination of the licensing conditions and BirchBob is only providing assistance. BirchBob will in principle not take over the wheel. Second, BirchBob's commercial interest lies rather in customized on demand services. This does not mean that in the future, standard licenses may not become a useful instrument. Especially when the clearinghouse model will become more common and market players are getting used to outsourcing transfer of technology services, they might start appreciating standard licenses as a way to diminish transaction costs while at the same time remaining in control of the licensing terms.

7.4 Concluding remarks

The emergence of clearinghouses like BirchBob is especially valuable in the light of the current trend of "Open Innovation".[7] The central idea

[6] Krattiger, 'Financing the Bioindustry', at 22 and Graff et al., 'Towards an Intellectual Property Clearinghouse', at 6–7.

[7] See in particular: Chesbrough, H.W., *Open Innovation: the New Imperative for Creating and Profiting from Technology*, Boston, MA: Harvard Business School Press, 2005.

behind open innovation is that in a world of widely distributed knowledge, organizations cannot afford to rely entirely on their own research, but should instead buy or license IP from other companies, research institutes or universities, or closely collaborate with such organizations in common research projects. In addition, internal inventions not being used should be taken outside the organization (e.g. through licensing, spin-offs and joint ventures). Technology exchange clearinghouses may facilitate quick advancement of open innovation.

BirchBob offers a wide variety of services to clients (technology holders and users) as long as they are prepared to pay for those services. If a client would be interested in granting standard licenses to technology users without thorough negotiations on the licensing conditions with each individual user, BirchBob could offer standard licenses to technology users in addition to the existing services. This shows that BirchBob's business model is dynamic. Reality does often not coincide with academically defined models, but, when translating BirchBob's future opportunities in terms of the clearinghouse categorization applied by van Zimmeren,[8] it is not excluded that BirchBob might develop towards a standard licenses clearinghouse or even a patent royalty collection clearinghouse. BirchBob could develop the necessary interface in line with the features described for those types of clearinghouses. However, this will be a step-by-step process and it remains to be seen to what extent clients are actually interested in such services being provided by a clearinghouse instead of being in control themselves of the negotiations and design of the license, collection of royalties and monitoring and enforcement.

REFERENCES

LITERATURE

Avau, D., 'Creatieve kenniseconomie: België in de spits van wereldwijde technologie marketing met BirchBob, *Incrowd,* May, 2005, 13

Chesbrough, H. W., '*Open Innovation: The New Imperative for Creating and Profiting from Technology*, Boston, MA: Harvard Business School Press, 2005

Graff, G. D. and Zilberman, D., 'Towards an Intellectual Property Clearinghouse for Ag-Biotechnology. An Issues Paper', **1** *IP Strategy Today* 3, 2001, 1–38

Krattiger, A. F., 'Financing the Bioindustry and Facilitating Biotechnology Transfer', **1** *IP Strategy Today* **8**, 2004, 1–45

[8] Van Zimmeren, see Chapter 5 of this volume.

Van Overwalle, G., van Zimmeren, E., Verbeure, B. and Matthijs, G., 'Models for Facilitating Access to Patents on Genetic Inventions', **7** *Nature Reviews Genetics*, 2006, 143–8

van Zimmeren, E., Verbeure, B., Matthijs, G. and Van Overwalle, G., 'A Clearinghouse for Diagnostic Testing: the Solution to Ensure Access to and Use of Patented Genetic Inventions?', **84** *Bulletin of the World Health Organization*, 2006, 352–9

'Clearinghouse Mechanisms in Genetic Diagnostics: Conceptual Framework', see Chapter 5 of this volume

LEGISLATION

Patent and Trademark Act Amendments of 1980, enacted December 12 1980 (P.L. 96–517), codified in 35 U.S.C. §200–212, and implemented by 37 C.F.R. 401

8 Case 5. The Public Intellectual Property Resource for Agriculture (PIPRA)

A standard license public sector clearinghouse for agricultural IP

Alan B. Bennett and Sara Boettiger

8.1 Introduction

Agricultural research has historically been publicly funded and delivered as a public good directly to farmers through seeds which incorporate advanced genetics or through the demonstration of improved agricultural practices. However, over the last twenty years, the results of agricultural research have increasingly been treated as private goods and protected through various forms of IP belonging to the primary innovator. IP protection has provided incentives to develop new crops that may otherwise not have been developed and, in particular, to invest in the increasingly expensive regulatory processes for approvals of genetically engineered crops. In contrast to many technology sectors, public and non-profit institutions have played a very large role in new technological innovations in agriculture, accounting for nearly one quarter of new patented innovations in this sector. However, this technology "portfolio" is fragmented across a large number of institutions and has not been strategically managed to enable the advancement of a number of projects. The Public Intellectual Property Resource for Agriculture (PIPRA) is a clearinghouse institution that is designed to integrate this fragmented IP portfolio through collaborative management. PIPRA's goal is to mobilize technologies from a wide range of public/non-profit technology providers to address specific projects for the improvement of subsistence and specialty crops that are not being addressed by commercial seed and agricultural biotechnology companies. PIPRA and its members believe this landscape of IP can be more effectively managed collaboratively and by using a set of shared principles. PIPRA's primary strategies to improve access to patented technologies are to: 1) provide a one-stop IP information clearinghouse for access to public sector patented technologies; 2) provide a resource for the analysis of patented technologies for implementation of specific projects; 3) develop gene

transfer and gene-based trait technologies that have maximum legal "freedom to operate"; 4) manage pools of public sector technologies to promote availability and reduce transaction costs associated with transfer of rights to patented technologies; and 5) support the development of IP management best practices and capacity enhancement in developing countries.

8.2 Background

The patent thicket in agricultural biotechnology

Public and non-profit institutions have a long history of developing new agricultural technologies and delivering those research results to seed companies, farm equipment manufacturers or directly to farmers as a public good. Land-grant universities and the affiliated Cooperative Extension Service in the United States provided an integrated system of public research and delivery of innovations to the agricultural sector. Similar institutions and activities also supported the development of so-called green revolution crop cultivars and their delivery to farmers on an international scale. This direct role of public universities and non-profit research centers in agriculture is strongly embedded in the culture of these institutions and in agricultural research, more generally.

So what happened? In the early 1980s in the United States a convergence of events contributed to a changing paradigm for technology transfer from universities to the agricultural industry. These events included: 1) scientific developments in the life sciences that promised to enable powerful innovations in both crop and animal genetics through biotechnology; 2) changes in the legal framework that allowed universities to own patented inventions resulting from federally sponsored research; [1] and 3) a Supreme Court decision allowing the patenting of living organisms.[2] Simultaneously, there developed a research-intensive private biotechnology sector that was both technologically and financially equipped to take early-stage inventions from universities and make the substantial investments in research and regulatory approval to bring new products to market – but these private firms relied on patent protection to justify the large follow-on

[1] P.L. 96–517; The Patent and Trademark Act of 1980 and amendments included in P.L. 98–620; 1984.

[2] *Diamond* v. *Chakrabarty*, 447 US 303 Docket Number: 79–136; http://caselaw.lp.findlaw.com/scripts/getcase.pl?court=US&vol=447&invol=303.

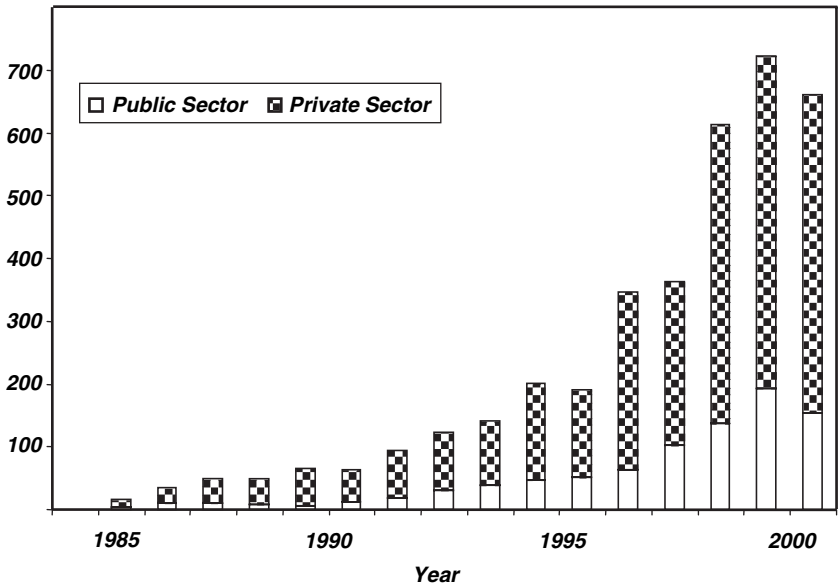

Figure 8.1 Patents issued in the US Patent and Trademark Office in the area of plant biotechnologies between 1985 and 2000 for both public and private sector organizations (reprinted from Delmer et al., 2003).

investments typically required to develop university innovations. As a result, beginning in 1980, universities began to seek patent protection on a wide range of technological innovations, including agricultural innovations. Figure 8.1 illustrates the trend in patenting in the area of plant biotechnologies between 1985 and 2000 for both public and private sector organizations.

During the 1990s, it became clear that universities and non-profit agricultural research institutions were constrained in their historical role of providing many new agricultural innovations – particularly biotechnology-derived innovations – directly to the agricultural industry or to farmers. This was especially apparent for specialty or horticultural crops which don't occupy the large acreage of agronomic crops but provide high regional economic value. While there are many contributing factors, access to the suite of proprietary technologies required to produce a genetically modified crop has been frequently cited as a barrier to the commercialization of public sector agricultural

research.[3] In Europe, a similar picture emerged in 2000, when a Swiss scientist developed "Golden Rice", genetically modified rice with elevated pro-vitamin A,[4] which triggered an IP audit. The audit revealed that seventy proprietary technologies had been infringed in the development of Golden Rice and illustrated the complex patent thicket that surrounded biotechnology innovations for crop improvement.[5]

Role of institutional leadership

As a result of the emerging and complex IP landscape in agricultural biotechnology, a group of university, non-profit research center and foundation presidents wrote a compelling article for the "Policy Forum" of *Science* magazine.[6] The article addressed the historical mission of public/non-profit institutions and lamented how IP and its management were now impacting their institutions' own ability to "develop new crops with the technologies it has itself invented". The article considered the structure of IP ownership in the agricultural sector and recognized that the public and non-profit research sector had invented nearly 25% of the reported innovations. However, this portfolio of inventions was highly fragmented across many institutions that did not necessarily collaborate well, particularly when it came to IP management (Figure 8.2).

The conclusion suggested that collaboration to unify this broad portfolio under a common philosophical framework may be a powerful approach to reconstruct a "commons" of patented technologies to support a range of agricultural innovations that were not being addressed by private firms – particularly projects addressing specialty crops and humanitarian objectives. The strong and public statement made by these major institutional leaders was a critical step in advancing the clearinghouse initiative that became PIPRA.

[3] Graff G., Wright B., Bennett A.B., Zilberman D. 2003a. 'Accessing Intellectual Property for Biotechnological Development of Horticultural Crops', **58** *Cal. Ag.,* 122–7.

[4] Ye, X.D., Al-Babili S., Kloti, A., Zhang J., Lucca P., Beyer P., Potrykus I. 2000. 'Engineering Provitamin A (β-carotene) Biosynthetic Pathway Into (Carotenoid-Free) Rice Endosperm', **287** *Science,* 303–5.

[5] Kryder DR, Kowalski DP, Krattiger AF (2000) 'The Intellectual and Technical Property Components of Pro-Vitamin A Rice (GoldenRiceTM): A Preliminary Freedom-to-Operate Review' ISAAA Brief #20. ISAAA, Ithaca, NY.

[6] Atkinson RC, Beachy RN, Conway G, Cordova FA, Fox MA, Holbrook KA, Klessig DF, McCormick RL, McPherson PM, Rawlings HR, Rapson R, Vanderhoef LN, Wiley JD, Young CE (2003) 'A Collective Strategy for Managing Public-Sector Intellectual Property in Agricultural Biotechnology', **301** *Science*, 174–5.

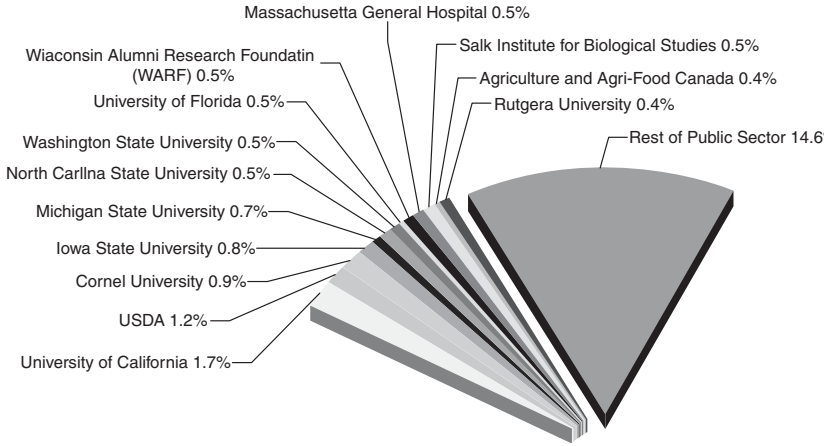

Figure 8.2 The breakdown of ownership of patented technologies assigned to public/non-profit research institutions across multiple public/non-profit institutions (data from Graff et al., 2003b).

8.3 The Public Intellectual Property Resource for Agriculture

A strategy of collaborative membership

PIPRA was established in 2004 with financial support from the Rockefeller Foundation and began to develop specific services and programs to address the high-level objectives that had been proposed through extensive consultation. The primary strategy of PIPRA was to establish a broad membership base that would represent the major agricultural technology developers in the world. Unifying the highly fragmented portfolio of agricultural IP under a common set of principles or within a framework of open and collaborative communication was viewed to be the most important first step. As a consequence, the barriers to join PIPRA were kept quite low – membership fundamentally requires an agreement to populate the PIPRA patent database with institutional information, to participate in PIPRA meetings and to agree at a high institutional level to support collaborative efforts that promote broad technology access. PIPRA's membership base is currently comprised of forty-six institutions in thirteen countries, although US institutions are predominant. The current members account for approximately 50% of the public/non-profit patented agricultural technologies.

An IP information clearinghouse

A major program and activity within PIPRA is to serve as a clearinghouse for patent information within the agricultural sector and to create a common source of information on public/non-profit patented technologies. This has primarily involved the establishment of a searchable database of PIPRA member's technologies that can be accessed by both members' technology management staff and by the public. The database contains information on patents and patent applications across seventy-two reporting jurisdictions and contains information on the licensing status of each technology which provides the basis to evaluate whether the technology is available for deployment in specific crops or geographic jurisdictions.

PIPRA recognizes that finding a patent in a database goes only part way toward accessing the technology. Among other challenges, know-how may be required, licenses may need to be negotiated, liability and stewardship issues may need to be addressed, and related public domain technologies may be worthy of examination. PIPRA's database was designed to provide a direct way to get assistance with these other critical areas of technology transfer. What sets PIPRA's database apart from others is not just the inclusion of licensing information, but the fact that PIPRA has collaborative working relationships with the owners of the technologies displayed. Connections to scientists and technology transfer offices can be facilitated along with assistance in licensing negotiation, and legal analysis can inform the decisions.

To add greater value to the information clearinghouse, PIPRA also developed the capability to evaluate freedom to operate for deployment of specific technologies. This capability is comprised of in-house staff with the skills to prepare dossiers characterizing the scientific and patent landscapes around specified technologies and a pro bono network of patent attorneys who provide detailed patent claims analysis and FTO opinions. The external legal resource has been a critical addition to expand the scope and impact of PIPRA's analytical capability and to provide rigorous evaluations of IP constraints and opportunities for the implementation of specific projects.

Technology exchange and standard license clearinghouse

PIPRA has also developed laboratories in order to design research tools and entire projects that are informed by IP and freedom to operate analysis. PIPRA's first project has been to develop "Enabling Technologies

for Plant Transformation" – involving the acquisition and testing of a suite of complementary technologies required for transfer of foreign genes into plant cells. To initiate this project, PIPRA convened a panel of experts to develop recommended design parameters that met technical and regulatory criteria as well as meeting legal criteria for access to the underlying IP. The recommended design parameters were then used to identify appropriate technologies that were extensively evaluated internally and by PIPRA's external network of attorneys. The results of this analysis provided the basis to identify the core proprietary and public domain technologies required to meet the technical objectives – with an emphasis on incorporating the required proprietary technologies from PIPRA member institutions. PIPRA has now combined the identified technologies into sets of research tools for distribution to the broader research community and has developed a pre-negotiated license to the pooled set of proprietary technologies that are incorporated into the research tool vectors. In the future, PIPRA will be in a good position to link its enabling technology pool with specific trait technology pools to fully enable project implementation relying primarily on PIPRA member technologies.

Strengthening capacity for IP management

Finally PIPRA is also leveraging the expertise embodied in its membership basis to strengthen the capacity for IP management in both the North and South. In collaboration with the Centre for Intellectual Property Management in Health Research (MIHR) it has developed an extensive handbook on best practices in IP management. The handbook is comprised of over 150 chapters that address issues of promoting broad technology access from developed country research institutions as well as providing blueprints for developing the capability to both protect and to access new technologies for developing country institutions.[7] This educational resource has now been deployed in curriculum for building institutional capacity for IP management in Latin America and Southeast Asia. It is anticipated that this will provide the basis for research institutions in a number of developing countries with emergent legal IP frameworks to rapidly develop their institutional capacity to both protect and access new technologies for agriculture.

[7] Krattiger A. 2007. *Intellectual Property Management in Health and Agricultural Innovation; A Handbook of Best Practices*, MIHR-USA.

8.4 Conclusion

The Public Intellectual Property Resource for Agriculture is fundamentally an IP clearinghouse that operates on several levels to effectively support the broad application of agricultural technologies developed in public-non/profit research institutions. Its primary strategy has been to adopt a highly collaborative program built on consensus views of its members – all of whom fundamentally believe that IP protection is an important tool to support innovation. PIPRA is working within the context of its members to support both commercial and humanitarian applications of technologies and to develop strategies and mechanisms to stimulate even more innovation globally.

REFERENCES

Atkinson RC, Beachy RN, Conway G, Cordova FA, Fox MA, Holbrook KA, Klessig DF, McCormick RL, McPherson PM, Rawlings HR, Rapson R, Vanderhoef LN, Wiley JD, and Young CE (2003), 'A Collective Strategy for Managing Public-Sector Intellectual Property in Agricultural Biotechnology', **301** *Science,* 174–5

Delmer D., Nottenburg C., Graff G. and Bennett A. B.(2003), 'Intellectual Property Resources for International Development in Agriculture; **133** *Plant Physiol.*, 1666–70.

Graff G., Wright B., Bennett A. B. and Zilberman D. (2003a), 'Accessing Intellectual Property for Biotechnological Development of Horticultural Crops', **58** *Cal. Ag.*, 122–7.

Graff G. D., Cullen S. E., Bradford K. J., Zilberman D., Bennett A. B. (2003b), 'The Public-Private Structure of Intellectual Property Ownership in Agricultural Biotechnology', **21** *Nature Biotech.*, 989–95.

Krattiger A. (2007), *Intellectual Property Management in Health and Agricultural Innovation; A Handbook of Best Practices*, MIHR-USA

Kryder DR, Kowalski DPand Krattiger AF (2000) 'The Intellectual and Technical Property Components of Pro-Vitamin A rice (GoldenRiceTM): A Preliminary Freedom-to-Operate Review', *ISAAA Brief* #20. ISAAA, Ithaca, NY.

Ye, X.D., Al-Babili S., Kloti, A., Zhang J., Lucca P., Beyer P. and Potrykus I. (2000), 'Engineering Provitamin A (B-Carotene) Biosynthetic Pathway Into (Carotenoid-Free) Rice Endosperm', **287** *Science*, 303–5.

9 Case 6. The Science Commons Material Transfer Agreement Project

A standard licence clearinghouse?

Thinh Nguyen

9.1 Introduction

Access to unique research resources, such as biological materials and reagents, is vital to the success and advancement of science. Many research protocols require assembling a large and diverse set of materials from many sources. Yet, often the process of finding and negotiating the transfer of such materials can be difficult and time-consuming. The ability to locate materials based on their descriptions in journal articles is often limited by lack of sufficient information about origin and availability, and there is no standard citation for such materials. In addition, the process of legal negotiation that may follow can be lengthy and unpredictable. This can have important implications for science policy, especially when delays or inability to obtain research materials result in lost time, productivity and research opportunities. These transactional barriers for material transfer may ultimately have more impact on the productivity of basic laboratory science than concerns related to patents or other intellectual property.[1]

Science Commons, a project of Creative Commons, is a non-profit initiative that promotes policy and technology that remove unnecessary legal and technical barriers to scientific collaboration and innovation. Science Commons's Material Transfer Agreement Project seeks to reduce unnecessary barriers to the transfer and reuse of basic research materials and reagents by proposing a scalable and flexible infrastructure for searching, negotiation, and tracking.

The MTA Project is a prototype of what van Zimmeren calls a "standard licence clearinghouse".[2] However, material transfer agreements are

[1] Walsh, J., Cho, C., and Cohen, W., 'View from the Bench: Patents and Material Transfers', 23 *Science*, 2005, 2002–3.

[2] van Zimmeren, E., 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume.

not necessarily, or even frequently, about licensing patents. The vast majority of common biological research materials are unpatented, and even when patents may apply, the use of such materials in basic research seldom implicates the need for complex patent negotiations, despite the occasional "reach through" royalty, grant back or other obligation on downstream innovation that may be premised on access to materials. The usual legal basis for such agreements, however, is located within very traditional, rather than intellectual, property rights: the ownership of physical things. These agreements, therefore, are traditionally viewed as a type of loan of property. While such a prototype involving the standardization of such agreements within a clearinghouse context may only tangentially touch upon the issues of building a true patent clearinghouse, they nevertheless offer a perspective from which to view the many challenges, as well as opportunities, that standardization offers any clearinghouse.

9.2 Material transfer agreements

Material transfer agreements (MTAs) are contracts that govern the transfer of tangible research materials from one research institution (the provider) to another (the recipient). They are most commonly employed in the transfer of "unique research resources" such as "cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones and cloning tools (such as PCR), methods, laboratory equipment and machines."[3] Non-biological and synthetic materials, such as certain nano-materials, chemical reagents and chemical substrates may be shared under MTAs as well.

This system for transferring these research tools can give rise to a variety of transaction costs associated with finding and bargaining for such tools. These problems are particularly acute where the volume of transactions is high and the sources of unique research resources required for a given research protocol are diverse. The resulting delays and failures to agree can impose a significant cost in terms of lost productivity and research opportunities.[4]

First, it may be difficult to locate relevant materials, because most of them are not widely publicized and not searchable on the web. The traditional method for a researcher to locate and assemble materials needed for research is to read relevant journal articles in the field of interest, design

[3] 'Principles and Guidelines For Recipients Of NIH Research Grants And Contracts On Obtaining And Disseminating Biomedical Research Resources' *64 Fed. Reg.* 72090 (23 December 1999).

[4] Campbell, E., et. al., 'Data Withholding Academic Genetics', **287** *JAMA*, 2002, 473–80.

a suitable research protocol, and contact the providers referenced, unless the materials are widely known to be available from a commercial vendor. For materials that are not commercially available, locating available supplies of materials is potentially time-consuming, because the provider of the materials may not be identified, may not have sufficient supplies of the materials, may not be able to produce more at a reasonable cost, may not wish to share them or may have moved to a different institution or job.

After a researcher has located the source of the materials, negotiation of the MTA may present the next hurdle. As the NIH Principles and Guidelines state, "each iteration in a negotiation over the terms of a license agreement or material transfer agreement delays the moment when a research tool may be put to use in the laboratory".[5] In many circumstances, the materials are subject to non-standard agreements, whose terms are not widely publicized. This makes it hard to predict whether a request for the materials may be simple or difficult to negotiate. Sometimes, a particular material may be subject to multiple MTAs with potentially overlapping or inconsistent terms.

This creates a number of possible factors contributing to delays or failure to obtain materials, particularly when a research protocol requires materials from many different sources. If the offered MTA is non-standard, then it must be carefully reviewed by a lawyer or specialist trained to understand legal issues and the institution's policies and objectives. These objectives can include ensuring rights to publish, disseminate and use research results and to license for commercialization and avoiding conflicting obligations. The reviewer must identify any objectionable terms and reject them or offer counter-proposals. In some cases, the reviewer will consult with business managers and researchers to clarify essential business objectives. However, this process can cause significant delays or failure to reach agreement, frustrating research agendas and schedules.[6]

While these negotiation practices may be useful in the context of high-value transactions with large pay-offs to the parties, such as royalty-generating transactions, it is less justified in the context of low financial value transactions like material transfer for basic research. Due to constraints in available legal resources, many technology transfer offices or licensing counsel must prioritize revenue-generating transactions, and resources to negotiate MTAs are limited. This is one factor that may contribute to longer turnround times for negotiating MTAs.

[5] *Principles and Guidelines,* at 72093.

[6] Streitz, W., and Bennett, A., 'Material Transfer Agreements: A University Perspective', **133** *Plant Physiology,* 2003, 10–13.

Some researchers avoid negotiation over MTAs through informal sharing. From an institutional perspective, such practices are unfavorable because they may subject an institution to legal risks, which might otherwise be mitigated by the use of MTAs. Such practices may also implicate the intellectual property management policies of the institution. Finally, informal sharing favors well-connected researchers and institutions, and therefore, may create or perpetuate disparities in opportunities for scientific research.

Science Commons proposes to reduce unnecessary transaction costs for sharing research materials by a creating voluntary and scalable infrastructure for rights representation and contracting represented by use standard agreements, web-based metadata and "human-readable deeds". These elements arise from design principles introduced by Creative Commons (CC) in creating the CC licences for copyrighted works, which have created a large and scalable infrastructure for authors, scientists, artists, and educators to license their works in standard but flexible ways. This has created a large and thriving community of users and a commons of copyrighted materials available under CC licenses.

9.3 Standard contracts

An important element of the success of open source software is the use of standard licences such as the GPL or other OSI-approved licences, which have provided a legal framework for collaborative software development. Such standard agreements reduce transaction costs by reducing negotiation costs within the communities that routinely use them and can facilitate regimes of frictionless exchange and re-use. Similarly, the CC licences provide a framework for the copying, re-mix and distribution of artistic works and other content.

One of the most prominent and successful efforts to standardize biological material transfers is the Uniform Biological Material Transfer Agreement (UBMTA), which was developed by the National Institutes of Health (NIH) in collaboration with research institutions and adopted by 320 signatories.[7] Institutions may sign and deposit a master UBMTA with the Association of University Technology Managers (AUTM) in order to be able to complete transactions by executing a short "implementing letter" or cover letter. A similar, shorter standard form called the Simple Letter Agreement (SLA) for non-profit use is published by NIH, which recommends its use in connection with NIH sponsored

[7] 'Signatories to the 8 March 1995, Master UBMTA Agreement', www.autm.net/aboutTT/aboutTT_umbtaSigs.cfm.

research.[8] However, use of such standards for intra-academic transfers is not universal, as signatories can opt to use them on a case-by-case basis, and some institutions may include in these MTAs additional modifications that would render them non-standard, and thus subject to individualized review and negotiation.

A further complication is that the UBMTA and SLA are not compatible with use by for-profit entities. This is because the UBMTA and SLA prohibit transfer to for-profit entities and restrict use to academic research. The lack of generally accepted standards for these transfers makes collaboration between academic and for-profit researchers complex and costly, even when only internal or evaluation use is contemplated.

The Science Commons MTA Project adopts a two-tiered strategy to reduce transactional barriers to exchanging materials for research. First, for intra-academic material transfer, we adhere to the NIH Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources ('NIH Principles and Guidelines') in calling for more widespread adoption and use of UBMTA or SLA in unmodified form. We are developing tools and infrastructure to facilitate listing, searching, contracting and tracking downstream impact for providers and recipients who are willing to take advantage of these existing standard MTAs.

The NIH Principles and Guidelines also encourage institutions to "simplify the transfer of materials developed with NIH funds to for-profit institutions for internal use by those institutions".[9] These guidelines recognize that while greater flexibility is required in this area, the same principles apply to considerations for internal use by for-profit entities. Science Commons, working with collaborators, has developed a set of new MTAs that use modular contract options to promote the development and evolution of standard MTAs for transfers between academia and industry. The new MTAs published by Science Commons will provide for a more flexible range of options, while at the same time adhering to the core guidelines articulated by the NIH Principles and Guidelines. For example, they distinguish between activities for internal use and commercialization, and they do not provide options that restrict publication or that contain reach-through royalties, grant backs, commercialization options or other obligations with regard to downstream inventions made by the recipient. We are also developing

[8] 'Simple Letter Agreement for the Transfer of Materials', http://ott.od.nih.gov/.
[9] *Principles and Guidelines,* at 72093.

a simple interface that can guide a user through key considerations and options associated with selecting a particular MTA.

9.4 Standard rights description framework

The use of semantic web metadata to identify rights associated with copyrighted works has contributed to powerful searching and filtering capabilities for web-based works available under Creative Commons licences. These metadata use the Resource Description Framework (RDF), a robust Web-based representation language for Universal Resource Identifiers (URIs) published by W3C.[10] This open framework allows physical resources in the world (such as unique research materials) to be represented in a machine-readable form that is designed to be compatible across a variety of software and operating system platforms. For example, more than 140 million objects on the web are tagged with Creative Commons licences, and they can be found by using advanced search options available from search sites such as Yahoo! and Google. This has demonstrated considerable potential to create a scalable, low-cost infrastructure for describing resources and associated rights and permissions.

Science Commons will use a similar framework to describe unique research materials and the MTAs under which they are offered. Each material that is listed on the web and available under a standard MTA can be associated or tagged with metadata, which allows for similarly powerful searching and filtering capabilities by software and search engines. For example, an academic researcher might be able to search for all available animal models for neurobiological research that are available under the UBMTA or SLA, and her counterpart at a for-profit laboratory can search for similar materials that might be offered under a standard Science Commons MTA. This will permit researchers to plan research protocols with greater visibility into the likelihood that unique research resources will be available quickly or whether more extended negotiations will be required.

The association of this metadata with scientific articles may raise exciting new possibilities. For example, authors can supply a unique link from materials described in the "materials and methods" section of a scientific article to the hosting material depository where they can be found and ordered. Then, a researcher referencing such a link can use the supplied metadata to identify and filter acceptable MTA offers

[10] Shadbolt, N., Berners-Lee, T., and Hall, W., 'The Semantic Web Revisited', **21** *IEEE Intelligent Systems*, 2006, 96–101.

and then order online if possible. The widespread use of such a system may eliminate much of the detective work currently involved in tracking down materials and enable greater automation of ordering and fulfillment.

The association with materials with the literature using metadata can also permit the research impact of materials to be tracked and analyzed by software, giving researchers and funding institutions additional measures of scientific impact. Creative Commons has demonstrated this capability with its CCMixter software, which allows metadata to be used to track and analyze downstream impact of creative works, such as remixes and other derivative works originating from a given work.[11] In the materials context, this may permit the impact of research to be evaluated not only in terms of journal citations but also the frequency of re-use of unique research materials generated by that laboratory.

In addition to metadata, Science Commons is developing "human readable deeds" for each standard MTA. These deeds will be hosted at unique web URIs to which users and software applications can link. Each, in turn, provides links to the relevant legal text and associated metadata for that MTA. Each deed describes a unique standard agreement in summary terms, as intended to be understood by non-legal audiences, including basic iconography that will enable researchers to identify at a glance the most relevant rights and obligations associated with a material. These can also be printed out and attached to materials to describe relevant MTA limitations, similar to the way that Material Data Sheets summarize salient physical and chemical properties of materials.

Together, these elements create the basic outlines of an infrastructure for enabling Web-based transactions in materials. Web-based transactions have revolutionized e-commerce, as evidenced by sites like Amazon.com and Ebay. Yet, so far, we have seen little evidence that these models are being adapted with nearly that level of success for solving material transfer problems. We believe that such success requires significant standardization of policies, contracts and technology. The elements of our MTA project will offer nucleating agents around which such efforts can grow and evolve. We are also collaborating with the iBridge to deploy the initial prototype of this MTA system through the iBridge network. This will provide us with an opportunity to conduct a beta test of our software and tools and obtain feedback from key stakeholders.

[11] Creative Commons, ccMixter, http://ccmixter.net/.

Reducing the time it takes for scientists to obtain basic research materials is vital for accelerating scientific discovery. Standardization of policy, contracts and technology is necessary in order to deliver the relatively frictionless transaction systems that have revolutionized web commerce. The system that we propose, which includes greater use of standard contracts, a web-based rights description framework, and other educational tools, is the first step in that direction. The possible benefits will accrue not only to immediate stakeholders, in the form of cost savings and increased productivity, but ultimately to society as a whole from greater innovation and scientific progress.

REFERENCES

Campbell, E., et. al., 'Data Withholding Academic Genetics', **287** *JAMA*, 2002, 473–80

'Principles and Guidelines For Recipients Of NIH Research Grants And Contracts On Obtaining And Disseminating Biomedical Research Resources', *64 Fed. Reg.* **72090** (23 December 1999)

Shadbolt, N., Berners-Lee, T., and Hall, W., 'The Semantic Web Revisited', **21** *IEEE Intelligent Systems*, 2006, 96–101

Streitz, W., and Bennett, A., 'Material Transfer Agreements: A University Perspective', **133** *Plant Physiology*, 2003, 10–13

Walsh, J., Cho, C., and Cohen, W., 'View from the Bench: Patents and Material Transfers', **23** *Science*, 2005, 2002–3

van Zimmeren, E., 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume

10 Case 7. The collective management of copyright and neighbouring rights

An example of a royalty collection clearinghouse

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10.1 Introduction

In a collective management system, owners of rights authorise collective management organisations to administer their rights – that is to negotiate with users, deliver licenses, collect fees and distribute them, and monitor unlicensed uses.

Copyright and neighbouring rights are exclusive rights and should normally be exercised individually by the owner of the right himself. But as early as the first half of the nineteenth century it appeared that certain rights, in the first place the right of public performance of musical works, could not in practice be exercised individually.

The number of venues at which musical performances took place and the number of copyright owners whose rights were involved were so large as to preclude altogether the possibility of individual negotiation between right owner and user. Performances by means of recordings and radio have multiplied the scale of the problem still further. In these circumstances the only feasible method of enforcing the performing right was the establishment of organisations capable of representing the rights of thousands of individual copyright owners and thus being in a position to negotiate with all music users.

Among the first organisations to have been established are the authors' societies SACEM (France, 1851), SIAE (Italy, 1882), GEMA (Germany, 1903) and PRS (United Kingdom, 1914).

At the outset, authors' societies represented their own national repertoire, but they rapidly entered into bilateral representation agreements with organisations of other countries and created a 'worldwide web', allowing any national organisation to license the use of, practically, the whole world music repertoire.

The advance of technology with uses of copyright works such as film, television, cable television, reprography and home copying made

individual licensing impracticable over a much wider field. The structures and methods of the performing societies began to serve as a model for other categories of authors, such as writers, playwrights, film directors, painters, sculptors and photographers.

However, in many countries these categories of authors are still not organised or, if they are, the scope of the management of their societies is limited to only one or a few forms of use of copyright works.

The recognition of neighbouring rights (i.e. rights of performers, producers, broadcasters) has also led to the establishment of collective management organisations. Although some basic neighbouring rights can be exercised on an individual basis, the rights of performers and phonogram producers with regard to the public communication and the broadcasting of phonograms called for collective management.

However, as collective management of neighbouring rights has started more recently, the international network of bilateral agreements, such as the authors' societies have created, is not fully established yet.

Finally, several national legislations have made collective management of copyright and neighbouring rights compulsory in some areas, such as reprography, home copying, lending and cable television, sometimes in combination with a non-voluntary licence system.

10.2 Forms of collective management

Most collective management organisations are non-profit-making private corporations, established on the basis of the voluntary initiative of copyright owners. However, in a number of developing countries, mainly in Africa, public or semi-public organisations are doing well and are probably the most suitable formula in the specific conditions prevailing there. But even private corporations are generally supervised by public authorities, which will be discussed later.

The scope of the management varies greatly, as well as regards the categories of works covered, as regarding the forms of use of the works. Some authors' societies manage all categories of works for all forms of uses (e.g. SABAM, Belgium; SGAE, Spain; SIAE, Italy); others manage only musical works but both for performances and for recordings (e.g. GEMA, Germany; SUISA, Switzerland); others again manage only musical works (e.g. SACEM, France) or dramatic works (e.g. SACD, France) and for performances only.

10.3 Methods of collective management

The 'raison d'être' of collective management organisations is to collect and distribute appropriate remunerations for the right owners, to

monitor all uses and eventually to enforce the copyrights or neighbouring rights in their custody. A reliable documentation system is therefore essential.

Documentation

Documentation and the exchange of documentation between collective management organisations present a very heavy burden. The most important problem is that of the 'dormant repertoire', that is works stored in the organisation's card index or database, which are very rarely or sometimes nevermore used. The dormant repertoire probably represents about 85% of all repertoires, particularly so in the area of pop music, where the production of new works is enormous and the life-span of the works is ephemeral. The organisations rely more and more on electronic data processing and international tools have been developed, updated daily, such as the IPI-list identifying authors, composers and publishers; the ISWC, identifying musical works, the ISRC, identifying recordings, the ISAN identifying audio-visual works. The ISTC, identifying textual works, is under development.

All collective management organisations' databases are operating with these identifiers and are all available on the CIS-net, an intranet for the authors' societies, working under the umbrella of CISAC, the International Confederation of Authors' and Composers' Societies.

It is planned, in the future, to incorporate these identifiers in all digital recordings and broadcasts as metatags, allowing the identification of the works and the allocation to the correct rights owners of the fees collected for any use of the works.

It will be clear that this infrastructure represents an important part of the administration costs of the collective management organisations.

Collection

The typical instrument of licensing by collective management organisation is the 'blanket licence' under which the user is entitled to make use of any or all works or other protected material in the organisation's repertoire for the purpose, and within the period indicated in the licence.

The 'blanket licence' is the most common method used for musical works, with the exception of concerts of classical music which are licensed on a per work basis.

Conversely, for dramatic and dramatico-musical works, the licensing on a per work basis is the rule and the blanket licence is applied only for broadcasting.

Tariffs and other conditions of licences are mostly negotiated with organisations of users.

In the majority of countries, there is some kind of government control on the licensing practice of the collective management organisations, either by approval of the tariffs and the standard agreements, or by special tribunals dealing with conflicts between organisations and users.

Distribution

The distribution rules of the collective management organisations are complex. Distribution of fees collected on a per work basis is fairly simple: the fees are allocated to the used work(s) and distributed among the relatively few rights owners of these works.

But the distribution of fees collected under a blanket licence is another matter. Here an elaborated points system is needed to take into account the relative importance of the works and uses. The number of allocated points reflects the length of the work and the artistic category to which it belongs (i.e. classical music, pop music, poem, story, stage play, opera, ballet etc.).

Artistic value or merit are not taken into consideration, as this would be contrary to the principles of copyright.

However, artistic evaluation may play a role in establishing the category in which the work is classified.

Essential for correct distributions are the data concerning the uses of the works, allowing distributing the fees accordingly. Obtaining and analysing full information concerning all uses of all works is, of course, impossible and would not be feasible for obvious cost reasons. Collective management organisations have to strike a balance between creating a reliable basis for the distribution and avoiding unreasonable costs. As a rule, broadcasting organisations and phonogram producers provide full information – as neighbouring rights owners they are interested parties in the distribution of the equitable remuneration for communication to the public of phonograms – and the outcome of the distributions based upon these data is extrapolated to the distribution of fees collected in other areas.

Another method, applied for fees collected in places such as bars, restaurants, shops etc., is a sampling system.

However, especially European collective management organisations are reluctant to apply extrapolation and sampling systems as they obviously favour the international repertoire. European organisations will go to great lengths in order to collect as full information as economically

reasonable, aiming at a reliable distribution and the least detrimental to the less important rights owners.

10.4 Cultural and social purposes

Again, European collective management organisations do not think that the administration of the rights of their members is their only purpose, but they feel that they also have responsibilities on a social and a cultural level.

At least authors' societies do so, and performing artists societies will probably do the same in the future.

Authors and artists are people who tend to lead a life which is often irregular and whose careers do not always fit into the administrative demands of traditional welfare schemes with the unfortunate result that they often remain outside any scheme.

Therefore, most authors' societies have organised specific health insurance and pension schemes.

On the other hand, the difficult economic situation has led public authorities, traditionally responsible for the funding of cultural activities in Europe, to reduce drastically the funds available. Therefore, the collective management organisations try to take care of some more vulnerable areas, such as performance of contemporary music, avant-garde theatre and poetry,and art cinema.

Anyhow, deductions from collected fees allocated to social and cultural purposes will not exceed 10%.

10.5 Costs of collective management

It is sometimes said against collective management that the costs involved are too high. But one should not overlook that in the absence of collective management, the transactional costs involved for users having to deal with individual rights owners, assuming that were possible, would be considerably higher.

The administrative costs of the collective management organisations are, in general, around 15–25% of their gross collections for music performances, around 10% for professional stage performances and around 5% for mechanical reproduction.

For several reasons, it is not possible to suggest a maximum acceptable percentage of administrative costs. Much depends on the intensity and the precision of the activities of the organisation. The operations of some organisations are fairly simplified, while the collection and distribution system of other organisations is much more sophisticated.

It has sometimes been argued that an alternative solution would be for the exclusive rights of copyright and neighbouring rights owners to be replaced by a system of non-voluntary licences, under which they would only be entitled to equitable remuneration. In fact, the international conventions governing copyright and neighbouring rights allow the possibility of non-voluntary licences, and a number of national legislations have introduced such systems.

But the mere existence of non-voluntary licences in respect of specific uses of copyright or other protected material will not in itself provide a complete solution. The right owners are still to obtain payment and they will always need a collective management organisation to identify the uses, to collect fees accordingly and even, in the case of a simple compulsory licence, to negotiate the appropriate remuneration; and last but not least, to ensure a correct distribution of the collected fees.

Another alternative, which has been actively promoted by American academic circles, are the so called 'Creative Commons licences'. In this system, the copyright owner allows the licensee to use the work, or other protected material, under more or less restrictive conditions: i.e. only non-commercial uses, and without creation of derivative works (translations, adaptations); or commercial uses, without creation of derivative works; or allowing creation of derivative works, but provided a cross-licence is granted; and so on.

However, this system presents several serious flaws. CC licences cannot be limited in time, and are irrevocable. The copyright owner cannot change his mind. Many legal questions remain. What happens if the conditions of the licence are not complied with? And, above all, CC licences have no mechanism to provide for payment. This makes CC licences unattractive for the author and artist who want to make a living out of their work. CC licences seem only appropriate for academic research and writing, and some avant-garde music or poetry. Anyway, CC licensing is only possible in an on-line environment.

10.6 Challenge of the new technologies

New technologies, in particular the digitisation of works, have proved a formidable challenge to collective copyright management. Digitisation has made possible new technologies of recording and copying without loss of quality; new kinds of carriers allowing multimedia recordings, such as CD-ROM, CD-I and the like; and last but not least, has allowed the creation and the development of the Internet, the most powerful instrument in history of dissemination of all kinds of data, including copyright material.

All these applications of digital technology have raised complex and difficult legal questions, which are beyond the scope of this paper and will not be discussed here. We will focus on the managerial and organisational aspects arising from these new ways of exploitation of works for collective management organisations.

Digital copying, in fact, can be managed along the same lines as the old analogue copying. In most countries, in the EU anyway, analogue home copying was allowed under a legal licence scheme. Collective management organisations distributed the proceeds among the different rights owners. Similar systems with appropriate tariffs, may work satisfactorily for digital home copying too. However, some rights owners, in particular phonogram and audiovisual producers, favour technological solutions, by incorporating in the original carriers a device allowing the making of only one copy, or a limited number of copies, or even prohibiting copying altogether.

For several reasons, which cannot be discussed here, authors and their collective management societies are not always happy with these solutions, which raise also delicate legal and policy issues.

Multimedia carriers, already, have required some reorganisation of the collective management organisations. As seen before, collective management is generally organised along categorical lines: organisations for authors, organisations for performers, organisations for producers. And authors, mostly, have separate organisations for writers, for composers etc.

But multimedia carriers reproduce all kinds of works, textual, musical, visual, audiovisual, implying licences from many kinds of rights owners. In order to allow this new technology to develop, collective management had to find ways of working together and, ideally, to form one-stop shops, where users could find all licences needed.

In several EU countries, tentative one-stop shops have been organised. Most are no more than clearing centres, identifying works and directing the user to the correct rights owner for licensing. Indeed, licensing multimedia is a very difficult task. The collective management organisation has to strike a balance between the respective value of several kinds of works, textual, musical, visual etc. Simply adding up the claims of all rights owners would lead to prohibitive tariffs. But finding a generally accepted balance is far from easy.

An effectively direct licensing collective management organisation is the French SESAM. But still, it associates only authors' societies; no performers' or producers' organisations. Taking their claims into account in one single licence has proven to be a bridge too far.

A real, all encompassing one-stop shop is still far away.

The Internet, however, has been, and still is, the fiercest challenge. Allowing transmission on-line, in real time, throughout the world, of all kinds of data, works and other protected material, it not only needs licensing covering all rights concerned but also worldwide licensing.

As seen before, authors' societies, in particular composers' societies, have developed a worldwide system of reciprocal agreements, allowing a society in any given country to license the world repertoire. Until the seventies, these agreements, as a rule, were exclusive. In the EU member states, as a result of the EU competition authorities taking action, they no longer are; but as a matter of fact the societies still continue to license in their own country only, for the obvious reason of avoiding unnecessary expenses resulting from multiplicating monitoring and enforcement. The EU Commission has acknowledged that practice until now. But on the Internet this was not longer possible. The societies, under the aegis of CISAC, then developed a new standard agreement, known as the Santiago agreement, allowing the society of the economic residence of the website to license worldwide.

However, the phonogram producers' collective management organisations developed another standard agreement, allowing every organisation to license worldwide, provided it charged the tariffs of the country(ies) of performance and not only the tariff of the country of the website. Besides, this agreement was limited to website broadcasts, whereas the Santiago agreement allowed licensing of all websites.

The EU Commission has approved the phonogram producers' standard agreement (decision of 8 October 2002 'Simulcasting')[1] and has aired some criticism of the Santiago standard agreement, which has been dropped by the authors' societies lately. The situation now remains unclear. The Commission has recently published a 'Recommendation on the cross-boarder collective management of copyright in the field of on-line music services' (18 October 2005) which will be discussed further.

10.7 Collective management and competition law

Collective management organisations are, by nature, monopolies and competition law looks on a monopoly a priori with suspicion. This has led to several conflicts in many jurisdictions.

In the United States, under pressure of the competition authorities, two and later even three music performance right societies have been created, in order to eliminate a monopoly in this field. Still today, the

[1] *OJEC*, L107/58, 30 April 2003.

blanket licence, the licensing method typical for collective management, is under legal scrutiny.

In the European Community, although a dominant position is not in itself condemned by the competition rules, but only an abuse of it, collective management organisations have already been brought to amend membership rules, and tariffs.

Here is a real problem. Copyright and neighbouring rights are, by nature, exclusive rights. If exclusive rights are collectively administered, this should not influence the exclusive nature of such rights. It is generally accepted that collective management of copyrights and neighbouring rights is not only useful for the rights owners but is also to the advantage of users, who would otherwise be confronted with unbearable transactional costs. It is obvious that the full advantages of collective management can only be obtained by means of one single organisation, at least in the same category of rights in each country.

As discussed earlier, several national legislations have recognised the advantages of collective management and have even gone so far as to make collective management compulsory for some forms of use of copyright works or other protected material. It is not very coherent to afterwards wipe out the advantages of the imposed collective management by strictly enforcing competition law rules.

But it cannot be disregarded that abuse of the monopoly remains a possibility and appropriate guarantees seem to be necessary.

This dilemma is even more difficult when it comes to one-stop shops which associate still more rights owners and acquire a still more important dominant position, but which, as seen before, are now indispensable in the new digital environment of multimedia and the Internet.

This has not escaped the attention of the EU Commission, but its attitude regarding the collective management organisations is somewhat ambiguous.

On the one hand, the Commission calls for the creation of one-stop shops as an answer to the market's need for fast and comprehensive licences and to reduce transactional costs. The Commission has done so already in the 'Green Paper on Copyright in the Information Society' (1995),[2] in the Copyright Directive (2001)[3] and again in the recommendation mentioned earlier.

But on the other hand, the Commission has never taken a clear stand on the applicability of competition rules on collective management organisations, in particular one-stop shops.

[2] Doc COM (95) 382 final, 19 July 1995. [3] *OJEC*, L167/10, 22 June 2001.

The EU Court of Justice has been, in general, rather favourable to collective management organisations, in its SABAM decision (27 March 1974)[4] and the Coditel decisions (18 March 1980 and 6 October 1982)[5] but has been critical of some tariffs: SACEM (13 July 1989).[6]

Be that as it may, in most countries collective management organisations are under scrutiny from two authorities: on the one hand, the general competition authority; and on the other hand, a specific authority, which may be a public office (Germany), a governmental service (Belgium, France) or a tribunal (UK, Canada).

A public office or service will generally look into the terms of membership, the participation of rights owners in decision making, the documentation, collection and distribution systems etc. A tribunal will put the tariffs to the test, which, in fact, is somewhat at odds with the exclusive nature of copyright.

In the presence of such supervising authorities, competition authorities will limit themselves normally to cases of abuse. Collective management organisations of copyright are thus among the most closely scrutinised enterprises in modern society. Maybe this is unavoidable, given the great importance of copyright management for the cultural, social and economical development of the information society.

REFERENCES

M. Ficsors *Collective Administration of Copyright and Neighbouring Rights*, Geneva, 1990.

D. Peeperkorn and C. Van Rij (eds.), *Collecting Societies in the Music Business*, Apeldoorn – Antwerpen, 1989.

[4] (1974) *ECR* 317; 2C*MLR* 283 (1974). [5] (1980) *ECR* 881; (1987) *ECR* 3381.
[6] (1989) *ECR* 2521.

11 Comment on the conceptual framework for a clearinghouse mechanism

Michael Spence

10.1 Introduction

The notion of a royalty clearinghouse for biotech patents is beguilingly simple. So many problems would seem to be solved if there were a one-stop shop in which scientists could determine whether their activities were liable to infringe some particular gene patent, to determine whether any relevant genetic invention could be licensed, to pay for its use and to proceed on their voyage of scientific discovery.

Van Zimmeren's fascinating paper makes it clear, however, that it may be a long time before the dream of such a one-stop shop becomes a reality. She calls it 'too big a leap forward'.[1] I would go even further and suggest that there is much about the idea of a one-stop shop that is not only unachievable, but also potentially undesirable, unless appropriate standards of genetic patentability are firmly in place. Real thought must be given to whether the potential problem of the anticommons is not, after all, that too many genetic patents are granted and too few defences to infringement and compulsory licences available. If it is, then clearinghouses may even exacerbate, rather then relieve, the problem. Moreover, the analogy of a patent clearinghouse and a copyright collecting society seems to me to be a false one.

In her paper, van Zimmeren considers the advantages of the various clearinghouse mechanisms, and in particular the royalty collecting clearinghouse, in terms of their ability to meet three types of problem. First, she shows how a royalty collecting clearinghouse could reduce the potentially large transaction costs – including search, bargaining and enforcement costs – that face scientists undertaking biotech projects. This is because a clearinghouse could coordinate the promotion of genetic inventions, on some models of the clearinghouse it could license them on standard terms and even collect royalties, and it could operate to identify infringements as a watchdog for the patent holders.

[1] van Zimmeren, 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume.

Second, van Zimmeren claims that a clearinghouse mechanism could prevent royalty stacking by offering the potential licensee a package of inventions for a particular project at a price-controlled rate. Third, she claims that a clearinghouse mechanism could, at least to some extent, prevent non-cooperative patent holder behaviour by requiring reciprocal positive comity or grant back clauses in the standardised licences.

10.2 Evaluation of the patent clearinghouse model in genetics

My difficulties with the clearinghouse model relate on the one hand to its vaunted advantages in relation to transaction costs, and on the other in relation to its alleged advantages concerning royalty stacking and non-cooperative behaviour.

Reduction of transaction costs

As for transaction costs, it is plausible that a clearinghouse could achieve some reduction of such costs, and be effective to facilitate licences for at least the most straightforward uses of the most straightforward inventions. Nevertheless, the difficulties that van Zimmeren points out in her paper are real. These difficulties are of three types. First, they relate to the problem of comprehensiveness. Transaction costs would only be reduced if the library of patents that a clearinghouse controlled were comprehensive, but there may be little incentive for the holders of the most valuable patents to join. Moreover, the more comprehensive the relevant library, the more likely it would be to give rise to competition law problems. Second, difficulties arise because, even in so restricted a field as genetic diagnostics and far more in more complex fields such as the licensing of transgenic plants and animals, biotech licensing arrangements are rarely 'standard'. Yet the reduction of transaction costs is usually seen as dependent upon standardised licensing. It may be impossible to develop an appropriate library of standardised licences for all but a limited range of uses of a limited range of inventions. In particular, the fact that the licensing of know-how could not be standardised means that a royalty collecting clearinghouse would only be appropriate for 'patented DNA sequences and mutations, and a handful of commonly used diagnostic tools'. Further, any library of standardised licences would need to be constantly updated or it could institutionalise the use of inappropriate arrangements by ossifying licensing practices at one point in the development of very fast-moving industries. Third, the administration of at least royalty collecting clearinghouses would

be expensive and require considerable expertise: not least because biotech patents are often uncertain in scope and it is difficult to determine when a licence is needed.

In addition to these difficulties I would argue that reducing transaction costs might – and I put it no more highly than that – have a perverse unforeseen consequence. As van Zimmeren points out, empirical work in the biomedical sciences is equivocal as to whether the anticommons effect can be demonstrated. Importantly, it suggests that many scientists, both in universities and in industry, currently ignore the question of whether their activities are covered by a patent, at least over so-called 'research tools'.[2] Thus, for example, 'only 2 percent of academic bench scientists have begun to check regularly for patents that might impinge on their research',[3] and even in industry the 'infringement of research tool patents … appears to be pervasive'.[4] Some have argued that this is why the anticommons effect is not currently as serious an issue as it might be: lax standards of patentability do not give rise to serious anticommons problems because no one pays attention to many of the patents issued. The reasons that these patents are ignored are numerous, including a general sense that there is, or ought to be, a so-called 'research exemption' protecting at least academic researchers from patent infringement suits when they use protected research tools without a licence.[5] But it may also be that this wilful ignorance is sustained by an awareness, however tacit, that transaction costs are prohibitively high. They are, after all, high both for the potential licensee (who is likely to use a genetic research tool if it is physically available to her without bothering about licensing), and for the potential licensor (who is unlikely to detect its use). If this is right, then reducing transaction costs without also thinking carefully about standards of patentability in relation to biotechnological inventions, may have the perverse effect of increasing the anticommons effect. This would particularly be the case if the clearinghouse came to see itself as an enforcement agency, a probability to which we will return.

So in relation to clearinghouse mechanisms as a means of reducing transaction costs, I would give a cautious endorsement. I am perhaps

[2] Walsh, J. P., Arora, A. and Cohen, W.M., 'Effects of Research Tool Patents and Licensing on Biomedical Innovation', in Cohen, W.M. and Merrill, S.A. (eds.), *Patents in the Knowledge-Based Economy* Washington: NAP 2001, 285 ('Effects of RTPs') at 324–8 and National Research Council of the National Academies – Committee on intellectual Property Rights in Genomic and Protein Research and Innovation, *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health* Washington: NAP 2003 ('Reaping') at 119–27.

[3] 'Reaping the Benefits', 122. [4] 'Effects of RTPs', 327.

[5] 'Reaping the Benefits', 28.

less enthusiastic than van Zimmeren, but I can see the attractiveness of such a proposal, provided that we can be confident about the standards of gene patentability and the range of available defences to infringement. One alternative way of reducing transaction costs without some of the undesirable consequences of the clearinghouse mechanism would be to have a public actor charged with the task of devising and encouraging the use, not of standard licences, but of standard clauses for licences, standard mechanisms for resolving common licensing problems. This is a possibility that Paul David and I have suggested elsewhere as a solution to some of the problems associated with transaction cost barriers to collaborative e-science.[6]

Prevention of royalty stacking

However, more important than my concerns about clearinghouse mechanisms as a means of reducing transaction costs in the licensing of biotech patents, are the difficulties that I have with a royalty collecting clearinghouse in relation to its supposed advantages of preventing royalty stacking and non-cooperative behaviour. In relation to these issues, I am even more cautious about the ability of clearinghouse mechanisms to control for the anticommons effect. Again the real problem seems to be standards of patentability and the (non)availability of defences and compulsory licences: the possibility of a clearinghouse mechanism ought not to be allowed to deflect attention from these issues.

The first thing to emphasise is that even if a clearinghouse mechanism could reduce all transaction costs to zero, so that everyone could easily pay for the use of a particular invention, that does not mean that everyone should pay for its use. This is particularly the case with upstream inventions that are useful as tools in research, and inventions that have been produced by the investment of public research funds. The appropriate scope of the research exception, and whether the public ought to be charged the patent premium on inventions that are the product of research funds the public purse has provided, are contentious and difficult issues. They are not resolved simply because licensing is possible, or even easy. Indeed, we have seen that many academic scientists, and some in the private sector too, seem to operate on the mistaken basis that a very broad research exemption is already available in most jurisdictions.

[6] David, P. A. and Spence, M., *Towards Institutional Infrastructures for E-Science: The Scope of the Challenge* Oxford: Oxford Internet Institute Research Report No. 2, 2003.

Second, there is the important institutional question of by whom the clearinghouse would be 'owned', and in whose interests it would act. Van Zimmeren suggests that 'a clearinghouse could be administered by either a not-for-profit or profit (private) organisation'. The issue here is whether the clearinghouse would operate to squeeze as much return as it could from the licences within its portfolio, an approach that might attract members and endear it to them, or attempt to fulfil a public duty by maximising activity in the biomedical sciences. If experience of the copyright collecting societies is any guide at all, then the former is more likely. The fact that some copyright collecting societies have funds for cultural benevolence does not alter their essential function as IP policemen. Indeed, without the agency of a clearinghouse, the holder of a genetic patent may enter into bilateral licensing negotiations as both an owner of technology to which the other party seeks access, and perhaps also a user of technology that the other party owns. This may temper her desire to exploit the patents that she owns to the full.[7] However, if a clearinghouse has control over the patents, then it only ever enters negotiations as 'owner' and not as 'user'. It is not surprising, therefore, that the copyright collecting societies have been found, as van Zimmeren points out, to be susceptible to anti-competitive behaviour. If the clearinghouses are big enough effectively to reduce transaction costs, and aggressive in the promotion of their members' interests qua patent holders only, anti-competitive behaviour is almost inevitable.

One context in which this problem of who owns the clearinghouse and in whose interests it acts would become particularly acute, is the context of royalty stacking. The suggestion of van Zimmeren's paper is that the clearinghouse could act as a price-control mechanism, to ensure that only a 'reasonable' total royalty was paid. At one level this makes sense. A clearinghouse would realise that an excessive total licensing fee might mean that a project was not undertaken and that no licensing fees at all were paid. So even if its intention were solely to maximise return from its patent portfolio, the clearinghouse would have an incentive to cap the total fee for an individual project to ensure some level of return. But pricing that total fee would be far from straightforward. The fact that the different patents were complementary, rather than substitutes, would have a tendency to inflate the price of the total package. In copyright, where pricing should be more straightforward, the control has been necessary both of competition law, and also, in many

[7] Indeed, there is some empirical evidence that this type of consideration curbs infringement suits in the biotech industry, see 'Effects of RTPs', 295.

jurisdictions, of specialist tribunals to which resort can be had if a collecting society does not license on reasonable terms. If the problems of patent thickets and royalty stacking emerge because too many patents are granted in the field on biotechnology, the clearinghouse, with its need for this elaborate type of pricing control, seems an odd way to resolve the problem.

Reduction of uncooperative patent holder behaviour

Finally, on the issue of uncooperative patent holder behaviour, the clearinghouse proposal also seems to skirt the real problem. There is an important difference here between *copyright*, where control over the use of a work may be tool for protecting an author's expressive autonomy, and *patent*, where it is generally assumed that control over the use of invention is a tool for maximising an inventor's return from her work. We may recognise that an inventor should have the right to prevent the use of her technology for a purpose of which she disapproves, but we would normally see the widest possible distribution of an invention as the purpose of patent law. The patent compulsory licences for non-use of the invention would be unthinkable in copyright law. If there is a problem, then, in relation to uncooperative patent holder behaviour, particularly as regards research tools, then there may be no good reason to rely on the circuitous method for prising inventions out of the patent holder's hands described in van Zimmeren's paper. A compulsory license provision, though itself not straightforward to devise, would seem a more obvious mechanism for prising control over the invention from patent holder's grasp, while still ensuring that she enjoys a reasonable income flow.

Conclusion

I would argue, therefore, that a royalty collecting clearinghouse may be a very useful way of reducing transaction costs, but that more radical solutions are likely to be needed if the problems of royalty stacking and uncooperative patent holder behaviour are really to be overcome.

10.3 Comparison copyright collecting societies and patent royalty clearinghouses

In closing, I think it important to stress that the analogy between copyright collecting societies and patent royalty collecting clearinghouses seems to me only very inexact. The term 'intellectual property' seems

to be of nineteenth-century American coinage[8] and has only arrived even more recently in many languages. Real differences exist between the purposes and contexts, both cultural and economic, in which these regimes operate. Thus, first, gene patents are most frequently for upstream inventions, while copyright usually protects works that are finished products. Thus if a collecting society wrongly prices a work, there may be an available substitute. At most a particular use of the work is frustrated. For a gene patent, there may be no substitute and, if the patent is an upstream patent for a research tool, a whole project may be frustrated and technical progress hindered. Second, the scope of a copyright work is in general less contentious than the scope of patented invention and so a copyright collecting agency can determine more easily whether a work has been used, than a royalty collecting clearinghouse could determine whether a patent has been. Third, members of a copyright collecting society generally have an interest in maximising the distribution of their work. We have seen that this may not be the case with patent holders, who may want to use their patents strategically to hinder the work of competitors. It is interesting that there is no copyright collecting society for computer programs, the copyright context most analogous in this respect. Fourth, the copyright collecting societies each control the use of very particular types of work in very particular contexts (mostly musical and literary works and mostly in relation to public performance and mechanical reproduction). Determining appropriate licences for those contexts is more straightforward than licensing gene patents that may be used for a variety of different purposes. This is another reason why the clearinghouse mechanism is most attractive in relation to specific uses of particular categories of invention. Fifth, pricing of copyright works licensed by a collecting society involves the pricing of substitutes and raises none of the complexities of pricing complementarities considered earlier. And the list goes on.

10.4 Conclusion

None of this is to suggest that there are not lessons to be learned from the copyright collecting societies. The way in which the copyright tribunals complement the work of the competition authorities is, for

[8] The term is often attributed to the case *Davoll v. Brown* 7 Cas 197 (1845) at 199, though Sherman and Bently cite other contemporaneous uses, B. Sherman and L. Bently, *The Making of Modern Intellectual Property Law,* Cambridge: CUP, 1999 at 95 fn 1.

example, very interesting. But it is to suggest that there are real difficulties in translating the copyright experience into the realm of patent.

Van Zimmeren's paper surveys the range of available clearinghouse mechanisms and explores ways that may be immediately achievable for reducing some transaction costs. None of what I have said should cast doubt on the desirability of clearinghouses that merely facilitate access. But it is important to recognise that doing so does not entirely solve potential problems of patent thickets and the anticommons. And I am more cautious than van Zimmeren seems to be, not only on the achievability, but on the desirability, of clearinghouses that attempt to do more.

REFERENCES

David, P. A. and Spence, M., *Towards Institutional Infrastructures for E-Science: The Scope of the Challenge* Oxford: Oxford Internet Institute Research Report No. 2, 2003

National Research Council of the National Academies – Committee on intellectual Property Rights in Genomic and Protein Research and Innovation, *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health* Washington: NAP 2003

Sherman, B. and Bently, L., *The Making of Modern Intellectual Property Law,* Cambridge: CUP, 1999, at 95 fn 1.

van Zimmeren, 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume

Walsh, J. P., Arora, A. and Cohen, W.M., 'Effects of Research Tool Patents and Licensing on Biomedical Innovation', in Cohen, W.M. and Merrill, S.A. (eds.), *Patents in the Knowledge-Based Economy,* Washington: NAP 2001

Part III

Open source models

12 Open source genetics

Conceptual framework

Janet Hope

12.1 Introduction

Intellectual property (IP) rights are most often thought of as regulatory tools employed by the state to facilitate bargaining and induce investment in the risky but socially valuable process of innovation. However, they can also be regarded as private regulatory tools that enable their owners to order markets by fixing prices and controlling the availability of protected goods and services. The strategic use of patents and other IP rights to discipline international markets was foreshadowed by free market economists more than a century ago, and has since been dubbed the 'knowledge game'.[1]

It is well established that IP rights can serve the public interest only if they strike an appropriate balance between upstream and downstream innovation. In the context of gene patenting, for example, the 'tragedy of the anticommons' is a familiar concept.[2] But the knowledge game is not predicated on a careful balance between the interests of initial and follow-on innovators. Rather, it depends on uniformly high standards of IP protection. The political history of international IP standard setting at the GATT Uruguay Round and beyond shows that the concentrated interests of elite knowledge game players are more than a match for the diffuse interests of those who engage in and benefit from downstream innovation. The outcome is a global IP ratchet in which minimum standards of protection are gradually pushed higher and higher, with little scope for downward adjustment.[3]

In light of this political reality, there is a need to study how private contracting can help mitigate the potentially adverse effects of broad

[1] Drahos, P., and J. Braithwaite, 'Chapter 3: The Knowledge Game', in *Information Feudalism: Who Owns the Knowledge Economy?*, London, Earthscan, 2002, 39–60.

[2] Heller, M. A. and R. S. Eisenberg, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research', **280** *Science*, 1 May 1998, 698–701.

[3] Drahos, P., 'Global Property Rights in Information: the story of TRIPS at the GATT', **13** *Prometheus*, 1995, 6–19.

patents on early-stage genetic inventions.[4] The formation of contract-based institutions such as patent pools, IP clearinghouses and open source licensing need not wait for domestic or international law reform. Similarly, while states may promote or facilitate such institutions, their existence does not depend on top-down interventions by state regulators. Private transaction-cost-lowering institutions have the advantage of being far more responsive to varied and dynamic local conditions than the relatively slow-moving, broad-brush instruments available to state actors. Further, active engagement in the design of cooperative solutions helps generate commitment to the resulting institutions on the part of industry participants and can lead to establishment of new channels of communication that enhance overall information flow. The success of such institutions in fields other than human genetics suggests that the use of IP rights as private regulatory tools is not limited to restricting competition and crushing or co-opting potentially disruptive innovation. It can also serve the opposite goal – that of enhancing broad access to knowledge, including the capability to use that knowledge in pursuit of a multiplicity of economically and socially beneficial activities.

Institutions designed to overcome the high costs of contracting for knowledge in a complex IP landscape may take an enormous variety of different forms. An underlying premise of this edited collection is that it makes sense to talk about diverse institutional forms as variations on a finite set of themes (patent pools, IP clearinghouses and so on). Despite the difficulties of working out a sensible taxonomy, this is a fair assumption because modelling – the translation or adaptation of solutions from one setting to another – has been shown to be a key driver of institutional innovation across a broad range of regulatory contexts.[5] Instead of designing new institutions from scratch, people tend to draw on ideas that are already out there, modifying them only to the extent necessary to suit their own projects and purposes. By floating a number of conceptually distinct models that differ from conventional or mainstream IP management, the contributors to this book are engaging in what John Braithwaite has called 'model mongering'.[6] Empirically,

[4] For a discussion of the role of private institutions in overcoming IP-related transaction costs, see Merges, R.P, 'Intellectual property rights and the new institutional economics', **53**(6) *Vanderbilt Law Review*, 2000, 1857–77 (Symposium: 'Taking Stock: The Law and Economics of Intellectual Property Rights').

[5] Braithwaite, J., and P. Drahos, *Global Business Regulation*, Cambridge, Cambridge University Press, 2000.

[6] Braithwaite, J., 'A sociology of modelling and the politics of empowerment', **45** *British Journal of Sociology*, 1994, 445–78.

model mongering plays an influential role in the modelling process, and hence in institutional innovation overall.[7]

The institutional form modelled here is that of 'open source'. Open source is an approach to technology development, IP licensing and commercialisation that has emerged within the software industry in response to conditions that parallel those now found in human genetics – namely, proliferating IP rights leading to restrictions on freedom of use and freedom to operate. The application of this model outside software has so far been mostly, though not exclusively, theoretical. In consequence, the modelling of open source in the context of life sciences research and development is perhaps not as advanced as the modelling of institutional forms with a longer history and a broader range of previous applications. Nevertheless, in recent years there has been an unmistakable groundswell of interest in open source biotechnology, and the modelling process is gathering momentum.

The chapter is structured as follows. First, the open source phenomenon is introduced in its original context of software development. Second, the essential elements of the open source model are identified in general terms that can be applied outside that context. Third, the chapter addresses a question that is consistently uppermost in the minds of people learning about the open source model for the first time: where does the money come from that would be needed to fund open source research and development in relation to genetic technologies? The chapter closes with some thoughts about how the real-world initiatives canvassed in other contributions to this book might fit into the conceptual framework presented here.

12.2 What is open source software?

In the early days of computer programming, most users wrote their own programs and exchanged source code (the form of software code that can be read and understood by human beings) according to the etiquette of a community made up of scientists and engineers employed in academic and corporate laboratories. As in the life sciences during the same period, there were few proprietary restrictions on sharing. Under these conditions there grew up a self-conscious community of 'hackers' – people who loved programming and enjoyed being good at it – to whom the unfettered exchange of technical information

[7] Braithwaite and Drahos, *Global Business Regulation*, 585–601.

represented both a fundamental necessity of professional creativity and the lifeblood of personal relationships.[8]

In the 1970s and early 1980s, things began to change. At the same time as life sciences research was undergoing its own transformation – marked in the US by the decision in *Diamond v. Chakrabarty*, the passage of the Bayh-Dole Act and the establishment of the Court of Appeals for the Federal Circuit – companies dedicated to producing proprietary software began to appear, triggering a diaspora of the best programmers from university laboratories and other public sector institutions. For the first time, restrictions were imposed on the sharing of source code. The result was a palpable loss of community among hackers.[9]

One who felt this loss most keenly was Richard Stallman, a member of the MIT Artificial Intelligence (AI) Laboratory. By Steven Levy's well-known account, Stallman went into deep mourning for the destruction of his beloved AI lab as it had once been, even to the point of telling people his wife had died and leaving them to discover for themselves that he was referring to the old lab culture instead of a real woman.[10] As he came to terms with his grief, Stallman determined to find a way of recreating the possibility for hackers to share source code across organisational boundaries.

The plan he eventually hit upon was the development of a suite of 'free' software. The word 'free' did not refer to price; rather, Stallman meant that software users should be at liberty to run a program for any purpose, to study how it works and adapt it to specific needs and to redistribute copies, as well as being free to improve the program and release those improvements. In other words, the software was to be '"free" as in "free speech", not as in "free beer"'.[11] The obvious starting point for this scheme was to create a free operating system. An operating system is the core computer program that tells other programs what to do; without it a computer cannot run. A free operating system would establish a platform on which other free software could be constructed – the foundation stone of a rebuilt community.

Stallman called the operating system project 'GNU', or '*G*nu's *N*ot *U*NIX'. The name was an allusion to the UNIX operating system, which existed in many incompatible proprietary versions and had become a symbol of the inefficiencies associated with proprietary restrictions

[8] For a classic description of the hacker community, see Levy, S., *Hackers: Heroes of the computer revolution*, New York, Penguin, 2001.
[9] *Ibid.* [10] *Ibid.*, p.425.
[11] See the Free Software Foundation web site, www.fsf.org.

on code-sharing. The GNU Project was launched in 1984, accompanied by the 'GNU Manifesto', a statement of purpose addressed to fellow programmers requesting their participation and support.[12] The Free Software Foundation (FSF), principal organisational sponsor of the GNU Project, was established the following year to promote the broader development and use of free software.[13]

One challenge to the success of the FSF's mission was the possibility that free software would be incorporated into proprietary (that is, non-free) applications. Of course, this would not prevent anyone from using the free version, but it would mean that contributors to the development of free software would have no guarantee of ongoing access to state-of-the-art technology – and would therefore be less likely to contribute in the first place. To overcome this incentive problem, Stallman devised an ingenious twist on the proprietary approach to software licensing. To appreciate his idea, it is helpful to first consider the proprietary approach.

Historically, software source code was not regarded as patentable subject matter, instead being protected under copyright law as an original work of authorship and as a trade secret. Vendors of proprietary software typically use both types of protection to stop competitors from imitating their products. The buyer of a proprietary software program – technically a licensee – generally receives only the binary or machine code version of the program; the source code is kept secret. Making modifications to a computer program, or using parts of the program code in another program, is very difficult unless a programmer has access to the source code. But even with such access, he or she would still be legally constrained by the terms of the copyright licence agreement. Under a typical proprietary software licence, the licensor retains the exclusive right to redistribute or modify the program and authorises the making of only a limited number of copies. Most licences also contain explicit restrictions on the number of users, the number of computers on which the program may be run and the making and simultaneous use of backups.[14]

Stallman's grand idea was to create a licence that would emphasise the rights of software users instead of software owners. He called this type of licence 'copyleft' because it had the opposite effects to those of a conventional copyright licence. (The copyleft symbol – a mirror image of the familiar circled 'c' of copyright – is often seen accompanied

[12] A copy of the GNU Manifesto is available at www.gnu.org/gnu/manifesto.html.
[13] Free Software Foundation website, www.fsf.org.
[14] von Krogh, G., and E. von Hippel, 'Special issue on open source software development', **32**(7) *Research Policy*, 2003, 1149–57.

by the caption 'all rights reversed', a play on the copyright slogan 'all rights reserved'.) With guidance from Eben Moglen, now a law professor at Columbia University and pro bono General Counsel for the FSF, Stallman drafted the archetypal copyleft licence – the GPL or 'GNU Public License', later renamed the 'General Public License'.[15]

Under the terms of the GPL, the copyright owner grants the user the right to use the licensed program, to study its source code, to modify it, and to distribute modified or unmodified versions to others, all without obligation to the owner. The only catch is that if the user chooses to distribute any modified versions, he or she must do so under these same terms. It is this final proviso that makes the GPL a copyleft licence, giving it its famous (or infamous) 'viral' character.

Part of the reason the GPL has gone such a long way to achieving its goal of creating a collection of usable code that grows over time as users contribute improvements back to the common pool is that it is a template licence. In other words, it can be applied by any programmer to his or her own code. In 1991, Linus Torvalds did just that when he released Linux, an operating system kernel built using tools made available by the FSF, to a usenet newsgroup. The first release of Linux was barely usable: according to Torvalds, it was 'a program for hackers by a hacker. I've enjoyed doing it, and somebody might enjoy looking at it and even modifying it for their own needs.'[16] But by the end of that year, close to one hundred people had joined the newsgroup, many of them active contributors to Linux's further development. By the end of the decade, GNU/Linux (that is, the Linux kernel together with other operating system elements supplied by the GNU project) was a major technological and market phenomenon, built from the voluntary contributions of thousands of developers around the world.[17]

Since then, Linux has become the flagship for an entire techno-social movement. Though based on 'free' software, this phenomenon is now generally referred to by a different term: 'open source'. Stallman wanted his fellow programmers to look beyond short-term expediency in their choice of programming tools, to see that the use of proprietary software raised serious ethical issues and to commit to providing and using an ethically acceptable alternative. To make his point he employed

[15] References in this paper to the 'GPL' are to version 2. Version 3 is currently in draft form.

[16] Torvalds, L., ¡torvalds@klaava.Helsinki.FI¿ Free minix-like kernel sources for 386-AT Article ¡1991Oct5.054106.4647@klaava.Helsinki.FI¿ in Usenet newsgroup comp.os.minix, 5 May 1991.

[17] Weber, S., *The Success of Open Source*, Cambridge, Mass., Harvard University Press, 2004.

the language of rights and freedom. But by the late 1990s, those who coined the term 'open source' wanted to see non-proprietary software more widely adopted, including in commercial settings, and they considered the language of freedom to be both confusing and unnecessarily alienating to businesspeople. In 1998, they established the Open Source Initiative as a certification body for open source licences and to advocate for the use and development of open source software as a mainstream commercial strategy.[18]

Whether as a result of this advocacy or because of deeper economic trends, both public and private sectors have embraced the use of open source software in a variety of forms. Open source software has penetrated government at all levels in countries around the world and is used for major enterprise applications by small businesses through to large corporations. Open source development is financially supported by several well-known companies, including IBM, and has been denounced by Microsoft as a serious competitive threat.[19] There are over one hundred thousand open source software development projects in existence, supporting a wide range of commonly used open source applications, many of which are crucial to the functioning of the Internet.[20] In the words of political economist Steven Weber, open source software is no marginal phenomenon, but a major part of the mainstream information technology economy – one that increasingly dominates those aspects that are becoming the leading edge in both market and technological terms.[21] It seems natural, then, to ask: could open source do for human genetics what it has done for software?

12.3. A generalised model of open source for the life sciences?

To provide a realistic answer to that question, it is necessary to come to grips with all of the technical, legal and economic differences between

[18] Perens, B., 'The Open Source Definition', in C. DiBona, C. S. Ockman, and M. Stone (eds.), *Open Sources: Voices from the Open Source Revolution*, O'Reilly, Online version, 1999, 1–11.

[19] V. Valloppillil, 'Open source software: A (new?) development methodology,' annotated version available on the Open Source Initiative website as 'Halloween Document 1 (Version 1.14)', 31 October–1 November, 1998, at www.catb.org/~esr/halloween/halloween1.html.

[20] The Sourceforge.net count of registered projects and users gives a first approximation of the size of the open source developer community: see http://sourceforge.net/. Open source software programs that help run the Internet includes Apache, Linux, FreeBSD and BIND.

[21] Weber, *Success*, 5.

the two fields.[22] Software code itself is quite different from any given genetic technology; moreover, the capital costs of development tend to be lower, the prevailing industry culture is generally thought to be less proprietary, and innovations are typically protected using different sets of exclusive rights. These and other differences need not constitute insurmountable obstacles to the translation of open source software principles into the life sciences. However, they do warrant detailed analysis. To conduct such an analysis – in other words, to decide which differences matter and which don't – it is necessary to construct a model of open source that distinguishes between features that are essential to its success and those that are merely incidental. Features that are essential must be preserved or translated to the new setting, while those that are incidental can be more freely adapted or even abandoned.

In software industry usage, the phrase 'open source' has several layers of meaning. It simultaneously denotes a defined set of licensing criteria, a somewhat more loosely defined development methodology and a largely undefined yet characteristic approach to commercial exploitation of technological innovations. Of these, licensing is fundamental: open source exploitation strategies rely on open-source-style collaborative technology development, which in turn relies on open source licences both as legal instruments and as embodiments of a social covenant.

What is the key to open source licensing? In the software context, the Open Source Initiative must certify software as 'open source' if it is licensed on terms that conform to the official Open Source Definition (OSD). The OSD itself is too long to reproduce here (the latest version is available on the Open Source Initiative website)[23]. However, an accepted summary is that a licence is open source if it allows anyone, anywhere, for any purpose, to copy, modify and distribute the software (where distribution takes place either for free or for a fee) without having to pay royalties to the copyright owner.[24] Note that there is no mention either in this summary or in the OSD itself of a copyleft-style obligation to make improvements available to other users. This is because a licence can be open source without including any such requirement. Copyleft licences, of which the GPL is just one example, are merely

[22] For an early discussion of these issues, see Burk, D., 'Open Source Genomics', **8** *Boston University Journal of Science and Technology Law* (Symposium on Bioinformatics and Intellectual Property Law, 27 April 2001, Boston, Mass.), 2002, 254.

[23] Open Source Definition Version 1.9, online at www.opensource.org/docs/definition.php.

[24] Rosen, L., *Open Source Licensing: Software Freedom and Intellectual Property Law*, New Jersey, Prentice Hall, 2004.

a subset of the overall class of open source licences, though they are among the best known and most widely used.

Of course, most genetic technologies are protected not by copyright but by a mixture of IP and other property and quasi-proprietary rights, patents being the most important. The technologies themselves are also more diverse than software programs with respect to both their material forms and the mix of tacit and codified information they incorporate. A faithful translation of open source licensing principles into the sphere of human genetics therefore requires more than a 'cut, paste and edit' from existing open source licences. Instead, it requires those who draft biotechnology licences to grasp the underlying policy objectives of the open source approach.

Three key objectives of open source licensing are (1) credible commitment, (2) competition and, optionally, (3) copyleft. All three features are designed to encourage follow-on innovators to contribute to cumulative development of open source technologies.

Credible commitment

Credible commitment essentially means that to be open source, a technology must be protected by IP or other proprietary rights and distributed on terms that are at least perceived to be legally enforceable. A technology that is made available under the open source model is not in the public domain, which has been described as a 'rough neighbourhood' where well-meaning scientists may get 'mugged' (i.e. have their inventions appropriated by others who have anticipated their work in a broad patent claim or who make improvements that the patent office, though not necessarily the scientific community, regards as patentable).[25] Rather, it is owned by the licensor, who makes a legally enforceable promise via the licence agreement not to interfere with others' freedom to use, improve or circulate the technology. The point is to assure potential users that their investment of time and resources in adopting the technology and making improvements to it will not be turned against them in a later 'IP ambush'. Without such assurance, potential users may be reluctant to invest in freely revealed technologies or contribute to further development, leading to poor uptake and/or unfulfilled downstream potential. The licence protects the licensee from the licensor, and the existence of a legally recognised property right protects both from third parties. This last point is important

[25] Jefferson, R., 'The BiOS Initiative biological open source as a new innovation paradigm', Public Seminar, CSIRO Black Mountain, 17 May 2006.

because an IP ambush need not come from the person who initially offers a new technology to users. For example, in the diagnostics context, a clinical researcher may develop a test and make it freely available to others without knowing that the relevant gene sequence is subject to patent rights. When the patent issues and is enforced, both the scientist and his or her colleagues may find themselves subjected to demands for licence fees or restrictions on administering the test.

Competition

Competition is the second key feature of open source licensing. In this context, competition refers to a level playing field between the licensor and other users or distributors of open source technologies with respect to the legal freedom to use and commercialise both the technology itself and any downstream innovations. (The sole permissible qualification to this statement regarding downstream innovations relates to copyleft licensing, discussed below.) An open source licence may not impose field-of-use or territorial restrictions, commonly used in proprietary licensing to protect the IP owner or other licensees from competition in a particular market segment. For example, a biotechnology licence granted 'for research and non-commercial use only' might be helpful to some researchers, but it would not be open source. Similarly, an open source licence may not impose a requirement to report to the licensor, or to disclose the means and manner of any internal use of the licensed technology. (In copyleft licences, it is external deployment, not internal use, which triggers the copyleft obligation to disclose source code.) An open source licence may not restrict the number of products a licensee is allowed to distribute, the identity or geographic location of the recipients, or the price the licensee asks them to pay – which may be anywhere from zero to the highest price the market will bear. The same goes for improvements or other downstream uses, with the qualification that under a copyleft licence, the licensee may be constrained to deal with others as he or she has been dealt with by the licensor. Any person to whom the technology is distributed may in turn become a licensee and exercise the same rights of distribution. As Steven Weber has remarked, open source licensing is based on IP, but it is a concept of property configured around the right to distribute, not to exclude.[26]

Seeing competition as central to open source licensing clarifies aspects of the model that might otherwise seem confusing, such as the common description of open source licences as 'royalty-free'. Open

[26] Weber, *Success*, 86.

source licensees must be free to use and distribute open source technologies or downstream innovations without payment of royalties to a licensor. This does not mean that a licensor cannot sell an open source technology or a product made using an open source process: commercial distributors of open source software routinely sell copies of their own software, together with open source software they have licensed from others, to paying customers. However, an open source licensing scheme ensures that anyone can become a licensee and every licensee is a potential distributor, so market pressure keeps prices down. In the software context, where commercial distributors must compete with distributors who charge nothing at all for access to the same technology, prices are likely to be lower than in biotechnology, where higher overall costs may mean fewer licensees are willing or able to offer gratuitous access to a second tier of users. Even a substantial fee may be perfectly compatible with open source principles, provided it is a one-off. What matters is that the fee structure must not create a continuing obligation that even in theory could give the licensor indirect control over the licensee's subsequent use or distribution of the technology.

The importance of free competition between open source licensors and licensees explains why the freedom to create a new branch of a collaborative development project, known in software as a 'code fork', is often regarded as the defining characteristic of open source. Under the terms of an open source licence, anyone who is dissatisfied with the conduct of a project leader – on technical, administrative, political or even purely personal grounds – is free to take the collaborative effort in a new direction. In practice, forking is rare, largely because the benefits are usually not worth the hassle and uncertainty of persuading others to join a new branch of the project. For example, where there are technical differences it is often easier to continue contributing to the main project and simply devote a few extra resources to tweaking the results to meet one's own needs. But the ever-present possibility of a fork makes project leaders responsible to their co-developers and ensures that no individual or group unduly dominates the process of technology development. Conversely, there is no danger that a potentially useful tool will be left on the shelf simply because of the waning interest or incapacity of an initial innovator.

In fact, open source project leaders do have considerable power to dictate the terms of collaboration, for example by excluding contributions that do not conform to their own vision for the outcome of the collaborative effort. It is also often the case that project leaders happen to be the initial innovators with respect to a given technology; a common practice is for an innovator to seed an open source development

project with his or her own IP, as Linus Torvalds did with Linux, and as CAMBIA has tried to do with its BiOS initiative, described elsewhere in this collection. All else being equal, it is natural for an initial innovator to remain in charge of ongoing development and to act as a champion of the technology. However, it is absolutely key to the open source approach that the initial innovator not use his or her ownership of the IP in that seed technology to retain control over its ongoing development or to insist on special rights such as obtaining a sneak preview of new contributions. Thus, an open source project leader's power is subject to the continuing confidence of other contributors, which may be withdrawn at any time, for any reason.

Copyleft

The final key aspect of open source licensing is copyleft, also sometimes known as 'reciprocity'. We have seen that copyleft licences impose an obligation on the licensee to make any downstream innovations that it chooses to distribute beyond the boundaries of its own organisation available under the same terms as the original technology. Such licences are also known as 'reciprocal' licences – a more general term intended to highlight the fact that in the context of cumulative technology development, open source licensors and licensees are likely to find themselves at different times on different sides of the same licence terms.[27] Unlike credible commitment and competition, reciprocity in this sense is a feature of some open source licences, but not all. An example of a non-reciprocal open source software licence is the Berkeley Software Distribution (BSD) Licence, which grants freedom to use and distribute the licensed technology subject only to a requirement that the licensee respect the author's moral right of attribution.

In the life sciences context, reciprocal open source licence terms have been likened to reach-through and grant-back provisions in proprietary patent licences, and it has been suggested that they may raise similar competition concerns.[28] However, this anxiety is unfounded because the analogy between such proprietary terms and copyleft (or patent-left) terms breaks down at the very point where conventional reach-throughs and grant backs become suspect. Consistent with the level playing field described above, an open source licensor gains no special

[27] Rosen, *Open Source Licensing*, 103ff.

[28] See Feldman, R. C., 'The Open Source Biotechnology Movement: Is it Patent Misuse?', **6** *Minnesota Journal of Law, Science and Technology*, 2004; Boettiger, S. and D. L. Burk, 'Open Source Patenting', 1 *Journal of International Biotechnology Law*, 2004, 221–231.

privilege in relation to downstream technologies distributed in accordance with an open source reciprocity requirement. The licensor may expect to benefit directly or indirectly from access to and freedom to operate with such technologies, but he or she does so only as a member of the public who is entitled to take a licence to the improvement on the same terms as anyone else. Open source reciprocity is not tit for tat; rather, it is a diffuse form of reciprocity of the kind known colloquially as 'passing it forward'.

It follows that any biotechnology licence that claims to be a reciprocal open source licence must not seek to retain any special privilege for the licensor in relation to improvements or other modifications to the original technology. Further, an open source licensor is prohibited from imposing conditions on the distribution of downstream technologies that would privilege a particular group, for example, licensees of the original technology. In this regard, open source licensing may allow fewer restrictions than would be permissible under competition law. For example, non-exclusive grant backs of licensee improvements are well known in conventional biotechnology licensing, and are commonly used to establish a club atmosphere that encourages cross-fertilisation of improvements among licensor and licensees so that a basic technology can continue to provide commercial advantage from which all parties benefit. In such a scheme, the original licence is non-exclusive; each licensee grants the licensor a non-exclusive, royalty-free right in any improvement developed by the licensee, together with the right to sublicense the improvement to other licensees of the same technology. The licensor circulates such improvements among all licensees on a royalty-free basis, with ownership in each improvement being retained by the party developing the technology. Such arrangements are generally considered harmless by competition authorities, and may even be favourable to innovation overall. But they are not open source.

In summary

'Credible commitment' is about providing potential follow-on innovators with legally enforceable rights so they will have the confidence to invest in the initial technology and incorporate it into new developments. 'Competition' is about what hackers call 'software freedom', which in the present context might be thought of as 'technology freedom' or 'gene freedom': the right to use the technology, improve on it, and sell or otherwise distribute either the initial innovation or one's own improvements without incurring any ongoing obligation to the technology owner. Finally, 'copyleft' licences seek to extend these

rights beyond the initial technology to follow-on innovations. A licensee who accepts a copyleft licence forgoes the usual right of excluding others from using any IP-protected improvements he or she might choose to distribute, but in return gains an assurance that he or she will have access to developments contributed by others.

12.4 Free revealing, or where does the money come from?

To this point, open source has been described as an approach to IP licensing that is designed to facilitate cumulative technology development by removing IP-related barriers to access and freedom to operate. From a social welfare perspective, the advantages of an open source approach are obvious. It is less obvious why a self-interested actor, such as a private biotechnology firm or public sector organisation that is expected to pay its own way, should be prepared to make the products of its R&D investments available to all-comers on such apparently altruistic terms. What is the economic basis of the open source model?

Open source business strategies often seem unworkable to patent lawyers and others whose professional lives have been devoted to playing the knowledge game, because the underlying assumption of the game is that any uncompensated spillover of proprietary knowledge developed by private investment must reduce an innovator's overall profits. This assumption implies that rational profit-seeking actors should not engage in 'free revealing' – that is, the voluntary disclosure of valuable technical information without direct compensation. In fact, however, many innovators do engage in free revealing; some even spend significant money and time to ensure that their innovations are seen in a favourable light, and that information about them is effectively and widely diffused.

While open source software licensing is perhaps the best known example of such active efforts to freely reveal proprietary information, routine, intentional free revealing has also been observed in a wide range of other commercial settings. Scholars in the field of innovation management have documented free revealing in relation to the development of methods for processing iron ore and pumping water out of mines in nineteenth-century Britain, the design of semiconductors and automated clinical chemistry analysers, the design of lithographic equipment and sporting goods such as mountain bikes and kitesurfers.[29] Free revealing among profit-seeking firms in industries where

[29] Von Hippel, E., *Democratizing Innovation*, Boston, MIT Press, 2005.

R&D is far more capital-intensive than it is in software development suggests that there are positive private rewards to be obtained from free revealing.

As noted earlier, open source licensing promotes innovation by making new technologies available on terms that allow users to make changes to the technology and to use or distribute the resulting modified versions or the technology itself as they see fit. This free revealing on the part of the technology owner enhances the value of the technology to users. Commercial exploitation of open source technologies involves the conversion of that enhanced value into private economic benefit.

How does free revealing on the part of a technology owner help to maximise its value to users? Open source tools are often technically superior because the development process is open to a diverse range of creative inputs and enables 'learning by doing' so that outputs are subject to more rigorous quality testing. Open source technologies are often cheaper and more accessible than proprietary tools because of the 'competition' aspect of open source licensing. They bring freedom from dependence on individual suppliers: something that large pharmaceutical companies, in particular, regard as advantageous. They can be adapted to suit the users' own needs and incorporated into other products without the need for time-consuming and unpredictable negotiations with the IP owner. All of these qualities are a direct consequence of the characteristics of open source licences.

Assuming that an open source approach enhances the attractiveness of a technology to users by improving its user-friendliness, quality, affordability or availability, how can these features be exploited for profit without restricting access to or freedom to operate with the underlying IP? The answer depends on the role that the technology plays in a licensor's overall business model. A licensor's relationship to the technology may be primarily that of a user, manufacturer, distributor, supplier of upstream inputs, or seller of complementary goods or services, or it may be a mixture of these. The decision to employ an open source exploitation strategy with respect to a particular technology may entail a shift in this relationship, for example from manufacturer to seller of complementary goods; but note that it does not imply that all of the technologies owned by that licensor must be open source.

Consider first the position of user-owners. Companies or other institutions (such as universities and public or private non-profit research institutions) that use a particular research tool as a core component of their business process or research programme can benefit directly from any improvement in the use value of the tool, for example through costs savings, efficiency gains or reduced R&D risk. For

example, a firm that conducts in-house gene sequencing as part of its overall R&D effort would benefit from improvements to sequencing technology. Pharmaceutical firms could benefit from improvements in chemical libraries, molecular synthesis techniques, protein assays, instrumentation for high-throughput measurement of biological assays, or data sets and analysis methods for predicting toxicological and other properties of selected molecules.

Clearly, this particular application of open source as a commercial exploitation strategy is only suited to fundamental enabling technologies that are not a source of competitive advantage for the companies involved. You're not going to find pharmaceutical companies releasing their latest blockbusters under open source licences. But there might be a place for open source where it complements proprietary business models by reducing costs, risks and product development time. Rather than open sourcing tools that are developed in-house, a big company might prefer to support open source development by universities and smaller firms. The SNP Consortium, while not an example of open source per se, was a concrete example of the same type of business logic at work in the pharmaceutical industry. To quote from the Consortium website, 'A high-quality, high-density SNP map is a research tool that will benefit everyone involved in genomic research. By collaborating, the members of the SNP Consortium will be able to create a commonly accepted SNP map more quickly, and with shared financial risk and less duplication of effort than if each company proceeded on its own.'

As for smaller firms, many biotechnology firms take a strongly proprietary approach to their IP on the basis that downstream users require a guarantee of exclusivity, but this need not always be the case. If the opportunity is big enough and the risk low enough, it may make business sense for downstream users to adopt and support an upstream technology that is not subject to IP rights. For example, as Arti Rai and her co-authors have pointed out, in the 1950s pharmaceutical companies were quite happy to take on drug development for the polio vaccine even though it was unpatented.[30]

It might be thought that the exclusive proprietary approach exemplified by the knowledge game has become too entrenched for a non-proprietary approach to be viable today. However, this overlooks the fact that the existence of an open source version of any given technology might sometimes be extremely useful as a competitive weapon.

[30] Rai, A., S. Maurer and A. Sali, 'Finding Cures for Tropical Diseases: Is Open Source an Answer?' *Public Library of Science: Medicine*, 2004. See also Smith, J. S., *Patenting the Sun: Polio and the Salk Vaccine*, New York, William Morrow & Co., 1990.

In the world of conventional IP exploitation, one player's R&D win is another's loss. In any given round of the knowledge game, the winner probably won't be interested in an open source approach. But the losers – who by definition outnumber the winners – may well be interested in supporting any new technological development that offers to erode the winner's competitive advantage. Open source offers a way to achieve this that may be more practicable than the ideal outcome for a profit-seeking firm, which is to become the new winner.

Of course, this calculation may also be made *ex ante*, and the institutional diversity of biotechnology industry participants means that open source may be used as a competitive weapon by non-profit as well as for-profit players. This dynamic was present in the case of the SNP Consortium, where researchers and pharmaceutical companies alike faced the threat that biotechnology firms would gain a proprietary stranglehold over a non-substitutable technical standard, and responded by working together to eliminate that possibility by placing the data in the public domain.

The benefits of an open source exploitation strategy for non-commercial players are discussed further below; but first, what about technology owners for whom the technology is valuable primarily as a product rather than a tool? How can they convert the improvements that might be gained by turning the technology over to a group of open source developers into profit for themselves?

One possibility is to leverage the improved use value of an open source technology to enhance the appeal of a complementary product. So, for example, a company like IBM that is primarily in business to sell hardware might distribute enabling software such as driver and interface code at no charge along with the hardware; the hardware is more valuable the better the data and the better the tools for manipulating the data. In biotechnology, the hardware could be a sequencer and the data analysis software might be open source. A non-software example would be if a manufacturer of microarray readers were to give away instructions for spotting microarrays in order to sell more readers: the fact that the information would be freely available would mean that overall use of arrays would increase.

Another possible income stream is the provision of services. In this model the technology is distributed on an open source basis in order to grow the market for the technology itself and associated offerings. Revenue is generated by selling the technology in a form that is easier or more convenient to use than the freely available version and by providing services such as training, consultancy, custom development, and after-sales support or accessories such as user manuals. This strategy is

well known in the software context, but it is actually more promising in the biotechnology context because the tacit, uncodified nature of much biotechnological information means that users of a technology may well be prepared to pay a premium in order to avoid some of the trouble and expense of optimising a published protocol.

A third possibility is to use an open source technology as a market positioner. For example, an open source product may generate little or no revenue, but could help to build the firm's overall brand and reputation, add value to conventional products, and increase the number of technology developers and users that are familiar with and loyal to the product line as a whole. Brand licensing and franchising are common business strategies that depend on good market positioning: in the open source context, both involve charging a fee for the right to use brand names and trademarks associated with technology that is itself open source. If – in what is admittedly an unlikely move – Affymetrix decided to open source its chip technology, an 'Affymetrix Inside' logo might be a successful branding exercise, even if others were able to make chips using Affymetrix technology.

How viable are all these strategies in real life? Interviews with participants in the Australian biotechnology industry suggest that they are perfectly viable under favourable conditions. For example, imagine a small company built around a patented genotyping technology whose main virtue relative to competing technologies is that it is cheaper to use. The company makes its technology available on liberal licensing terms akin to those employed by open source software developers. Instead of making money from licence fees, it offers genotyping services directly to plant breeders who work on particular crops. It also offers consultancy services to anyone who wants to 'port' the technology to new crops or other organisms. The licence terms leave the company open to competition in both markets, but because the technology is at an early stage of development, not many competitors have the know-how to compete successfully. Offering services allows the company to maintain that competitive edge by being on the spot as kinks are ironed out through trial and error in new use environments. At the same time, the company sells franchises to organisations in other parts of the world that might want to operate a similar type of business. The natural geographical segmentation of the market for crop-specific agricultural biotechnologies makes market segmentation using IP rights unnecessary. The key for this company is to serve small markets that are of no interest to larger players and in which a low-cost solution is attractive despite drawbacks, such as lack of automation, which would be a problem in more industrialised settings.

This example – hypothetical, but based on a real firm – is drawn from agricultural biotechnology. But we could imagine a similar scenario in human genetics; for example, where the technology in question is a diagnostic test. This time, let us suppose that the initial innovator works not for a private company but in the clinical laboratory of a non-profit organisation, such as a university or a hospital, that offers tests developed in-house on the basis of sequence information drawn from genetic studies of patients and their families. Let us further suppose that there are tens or hundreds of mutations associated with the relevant disease and that the current form of the test detects only some fraction of these, so that people whose test results are negative receive only a partial assurance that they are unlikely to be affected by the disease.

Clearly, the quality of the test – and hence the quality of the service the lab provides to patients, their families and the broader community – would be enhanced if it could be combined with tests developed elsewhere for other mutations associated with the same disease. There are also positive network effects to growing the user base in terms of reliability and quality assurance. Thus, the greater the number of laboratories that use the test and contribute to the creation of a more comprehensive version, the better for all. The marginal cost of developing the test itself, given that our hypothetical institution is funded to perform the underlying research in any case, is minimal. Further, the implementation of a new diagnostic test does not require the developer to clear the kinds of regulatory hurdles that make pharmaceutical development so capital-intensive. Thus, the argument that there would be no incentive or capacity to develop or improve the test in the absence of exclusive proprietary control or a high profit margin is not convincing in this context.

In fact, given that most of those who develop diagnostic tests are non-profit users rather than for-profit distributors, it's reasonable to assume that the net economic impact of a copyleft-style open source licence on a partial test for a complex genetic disease would be positive. Given a broad enough patent right on the initial licensed technology, a copyleft-style approach would protect all users from having to pay licence fees to subsequent developers in order to gain access to the most comprehensive version of the test. The only losers would be the few industry participants whose business model relies on obtaining licensing revenue from other test providers or charging monopoly rents. If it is considered desirable to encourage private research and development activity in the sector, such activity could be supported by the provision of services, complementary goods such as test kits or other revenue streams that do

not rely on controlling access to the test itself. The in-principle viability of such alternative revenue streams may be verified by a glance at the web page of any diagnostics company.

All of these observations point to the desirability and feasibility of implementing a copyleft-style open source licence in relation to diagnostic tests based on gene patents. One factor that at first glance appears to point the other way is the cost to the initial innovator of obtaining patent protection – necessary in order to be able to make a 'credible commitment' to other users, especially those who might contribute to the evolution of a more comprehensive or otherwise improved test. Patents are a much more expensive form of IP protection than copyright; a single patent costs in the order of USD 10,000, not including maintenance and enforcement. Clearly, the total amount paid in licensing fees to a submarine patent-holder by all users of a non-free technology can easily exceed this cost, but there is a collective action problem in inducing all those who would benefit from a copyleft-style patent licence to contribute to patent and licensing expenses.

However, there are several reasons why the high cost of patents relative to copyright protection need not prevent the application of the open source model in areas like the life sciences where patents are the prevalent form of IP protection. First, in some technology areas, the open source business strategies described above may bring in sufficient revenue to cover patent costs; if this seems incredible, consider that patent owners in some fields consider it profitable to grant royalty-free patent licences in order to have their licensed technologies included in industry standards. Second, recall that an open source licensor is in fact permitted to charge licensees whatever the market will bear, provided such a fee is a one-off. (In addition, there is no rule in open source against 'dual licensing' – that is, offering the same technology under both open source and proprietary licences.) Third, the open source model may be combined with other models such as the IP clearinghouse or collecting society models discussed elsewhere in this book. (Patent pooling is incompatible with the open source approach because a patent pool has a limited membership.) Finally, the financial support needed to cover patent costs might also be found among those who have an interest in promoting innovation in the field as a whole or in finding solutions to technological problems, as distinct from promoting a particular technological solution. Such players may be found in the public or private sectors, and they may or may not be profit-seeking. Governments and government funding agencies, private charities and disease-specific research foundations, patient subscriptions, insurance companies or nationalised health care providers, industry R&D

corporations, downstream users to whom solving a particular technical problem represents an overhead rather than a potential competitive advantage, all fall into this category.

12.5 From principles to practice: implementing an open source approach

This chapter has portrayed the prospects of translating the open source model into human genetics in a positive light; but the process is unlikely to be straightforward.

As an example, biotechnology licensing is inherently more complex than software licensing, and innovators in this field will not have the advantage enjoyed by their software counterparts of conducting their early experiments in open source licensing under the corporate radar. These considerations point to the necessity of enlisting lawyers and other technology transfer experts in licence development. Similarly, while in theory any IP owner can launch an open source project without first consulting potential contributors as to the terms of the licence agreement, in practice the project is much more likely to be a success if the task of building a technological community is taken seriously from the start – even before a licence is drawn up. In this context, there is a role for institutions such as PIPRA and Science Commons in facilitating the establishment of open source initiatives as part of their broader mission of promoting and supporting institutional innovation of the kind canvassed in this collection.

What of the remaining case study represented here, CAMBIA's BiOS initiative? BiOS has garnered considerable publicity as the most thoroughly implemented open source initiative in the life sciences arena so far. As such, it will no doubt be closely monitored by both proponents and opponents of the open source model. The BiOS licences, while not explicitly drafted as templates, may well be used for that purpose. It is likely that open source biotechnology initiatives will at least look to the BiOS example in designing their own institutional frameworks.

Yet the BiOS licences are not in fact open source by the analysis presented above; that is to say, if the technology in question were software, the Open Source Initiative would refuse to certify them and open source purists would refuse to adopt them. The fundamental reason is that the BiOS licences give the licensor too much control over downstream development of the licensed IP and technology. There is insufficient freedom to 'fork the code' – that is, to reject the licensor's leadership of the ongoing process of cumulative innovation. As noted above, this freedom is the core principle around which the entire open

source model is built, because without it, contributors to an open source project risk becoming unpaid workers on someone else's project instead of free participants in a mutually beneficial collaboration.

This is not mere pedantry, but a question of institutional design – of striking the right balance between owners and users. It may be that the BiOS initiative succeeds despite depriving licensees of the rights they could expect under a 'truly' open source licence. After all, there are many other institutional forms besides open source: the fact that a particular initiative deviates from key elements of the original open source design does not imply that it is doomed to failure or somehow illegitimate. But unless those deviations are explicitly shown to be driven by some generic technical, legal or commercial difference between software and the life sciences, the success or failure of the BiOS initiative should not be taken as a strong proof of the success or failure of the translation of open source into the life sciences context.

12.6 Conclusion

This chapter has outlined the key features of the open source model in terms that are sufficiently general to be applied outside software in the context of human genetics research and development. It also addresses one of the main concerns that arises in connection with this translation – the question of where the money would come from to support both technological innovation and IP-related costs under an open source regime. Finally, it suggests that implementation of the open source model in the context of human genetics, while feasible, is likely to require considerable input from licensing experts and others whose model mongering activities are carried on at a very practical level.

REFERENCES

Boettiger, S. and D. L. Burk, 'Open Source Patenting', **1** *Journal of International Biotechnology Law*, 2004, 221–31.

Braithwaite, J., 'A Sociology of Modelling and the Politics of Empowerment', **45** *British Journal of Sociology*, 1994, 445–78.

Braithwaite, J., and P. Drahos, *Global Business Regulation*, Cambridge, Cambridge University Press, 2000.

Burk, D., 'Open Source Genomics', **8** *Boston University Journal of Science and Technology Law* (Symposium on Bioinformatics and Intellectual Property Law, 27 April 2001, Boston, Mass.), 2002.

Drahos, P., 'Global Property Rights in Information: the Story of TRIPS at the GATT', **13** *Prometheus*, 1995, 6–19.

Drahos, P., and J. Braithwaite, 'Chapter 3: The Knowledge Game', in *Information Feudalism: Who Owns the Knowledge Economy?*, London, Earthscan, 2002, 39–60.

Feldman, R. C., 'The Open Source Biotechnology Movement: Is it Patent Misuse?', **6** *Minnesota Journal of Law, Science and Technology*, 2004.

Heller, M. A., and R. S. Eisenberg, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research', **280** *Science*, 1 May 1998, 698–701.

Levy, S., *Hackers: Heroes of the computer revolution*, New York, Penguin, 2001.

Merges, R.P, 'Intellectual property rights and the new institutional economics', **53**(6) *Vanderbilt Law Review*, 2000, 1857–77 (Symposium: 'Taking Stock: The Law and Economics of Intellectual Property Rights').

Perens, B., 'The Open Source Definition', in C. DiBona C. S. Ockman and M. Stone (eds.), *Open Sources: Voices from the Open Source Revolution*, O'Reilly, Online version, 1999, 1–11.

Rai, A., S. Maurer and A. Sali, 'Finding Cures for Tropical Diseases: Is Open Source an Answer?' **1** *Public Library of Science: Medicine*, 2004.

Rosen, L. (ed.), *Open Source Licensing: Software Freedom and Intellectual Property Law,* New Jersey, Prentice Hall, 2004.

Smith, J. S., *Patenting the Sun: Polio and the Salk Vaccine*, New York, William Morrow & Co., 1990.

Von Hippel, E., *Democratizing Innovation*, Boston, MIT Press, 2005.

von Krogh, G., and E. von Hippel, 'Special issue on open source software development', **32**(7) *Research Policy*, 2003, 1149–57.

Weber, S., *The Success of Open Source*, Cambridge, Mass., Harvard University Press, 2004.

13 Case 8. CAMBIA's Biological Open Source Initiative (BiOS)

*Nele Berthels**

13.1 Introduction

CAMBIA is a private non-profit research institute unique in its kind. Located in Canberra, Australia, CAMBIA is not only developing new life science technologies, but also pioneering new business models driven by its mission to increase fair access to the tools of innovation as a fundamental human right.[1] Founded by molecular biologist and social entrepreneur Richard Jefferson about fifteen years ago, CAMBIA has been applying new practices both in life sciences and IP management to foster innovation and collaboration throughout the developed and developing world.

The reason behind this mission is at least two-fold: humanitarian and economical. The crushing reality that the world is faced with an estimated four billion people living in extreme poverty, hints to structural problems at many levels.[2] CAMBIA advocates sustainable and equitable development through active participation of developing countries so that their needs can be addressed. A prerequisite is that the working tools are made available and accessible to all.

Access to these tools in the field of life sciences seems to be increasingly hampered by high levels of patenting, broad scope of patents and restrictive licensing.[3] All players in the field of innovation appear to be affected. Even purely academic scientists experience the effect of licensing on new techniques and might not be immune from patent infringement, although this has yet to emerge as a significant impediment to their activities.[4] Moreover, concern is raised that inventions

* This chapter was researched through interviews with Richard Jefferson.

[1] CAMBIA BiOS Initiative – Biological innovation for Open Society. Open Source, Open Science, Open Society. Implementation phase 2006–2008. January 31, 2006. Available at www.bios.net.

[2] CAMBIA BiOS Initiative – Biological innovation for Open Society.

[3] Editorial, 'Open-source Biology', **431** *Nature*, 2004, 491.

[4] Yancey, A., and Stewart, C.N., 'Are University Researchers at Risk for Patent Infringement?', 25 *Nat. Biotechnol.*, 2007, 1225–8. Centre for Intellectual Property Policy (CIPP), 'The Research or Experimental Use Exemption: a Comparative Analysis.'

from publicly funded research projects are increasingly being acquired by private companies or licensed exclusively. Large companies tend to spend enormously to acquire extended IP portfolios without necessarily gaining the freedom to operate they need. Such portfolios are typically used in cross-licensing negotiations, effectively excluding small players with no such bargaining chips. This strategy has been likened by Jefferson to 'mutually assured destruction (MAD) by patent estate'. Cross-licensing is also preferred for its effects on marketplace perception, with heavy involvement in IP litigation usually ill perceived by the public. More enlightened large companies therefore realise there might be an alternative solution to do business, or to complement their actual business.

Do patents hamper access to enabling tools in developing countries? Probably not directly. Patents on research tools are mostly granted in developed countries. Nevertheless, patent protection generally goes hand in hand with price increases, thereby hitting developing countries particularly hard.[5] Do patents hamper research on technology that is specifically relevant to developing countries? Probably not directly, either. However, the economic implications of patenting, and existing patent law and regulations, do not particularly stimulate research in the interest of developing countries.[6]

Efforts to stimulate development-orientated research were initiated in 2004 when CAMBIA received support from the Rockefeller foundation and IBM to establish the Biological Innovation for Open Society (BiOS) Initiative.[7]

BiOS develops, promotes and validates new tools for continuous invention, improvement and delivery of biological technologies.[8] 'Biological innovation' is interpreted as innovation in the life sciences, encompassing agriculture and medicine in the broadest sense. The technology available to BiOS users aims at encouraging innovations in these fields.

Inspired by the open source software movement where operating systems, programming languages and standards are shared and continuously improved by the open-source software community, CAMBIA's 'Open Society' initiative strives to make research tools freely available

CIPP Publications, 2004. Available at www.cimcgill.ca/data/publications/00000007.pdf.

[5] Commission on Intellectual Property Rights, 'Integrating Intellectual Property Rights and Development Policy', 2002, Available at www.iprcommission.org.

[6] Ibid.

[7] Dennis C. 'Biologists Launch "Open-Source Movement"', **431** *Nature*, 2004, 494.

[8] About BiOS. Available at www.bios.net.

under open source licenses. A clear distinction is made between research tools that are to be made available open source, and the applications created by those tools, that can be commercialised on a competitive and proprietary market under non-open source conditions.

Using Internet communications tools and open source instruments, BiOS promotes a paradigm shift in biotechnology at three levels: creating transparency in IP information through Patent Lens, developing cooperative open access technology through BioForge, and creating 'innovation system structural reform' through the BiOS Licenses.[9] In this chapter, the three main BiOS activities will be discussed in further detail.

13.2 Main BiOS activities

Patent Lens

Patent Lens[10] is a free online resource designed to provide transparent information related to patenting. Originally limited to life science patents, Patent Lens now includes patents in all fields of technology. Its free, searchable patent database incorporates data from WIPO, USPTO, EPO, IP Australia, and over seventy national patent offices. It includes full-text patent documents and information on patent family and legal status. Patent databases of China, Japan and Korea are yet to be included. Patent Lens is BiOS's answer to commercial providers of patent information such as Derwent™, Delphion™ and MicroPatent™ which were recently all incorporated into The Thomson Corporation, with market monopolizing consequences.[11]

Patent Lens also provides tutorials on IP, information on patent policies and practices, and actual news and views, for example, on the complex linkages between trade policy and innovation systems in the light of TRIPs and country-specific enforcement mechanisms.[12]

Patent Lens further provides IP landscape papers on key platform technologies, thereby focusing on freedom to operate in commentable, reader-updateable interfaces.

Navigating IP landscapes in high-tech industries such as biotechnology requires highly specialised legal expertise that is very expensive.

[9] The CAMBIA BiOS Initiative – Biological innovation for Open Society. Implementation phase 2006–2008.
[10] www. patentlens.net.
[11] The CAMBIA BiOS Initiative – Biological innovation for Open Society. Implementation phase 2006–8.
[12] Ibid.

Through Patent Lens, BiOS attempts to elucidate some of the complexity of patenting, and reduce its costs. It reckons that clear and reasonable strategies are prerequisites to limit financial risk and legal exposure, irrespective of the company's size. It is, however, unlikely that Patent Lens can substitute legal and professional advice provided by patent attorneys and lawyers, but it may nevertheless act in a complementary manner.

Efforts to enhance access to patented technology have resulted in the pooling of patents in pre-competitive 'commons'.[13] Patent pools have been established in IT and electronics, and have been proposed for biotechnological inventions.[14] Yet, BiOS wants to go one step further because 'cooperative innovation by beneficiaries of the pool can be an effective tool to forge a robust commons only when empowered by transparency and definitive knowledge of the true technology patent landscapes'. Open source's low transaction costs are certainly beneficial. However, CAMBIA reckons that a vulnerable point is the lack of clarity on the value of patents included in the pool, and the possibility that a critical patent be excluded from the pool or may arise later rendering the pool useless and irrelevant.[15]

BiOS wants to address these issues by evolving Patent Lens into 'a facility for generating, linking and dynamically annotating patent landscape analyses through web interfaces by distributed and diverse users' and to provide high-level decision support based on those landscapes and their embedded knowledge.[16]

BioForge

BioForge is an online information portal for open source biotechnology projects analogous to the Sourceforge.net open source software repository.[17] BioForge aims at catalyzing 'a large community of innovators to produce high quality and relevant biological technologies for the empowerment of diverse problem-solvers in the developed and developing world, and secure these technologies in a new, protected, universally-accessible commons'.[18]

[13] Jefferson, R., 'Science as Social Enterprise: The CAMBIA BiOS Initiative', **1** *Innovations: Technology, Governance, Globalization*, 2006, 13–44.
[14] Verbeure, B., van Zimmeren, E., Matthijs, G., and Van Overwalle, G., 'Patent Pools and Diagnostic Testing', **24** *Trends in Biotechnology*, 2006, 115–20.
[15] The CAMBIA BiOS Initiative. [16] Ibid.
[17] BioForge: an online community for biological innovation. Available at www.bioforge.net.
[18] Ibid.

BioForge offers alternatives to existing patented technologies and strives to develop new technologies that particularly target developing countries' needs. Some current BioForge portfolios include:

- the 'Crop Molecular Enabling Technologies' portfolio on CAMBIA's TransBacter™ plant transformation system to bypass the patent-stacked Agrobacterium-mediated gene transfer technology, and the GUS™ and GUS-PLUS™ reporter-gene system to screen for transgene behaviour, resp. The pCAMBIA transformation vectors were developed to be compatible with these technologies;
- the 'Genetic Resource Analysis' portfolio build around CAMBIA's Diversity Array Technology (DArT™) to analyse genomes and enhance molecular breeding activities. This technology is currently used commercially by licensees in the plant and animal breeding industry;
- the 'Cancer diagnostics and therapeutics' portfolio build around CAMBIA's recently acquired patents covering key aspects of the use of the human telomerase gene and proteins for cancer diagnostics and therapeutics.

Future BioForge portfolios are envisioned on homologous recombination (HARTs),[19] apomixis,[20] and medical and agricultural diagnostic systems. The latter includes the first commissioned project on BioForge, supported by the Lemelson Foundation, relating to bio-indicators that allow farmers to make independent, informed decisions on crop growing, pest control, sensible use of fertiliser etc.

The open source philosophy of BiOS entails that all BioForge portfolios and related know-how are available for use by anyone who agrees to the terms of the BiOS License, however as with all patent licenses, freedom to operate cannot be ensured as dominating patents may exist or arise. This is a fundamental challenge in creating a commons.

While at first glance, with over 2000 users registered on the BioForge, it seems a tentative success. But there are few if any new projects or much substantive research work product emerging on the publicly available site. It is worth asking whether the scientific community has really bought into the concept and whether there are improvements that must be made.

[19] Homologous Allelic Recombination (or Replacement) Technologies (HARTs).

[20] In botany, apomixis is an uncommon but naturally occurring form of asexual reproduction. Apomixis seeds are clones of the mother plant. Introducing apomixis in plants could be used to avoid the 'terminator technology' by which genetically modified plants adopt a suicide mechanism in their second generation seeds.

BiOS Licenses

The exploration, validation and promulgation of BiOS Licenses is BiOS's third level of activity. Today, a growing number of institutions and companies, including BASF,[21] use BiOS Licenses. In this legally binding agreement, enabling technologies, e.g. of BioForge's portfolios, are available worldwide and royalty-free for all, based on the following non-exhaustive elements:[22]

- All licensing agreements are non-exclusive.
- An owner of technology made available for use under a BiOS-compliant agreement, or an improvement to such technology, may not assert IP rights over that technology or improvement against any other entity that abides by the terms of a BiOS-compliant agreement.
- All BiOS licensees covenant to share improvements, making them available for use, even though they may be patented, to all other BiOS licensees.
- Participants share biosafety data and any other information needed to meet regulatory requirements for use in commercial products.

Open source licensing typically expects that licensees may sublicense to an infinite number of sublicensees under the same conditions. This facilitates 'viral' spreading as exemplified in open source software, and embodies the 'access to all' philosophy. BiOS designed a protected commons for open access and sharing of both patented and non-patented technology,[23] while the ownership of technology remains with the owner. The protected commons allow non-public disclosure among BiOS licensees meaning that information is shared on confidential grounds without risking invalidation of future patent applications or misappropriation of information by third parties.[24] Cornerstones of the protected commons are the BiOS License and associated support and material transfer agreements covering both patented and unpatented enabling technology, as well as know-how, materials, biosafety data and data needed for regulatory approvals.[25]

The BiOS License demands that improvements made to enabling technology – which are protected by IP – are shared among other BiOS licensees, but the products or materials made, created or obtained by using an enabling technology, do not fall under this provision. A clear

[21] Richard Jefferson on Swiss TV. 2007 World Economic Forum, Davos, Switzerland. Available at www.cambia.org.
[22] About BiOS (Biological Open Source) Licenses and MTAs. Available at www.bios.net.
[23] Ibid. [24] BiOS Agreement FAQs. Available at www.bios.net. [25] About BiOS.

distinction is made between 'Improvements' and 'Products' to assure that there is a continuous improvement of the core toolkit through sharing of technical improvements 'while still being as supportive as possible to entities involved in delivering products to the marketplace, whether via for-profit or public good mode'.[26]

The BiOS License does not prevent any party from patenting improvements made to BiOS-licensed technology. However, these patented improvements have to be granted back to the licensor and to all other BiOS (sub)licensees under the same open source conditions. This 'grant back' concept strives to guarantee the use of improvements without infringing IP rights.[27] However, CAMBIA takes steps to educate licensees and users of unanticipated or looming freedom to operate issues that could dominate the rights granted under a BiOS agreement. Grant back will only fully contribute to BiOS 'viral' character when complete alternative technology platforms become available.[28] Currently, researchers have to complement enabling technology obtained under open source conditions with regularly patented and licensed technology.[29] The owners of the latter might disagree on open source licensing of improved enabling technology which incorporates their technology.[30]

The BiOS License does not impose an obligation to patent improvements or maintain patents, but patenting can nevertheless be requested as well as supported by BiOS's contributors. Indeed, strategic patent applications and patents are an essential part of the BiOS License's enforceability, 'just as legally enforceable copyright is at the foundation of the University of California Berkeley-based open source Berkeley Software Distribution (BSD) license'.[31] Access to technology under open source conditions only makes sense when malpractices are discouraged. Therefore, it is crucial to BiOS and the owners of technology to enforce patents and litigate infringers who are not agreeing to the BiOS license. BiOS therefore has to ascertain substantial financial means to obtain and enforce their patent portfolio.

In order to sustain and maintain BiOS's services the 'Technology Support Services Subscription Agreement', entitling BiOS licensees to receive licensed material, aims at covering some of the costs involved. To

[26] Researchers & Non-profits FAQs. Available at www.bios.net. [27] About BiOS.
[28] Boettiger, A., and Wright, B.D., 'Open Source in Biotechnology: Open Questions', **1** *Innovations: Technology, Governance, Globalization,* 2006, 45–57.
[29] Chilton, M., 'Adding Diversity to Plant Transformation', **23** *Nat. Biotechnol.*, 2005, 309–310.
[30] Boettiger, A., and Wright, B.D., 'Open Source in Biotechnology: Open Questions.'
[31] www.opensource.org/licenses/bsd-license.php.

academic and non-profit institutions, these costs are 'solely to cover for the costs of production and distribution'.[32] Moreover, 'cost recovery for non-profit institutions, small and medium enterprises, and institutions in disadvantaged locations may be partially or completely covered by in-kind support of various sorts such as making infrastructure available for cooperative research, exchanges of staff, helping a student etc.'.[33] For-profit licensees are asked to pay a non-compulsory annual fee 'at rates related to the size of the enterprise', for at least three years, with a suggested fee schedule posted as a public access document. However, companies that cannot afford the suggested fee can make an in-kind contribution, e.g. by offering traineeships.[34]

Despite the associated cost for obtaining material, BiOS believes that businesses using BiOS's open source facilities can make the necessary profit due to cost savings on accessing technology, litigation and developing early-stage innovation. However, their willingness to provide licenses in the absence of such a Support Agreement, if not materials, shows a flexibility to accommodate the diversity of private sector capabilities.

13.3 Conclusion

Problem-solving mechanisms resonant with the open source philosophy may hold promising benefits for the economic sectors which could benefit from biotechnology, and the community at large. A critical point of CAMBIA's BiOS Initiative is the drafting of 'open' licensing agreements while safeguarding proprietary information in a protected commons with a view to increasing the leverage and protection over that commons. Some regard BiOS's approach not as pure open source since CAMBIA relied on grants from foundations to develop the technology rather than on volunteers.[35] BiOS is also criticised for violating software's core principle of open source by not providing the licensee with enough freedom to reject the licensor's leadership over downstream development of the licensed technology.[36] CAMBIA accepts such criticism as indicative of a naïve expectation that one size fits all.

[32] BiOS Materials Request Form. Non-profit institutions only. Available at www.cambia.org.
[33] BiOS Agreement FAQs. Available at www.bios.net.
[34] About BiOS Agreements. Available at www.bios.net.
[35] 'The Triumph of the Commons: Can Open Source Revolutionise Biotech?' *The Economist*, Feb 10, 2005.
[36] Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume. Also see Boettiger, A., and Wright, B.D., 'Open Source in Biotechnology: Open Questions'.

As biological innovation, biotechnology and software are drastically different in many aspects,[37] a different approach regarding open source licensing could be justified but should nevertheless strive for mutual gain in order to succeed. Yet, BiOS wants to make open source work where both fields meet: at the level of enabling technologies, the toolbox that BiOS sees as increasing innovation efficiency when freely accessible to all. Products or services, to the contrary, can be commercialised and theoretically sold with lower costs and a lower legal exposure.

Costs associated with innovation using biotechnology are currently high. It is therefore likely that funding from philanthropic organisations and governments to address agricultural and health problems in developing countries remains vital. However BiOS's approaches of transparency and leverage through creation of platform public resources may make such expenditures more efficient and effective, and ultimately may drive such costs down.

Open source biological innovation is a relatively novel concept with CAMBIA's BiOS Initiative currently being in an implementation and exploration phase. As a new kid on the block, there are already positive signs of successful participation from research institutes worldwide, as well as from some large companies who engage in BiOS licensing. Hence, BiOS has already proven that some large players in the field are willing to shift paradigms, or at least make tentative explorations in this arena. In recent years, BiOS also engaged in joint ventures with the International Rice Research Institute (IRRI)[38] and with funding from the Rockefeller Foundation and the Government of Norway it has created and provided the informatics platform – gratis – that underlies the Public Intellectual Property Resource for Agriculture (PIPRA).[39]

At present CAMBIA's most popular services are the widely respected and broadly used Patent Lens, and the provision of pCAMBIA transformation vectors to researchers worldwide under open source conditions and therefore at a nominal cost. The challenge CAMBIA faces is to continue teaming up with large players in the biotech field to invigorate credibility.

To really evaluate the full potential, early successes booked with open source in biotechnology have to be further sustained, complementary to the existing business models, and to serve as inspiration or enablers of new business models in biological innovation. However, the concepts articulated by CAMBIA's BiOS Initiative, and the Patent Lens really

[37] Bains, W., 'Open Source and Biotech', **23** *Nat. Biotechnol.*, 2005, 1046.
[38] Press release of December 13, 2005. Available at www.irri.org/media/press/press.asp.
[39] www.pipra.org.

are sector agnostic, and both information from, and engagement with diverse innovation requirements across sectors may bring the critical mass of experience and practitioners together.

REFERENCES

Bains, W., 'Open Source and Biotech', **23** *Nat. Biotechnol.*, 2005, 1046.

Boettiger, A. and Wright, B.D., 'Open Source in Biotechnology: Open Questions', **1** *Innovations: Technology, Governance, Globalization*, 2006, 45–57.

Centre for Intellectual Property Policy (CIPP), 'The Research or Experimental Use Exemption: a Comparative Analysis', CIPP Publications, 2004 (available at www.cipp.mcgill.ca/data/publications/00000007.pdf)

Chilton, M., 'Adding Diversity to Plant Transformation', **23** *Nat. Biotechnol.*, 2005, 309–10.

Commission on Intellectual Property Rights, 'Integrating intellectual property rights and development policy', 2002 (available at www.iprcommission.org)

Dennis C., 'Biologists Launch "Open-Source Movement"', **431** *Nature*, 2004, 494.

Editorial, 'Open-source Biology', **431** *Nature*, 2004, 491.

Hope, J., 'Open Source Genetics: A Conceptual Framework', Chapter 12 of this volume.

Jefferson, R., 'Science as Social Enterprise: The CAMBIA BiOS Initiative', **1** *Innovations: Technology, Governance, Globalization*, 2006, 13–44.

'The Triumph of the Commons: Can Open Source Revolutionise Biotech?', *The Economist,* Feb 10, 2005.

Verbeure, B., van Zimmeren, E., Matthijs, G., and Van Overwalle, G., 'Patent Pools and Diagnostic Testing', **24** *Trends in Biotechnology*, 2006, 115–20.

Yancey, A., and Stewart, C.N., 'Are University Researchers at Risk for Patent Infringement?' **25** *Nat. Biotechnol.*, 2007, 1225–1228.

WEBSITES

CAMBIA BiOS Initiative – Biological innovation for Open Society (available at www.bios.net)

Patent Lens: a free online patent information resource (available at www.patentlens.net)

BioForge: an online community for biological innovation (available at www.bioforge.net)

14 Case 9. Diversity Arrays Technology Pty Ltd. (DArT)

Applying the open source philosophy in agriculture

Andrzej Kilian

14.1 Background

Diversity Arrays Technology Proprietary Limited (Pty Ltd) was founded in 2001 in Canberra, Australia, with support from the Biotechnology Innovation Fund of the Federal Government's 'Backing Australia's Ability' program. The company was set up as a wholly owned subsidiary of CAMBIA, a non- profit research institute based in Canberra, as one of the mechanisms to deliver this author's invention, Diversity Arrays Technology (DArT). After nearly two years of operating with this status, the company became privately owned in July 2003 with the mission of improving the efficiency of using natural resources through modern genetic and information technologies. At the time of writing, the company continues to focus on development and delivery of DArT under an 'open source'-style licence. More recently the company has been moving towards more general genetic analysis services with increasing investment in informatics tools. At the same time, pressured by a significant increase in demand for its technology and services, the company is investing more resources in the international expansion of operations through creation of a network of similar organisations in several countries. This case study for 'open source' licensing constitutes a practical demonstration of the viability of service-based, non-proprietary business models in the field of biotechnology.

History

The roots of the company are strongly aligned with the initial stages of development of its main technology platform – DArT. In my role as Director of Genomics in CAMBIA I was charged with the task of developing technologies relevant to less developed countries' agriculture. With a background in population and molecular genetics, I perceived

a big opportunity for whole-genome profiling to positively impact crop improvement but required appropriate instrumentation to develop a proof of concept for my invention of 'genotyping by hybridisation'. It was made possible when my small team received low-cost microarray equipment from Genetic Microsystems (GMS) Inc. as part of a beta-testing arrangement and we tested the technology using rice genome in 2001.[1]

With this proof of concept in hand, some support from one of the Australian Government's R&D corporations (the Grains Research and Development Corporation – GRDC) and a modest philanthropic donation to CAMBIA from the Rockefeller Foundation for further development of DArT, we successfully applied for project support to the Biotechnology Innovation Fund, part of the Australian Federal Government's 'Backing Australia's Ability' programme. Together with several small research grants this modest 'seed money' helped to establish DArT PL, albeit still fully integrated within the management structures of the parent organisation.

Technology

DArT was developed to complement existing technologies for DNA polymorphism detection and quantification. Its success can be mainly attributed to the ease and very low cost of marker discovery, elimination of assay development costs and the low cost of data production, offering an affordable genome profiling option for practically any organism.[2]

The major enabling component of DArT is the use of complexity reduction systems and utilisation of 'genomic representations'. The collection of samples representing the genome (its 'genepool') is processed using a combination of restriction digestion and amplification, the fragments from such representation are individualised (usually cloned in bacteria) and individual fragments arrayed on a solid support. The main platform for practicing DArT is 'microarray' technology, comprising as the dominant components (1) a spotting device (arrayer) used to create arrays of thousands of microscopic 'spots' of DNA and (2) a scanner, a high resolution imaging device capable of detecting the outcomes of hybridisation of fluorescently labelled nucleic acids (targets) to the microarray of DNA 'probes'.

[1] Jaccoud, D., Peng, K., Feinstein, D., and Kilian, A., 'Diversity Arrays: a Solid State Technology for Sequence Independent Genotyping', **29** *Nucleic Acids Res.*, 2001, e25.

[2] Technical details explaining DArT with many practical examples are available at www.diversityarrays.com/ and in many papers we and our users have published over the last few years.

For those with any DNA marker experience the technology can be simply described as 'parallel reverse Southern blot' or 'parallel reverse Restriction Fragment Length Polymorphism (RFLP)', as DArT shares with RFLP both the hybridisation-based marker detection and polymorphism detection based primarily on the pattern of restriction enzyme digestion. The use of restriction enzymes which show very high level of specificity and robustness is the main reason for high data quality of DArT assays. Importantly, DArT removes practically all limitations of RFLP technology, mostly the slow, low plex, technically demanding assay which translated to high cost and limited throughput.

Patents

The critical formal IP for practicing DArT technology is encapsulated in one patent family called 'Genotyping by hybridisation' (US Patent no 6,713,258 B2, Australian patent no AU 2001260520 B2, New Zealand Patent no 521626, patent pending in additional countries). The patents cover the field of highly parallel genetic analysis based on the use of complexity reduction methods in combination with nucleic acid hybridisations. While initially owned by CAMBIA, during the preparation of this case study for the present book the patent family was reassigned from CAMBIA to Diversity Arrays Technology Pty Ltd. This change in ownership will not have practically any impact on the technology delivery process, as DArT PL will maintain its current licensing and business models as described below.

14.2 Licensing

In order to understand the licensing aspects of DArT one needs to remember that this technology was invented when I was working in CAMBIA. CAMBIA's general licensing policy was non-exclusivity and DArT was supposed to be licensed to users under this condition. In fact the initial arrangement gave Diversity Arrays Technology Pty Ltd exclusive rights in the developed world when the company was wholly-owned by CAMBIA. However, the intention always was to keep the technology generally accessible through non-exclusive licensing and exclusive rights were removed when DArT PL became privately owned.

While separating their operations in June 2003 DArT PL and CAMBIA agreed to offer parallel licensing based loosely on 'open source' principles, more specifically on the idea that improvements to the technology should be subject to a 'grant back' provision from

licensees to whichever organisation had been the source of the licence.[3] The idea of including grant back provisions in the licence was based on the assumption that the initial technology developers/inventors could play an important role in the future technology development. Under this arrangement CAMBIA offers DArT through its BIOS initiative (www.bios.org) while we at DArT PL are offering a licence to practise the technology in the context of a complete technology package (software tools, know-how/training, libraries of markers etc.).

Since the separation of CAMBIA and DArT PL the legal team at CAMBIA/BiOS has developed a licence for DArT that is promoted as an open source licence. While the strict adherence of CAMBIA's BiOS licences to open source principles has been publicly questioned,[4] the licence does offer access to the technology as in the original agreement with DArT PL. However, as the list of BiOS licensees is not publicly available it is impossible to judge the extent of DArT's uptake or development through this channel.

One sense in which DArT PL is adopting an open source approach is that it is not using its IP as a means of excluding competition, but rather to attract partners for joint delivery of the technology in new market segments (new applications or new geographic regions with little penetration). This is quite different from a traditional biotechnology company's approach, but is an important component of the overall business model.

The operation of DArT PL (and its network) does not require control over IP, but it does depend on ensuring freedom to operate (FTO). Based on our review of the IP landscape and the lack of any challenges to our FTO during several years of business activity in both companies (DArT PL and Triticarte PL), DArT (and its products/outcomes) has full FTO for its operations. This includes not requiring a licence to the so-called 'non-coding DNA' patent owned by Genetic Technologies (Melbourne), which has recently started to be enforced in the field of agriculture.

Interestingly, a few years after the separation of DArT PL from CAMBIA the level of interest in licensing just the right to practise the technology in general is very low (practically non-existent), while at the same time the level of interest in our genotyping services and technology

[3] A legal definition of 'improvements' and 'grant back' can be found at www.diversityarrays.com/pub/Legal.pdf.

[4] For example, by Hope, J. 'Biological Open Source'. Message posted to http://opensource.org/ Internet Mailing List, 15 November 2006. Archived at www.nabble.com/APL-license – What-about-the-enforced-logos–to7226746.html#a7351547. Also see Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume.

provision in general is rapidly increasing. I mention below a few possible reasons for this apparent paradox with respect to large companies. For small organisations, it seems there is an additional minimum investment entry barrier, as the instrumentation package enabling operation is likely to be prohibitive. Furthermore, there is an apparent structural incompatibility of non-profit/academic organisations with implementing a technology like DArT in a cost-effective manner, primarily due to relatively short-term (project/grant) focus and pressure on publications/knowledge building rather than provision of service. The DArT PL business model was therefore designed to take these considerations into account, in that it is not dependent on revenue derived from licensing out the technology in isolation from other offerings.

14.3 Business model

In the initial phase of technology development and commercialisation it became apparent that large(er) corporations have little interest in DArT with the lack of an option to take an exclusive licence being most likely the main disincentive. However, another reason was that large commercial entities tended to be strongly focused on the many Single Nucleotide Polymorphism (SNP) platforms developed by means of very large investments, primarily in the Human Genome Project. Yet another possible reason for lack of serious interest in DArT was the fact that many major players had already invested in alternative molecular marker technologies like Amplified Fragment Length Polymorphism (AFLP) and Simple Sequence Repeats (SSR) and were not willing to write off this investment.

With this initial experience, DArT PL had to develop a business model quite different from the one used by most biotechnology companies. An important difference was the way of accessing capital, which in the biotech area is traditionally sourced from the venture capital (VC) market. Not only was there a very limited level of intellectual property (IP) control, but also it was clear that DArT would not be able to compete effectively in the market segment that had the largest potential profit margins (biomedicine).[5] Without the two critical elements needed to make a business case for VC (control of the IP rights and rapid profit growth potential) we had to look for alternative investors. It became apparent that the most likely candidates for such a role would

[5] Investment of hundreds of millions of public and private dollars in Human Genome Project and high throughput platforms resulted in ample availability of technologies for human genotyping.

be the organisations involved in technology development for primary industries, as they have a mandate and resources to invest in R&D for their stakeholders (farmers), yet usually do not require exclusivity with respect to the technology or its products.

Importantly, the need for an alternative path was not only acceptable – it was indeed a major stimulus for developing the company further. First, not selling the shares to an investor interested in profit maximisation allowed us to keep our focus on maximising impact in our area of interest, which includes international agricultural research, an area of clear market failure. An additional stimulus was coming from the fact that we were moving the experimentation out of the lab into the business arena: testing whether a successful company could be built with little capital in the fairly competitive field of genome/nucleic acids analysis. While we drew inspiration for finding the way forward from many people and traditions, the book by Dee Hock,[6] the founder of Visa International, deserves a special mention, as his concept of 'chaordic' organisations helped us to develop a general framework for technology delivery.

Instead of concentrating on fighting any possible competition, we focused on developing collaborations and partnerships in recognition of the need to effectively manage the demand/supply balance and help us with product development. In our view, this is especially critical at the early stages of technology (and market) development. Our first partnership was with the Value Added Wheat Cooperative Research Centre, through the creation in 2003 of a joint venture company, Triticarte Pty Ltd, to deliver a wheat and barley genotyping service. Since the Tritcarte PL worked well as 50–50 partnership (mainly due to the commonality of vision of the two parent organisations and its officers), we are planning to use this model in expanding our international network.

14.4 Company products

DArT PL had to develop its products very quickly in order to survive in the marketplace. The company's initial offering – contract R&D – is still an important source of revenue, but already the majority of revenue comes from the provision of genotyping services using DArT arrays. A new product for the company is its value-added genotyping service – that is, provision of comprehensive genetic analysis including both data production and downstream processing.

[6] Hock, D., *Birth of the Chaordic Age*, Berrett-Koechler Publishers Inc., 1999.

Contract research

The development of DArT for new species continues at an increasing rate, with at least one new species initiated every month. Interestingly, as DArT has already been developed for all the more economically important species, developing the technology for new species almost invariably involves working with smaller/less well-resourced players in various consortia. These consortia are most often private–public partnerships which aim at pre-competitive technology development. While DArT PL does not claim exclusive rights to any new technologies developed, we do make a commitment to deliver inexpensive genotyping services using the product of our consortium efforts.

Genotyping services

With arrays developed for approximately thirty species (mostly crop plants), we are now offering an inexpensive genotyping 'DNA to data' service, often through scientific collaboration projects. As in any other service-based organisation, timeliness of service and the quality of data generated is critical for us. Establishing comprehensive informatics support for sample tracking (DArTdb) and automatic data extraction (DArTsoft) was critical to achieve sufficient throughput and ensuring high data quality. Returning business and customers' feedback suggests that our service is of high quality.

Genetic testing/knowledge

In recognition of the limitations on efficient downstream data analysis (i.e. extracting useful information from data), we devote an increasing amount of time to the development of software tools which add value to our data. While we are considering commercialisation of these tools as separate products, our vision is to combine them with our data production service and move towards genetic knowledge generation. Our decision is motivated not so much by a perceived business opportunity, but by the realisation that very few of our clients are capable of extracting information imbedded in data we report. This is especially true for clients from small breeding programmes or public institutions, but even large(er) organisations are likely to capture more effectively the value of whole-genome profiles when supported by the more advanced data processing algorithms we have developed. There is little doubt that in the long run the availability of such value-added services may translate into greater commercial success.

14.5 Lessons for biomedicine

Assuming that survival in the marketplace and modest, but consistent, growth is a mark of success I can list several factors which in my opinion helped us to get where we are right now:

1. Excellent team. We were very fortunate to assemble a group with a great mix of talent and complementary skills at the very early stage of company development: the manager, Eric Huttner, combining biotech business and good science background; Peter Wenzl, a talented and dedicated Principal Scientist; Grzegorz Uszynski, a creative and very productive IT manager. Apart from these most senior staff we have a dozen biology and IT personnel with great dedication and talents. Development of technology and the company under the guidance of the inventor has been important, in that the pricing structure for technology development and services is designed to maximise the impact of technology, not the profit.
2. The unique strength of DArT as a technology, fitting very well into a market niche characterised by very low margins, albeit fairly high volume.
3. Collaborative spirit. Many, if not most, of our technology development projects have been executed as a collaboration/co-development of the technology with users. This was done through a scientific visits programme to our company with over twenty scientists from practically all continents spending from a few months to over a year working on developing arrays and/or generating data. This enabled us to develop a lot of products on a shoe-string – a critical aspect of operating in an area with practically no profit margins.

It is difficult to generalise our experiences to biomedicine, as each technology will have its own specific constraints and opportunities. A significant issue the two fields have in common is access to capital and the likely need to step out of the box to develop a business model which can work for a particular technology or product(s). I expect that in the current economic environment and investors' mindset, only some biotech businesses will have a chance to succeed with an open source IP regime. Possibly the best opportunity could be for those who will be able to find a specific niche, likely in an area of limited financial opportunity, where competition with mainstream companies would be less intense. In order to change this pessimistic outlook one would like to see more resources available to those wishing to pursue non-standard business models, with positive social impact rather than driving the maximum profit.

REFERENCES

Hock, D., *Birth of the Chaordic Age*, Berrett-Koechler Publishers Inc., 1999.

Hope, J. 'Biological Open Source'. Message posted to http://opensource.org/ Internet Mailing List, 15 November 2006. Archived at www.nabble.com/APL-license – What-about-the-enforced-logos–to7226746.html#a7351547

'Open source genetics. Conceptual framework', Chapter 12 of this volume

Jaccoud, D., Peng, K., Feinstein, D., and Kilian, A., 'Diversity Arrays: a Solid State Technology for Sequence Independent Genotyping', **29** *Nucleic Acids Res.*, 2001, e25

15 Critical commentary on 'open source' in the life sciences

Arti K. Rai

15.1 Introduction

The conceptual paper and case studies in this section evaluate possible extensions of the "open source"-style private ordering that has emerged in software to the life sciences. In evaluating such extensions, it is important initially to note the historical context in which open source emerged in software and the many flavors in which open source software currently comes. From this clarification of first principles, we can then imagine what open source in the life sciences might look like.

15.2 Background and clarification of principles

The concept of open source in software has its origins in the quasi-Mertonian ethic that prevailed among academic laboratories in the 1960s and 1970s. At the time, packaged software was relatively unusual, and labs regularly exchanged software and underlying source code for purposes of modification and improvement.[1] The emergence of packaged software offered without underlying source code began to erode this Mertonian ethic. As Janet Hope points out,[2] one response to such erosion was Richard Stallman's GPL license,[3] which utilizes copyright licensing to mandate an expanding "commons" of source code. The GPL license not only sets up a situation where the source code commons can not be made proprietary, but by so doing it may create incentives to contribute in the first instance. A large percentage of open source software licenses continue to employ some version of Stallman's "copyleft" approach.

[1] *See* von Hippel, E. & von Krogh, G., 'Editorial: Special Issue on Open Source Software Development', **32** *Research Policy*, 2003, 1149.

[2] See Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume.

[3] GNU General Public License Version 2 (June 1991), http://www.gnu.org/licenses/gpl.txt.

On the other hand (contrary to Janet Hope's argument that licensing is "fundamental" to open source)[4], various other flavors of open source – perhaps most notably the Berkeley Software Distribution (BSD) license – essentially amount to a dedication of source code to the public domain. Those who improve upon source code distributed under BSD licenses may feel a norm-based obligation to contribute their improvements back, but they are under no legal obligation to do so.[5] In the case of BSD and similar open source licenses, emphasizing the licensing component of open source is excessively formalistic.

As the example of BSD illustrates, open source could be seen as a mode of production rather than a legal architecture. Indeed, to the extent open source presupposes – to use Janet Hope's terminology[6] – "credible commitment" and "competition", these features may follow from the simple reality that a core amount of material has been irrevocably made available for all to use. For this reason, some of us have used the term "open and collaborative research" instead of open source; in using this terminology, we wish to emphasize the organization of production and what is done with the results of production, rather than details of licenses.[7]

15.3 Open and collaborative life sciences research

Role of law/licensing

Non-legal, social norm-based approaches may have particular salience in the life sciences. For example, in the case of life sciences software – which is produced by, and for, a relatively small scientific community – empirical work that I have done indicates that copyleft licensing is much less common than in open source projects as a whole.[8] Various genome annotation projects also use a distributed approach without necessarily relying on copyleft.[9] Similarly, Josh Lerner and Jean Tirole have found

[4] See Hope, Chapter 12 of this volume.

[5] In distinguishing obligations imposed by positive law from obligations imposed by social norms, I follow the convention of many US legal scholars, who distinguish these sets of obligations. *See, e.g.*, Ellickson, R., *Order Without Law: How Neighbors Settle Disputes* (1991).

[6] See Hope, Chapter 12 of this volume.

[7] Rai, A.K., 'Open and Collaborative Research: A New Model for Biomedicine', in Robert W. Hahn (ed.), *Intellectual Property Rights in Frontier Industries: Software and Biotechnology*, 2005, 131.

[8] Specifically, as of February 2005, 47.4% of active projects in the 'bioinformatics' area of SourceForge used GPL licensing. This compared with 72% of projects in SourceForge as a whole. Unpublished data, on file with author.

[9] *See, e.g.,* BioDAS, www.biodas.org.

that strong copyleft licensing is less common where the community of users is relatively specialized.[10] As noted earlier, where a copyleft license used is not being used, the license is functionally much closer to a dedication to the public domain.

Moreover, an emphasis on law/licensing can sometimes pose, rather than resolve, problems. Two challenging issues involve, first, the need for an underlying property right and, second (at least for copyleft licenses), the need for line-drawing based on the economics of the industry in question.

As an initial matter, efficient licensing requires an underlying property right. Absent such a right, those who wish to impose restrictions must do so entirely through contract. The resulting contractual restrictions can do more damage than good. The case of the publicly funded International HapMap project provides a good illustration of the problems associated with using licensing absent a property right. For a period of time, the HapMap project used a click-wrap license that required those who sought access to data on human genetic variation (so-called single nucleotide polymorphism or "SNP" data) to refrain from combining it with their own proprietary SNP data in order to seek product patents on haplotypes (patterns of SNPs that are inherited together). In order to prevent leakage of the data outside the confines of this click-wrap license to those who would then have no obligation to the HapMap, the license required those who sought the data to refrain from disseminating such data to anyone who had not agreed to the license. Conventional publication of the data was not possible. This condition is no longer imposed because it is believed that the database has reached a sufficient density to be self-sustaining and to defeat subsequent patent claims. However, the old requirements illustrate the difficulties that may arise where there is no underlying property right.

The HapMap project also illustrates the line-drawing problem that can arise when a copyleft approach is taken outside the context of software. In software, there is no real need for such line-drawing: there is little evidence that conventional IP rights are useful as incentives at any stage in the development process. But in other industries, where patents may be important as incentives, there is a need to delineate carefully the scope of information that must be put back into the commons. The HapMap license employed a complex and ambiguous licensing policy

[10] Lerner, J. & Tirole, J. 'The Scope of Open Source Licensing', **21** *Journal of Law, Economics, and Organization,* 2005, 20.

that appeared to prohibit product patents on haplotypes but allow certain types of process patents.[11]

A careful drafter may be able to craft language that draws appropriate lines between what materials fall within the commons and what remains outside. For example, as the case study on BiOS notes,[12] this group has licenses that do make relatively clear and careful distinctions. Under the BiOS license, patents on improvements to the enabling technology – a suite of tools for creating transgenic plants – must be "granted back" and made available to other users of the commons.[13] But patents on end-product transgenic plants are not subject to a grant-back requirement.

However, the BiOS strategy of drawing *ex ante* distinctions may fare poorly when applied to enabling technology that is likely to lead in diverse, and perhaps unanticipated, directions. Where these different directions vary in levels of capital investment required, patents will have different degrees of importance.[14] For example, in the case of synthetic biology, relevant platform technologies could be used for products ranging from relatively simple tests for environmental toxins[15] to therapies that require clinical trials and regulatory approval.

Indeed, even within a single area of end product application, the level of capital investment required may change. For example, in the US, diagnostic genetic tests have generally not required much in the way of capital investment. This is because such tests have typically not been classified as the types of "medical devices" that would be subject to the US Food and Drug Administration's most exacting regulatory requirements. But that situation may soon change, at least for certain types of diagnostic tests.[16]

[11] *See* Eisenberg R.S. & Rai, A.K. 'Harnessing and Sharing the Benefits of State-Sponsored Research: Intellectual Property Rights and Data Sharing in California's Stem Cell Initiative', **21** *Berkeley Tech. L.J.,* 2006, 1187, 1207–9.

[12] See Berthels, N. 'Case 8. CAMBIA's Biological Open Source Initiative (BiOS)', Chapter 13 of this volume.

[13] CAMBIA BiOS License for Plant Enabling Technology, § 3, www.cambia.org/daisy/PELicense/751/1169.html.

[14] More specifically, the relevant variable is capital investment that would not be appropriable absent a patent right.

[15] Chu, J. 'A Safe and Simple Arsenic Detector', *Technology Review,* 25 January, 2007.

[16] US Department of Health and Human Services, Draft Guidance for Industry, Clinical Laboratories, and FDA Staff: In Vitro Diagnostic Multivariate Index Assays, 26 July 2007, available at www.fda.gov/cdrh/oivd/guidance/1610.pdf.

Role of competition

As noted, Hope argues for the centrality of competition to open source. She further notes the BiOS licenses are not truly open source because it does not allow for competition – for "forking" of the code.[17] As a practical matter, because forking in open source software is rare in any event,[18] this divergence from open source may be more apparent than real.

Will the project be sustainable?

Finally, it bears emphasis that the extent to which either norms or copyleft licensing is likely to yield further project growth may be quite sector-specific. While certain bioinformatics projects (e.g. BioPerl)[19] appear to have had some success in inducing such contributions,[20] BiOS has had much more limited success.[21]

15.4 Conclusion

Successful translation of open source principles into the life sciences will require far more than simple cutting and pasting. In part, this is because even open source projects in their native context show a great deal of diversity. An emphasis on legal formalities fails to encompass that diversity. Equally important, the life sciences context involves a set of participants, and a set of economic realities, that is quite different from software. Even open source bioinformatics software appears to look systematically different from open source software in other contexts.

REFERENCES

Berthels, N. 'Case 8. CAMBIA's Biological Open Source Initiative (BiOS)', Chapter 13 of this volume.

[17] Hope, see Chapter 12 of this volume.
[18] Raymond, E., 'The Magic Cauldron', available at www.catb.org/~esr/writings/magic-cauldron.
[19] www.bioperl.org.
[20] Stajich, J. et al., '*The Bioperl Toolkit: Perl Modules for the Life Sciences*', **12** *Genome Research*, 2002, 1611.
[21] Statement of Richard Jefferson, Washington University conference on Open Source and Proprietary Models of Innovation, 4 April 2008. According to Jefferson's oral presentation, many organizations have licensed the BiOS technology, but none has contributed improvements back.

Chu, J. '*A Safe and Simple Arsenic Detector*', *Technology Review*, 25 January 2007.

Eisenberg R. S. and Arti K. Rai, 'Harnessing and Sharing the Benefits of State-Sponsored Research: Intellectual Property Rights and Data Sharing in California's Stem Cell Initiative', **21** *Berkeley Tech. L.J.*, 2006, 1187, 1207–9.

Ellickson, R. *Order Without Law: How Neighbors Settle Disputes*, Harvard University Press, 1991.

Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume

Lerner, J. and Tirole, J. 'The Scope of Open Source Licensing', **21** *Journal of Law, Economics, and Organization*, 2005, 20.

Rai, A. K., 'Open and Collaborative Research: A New Model for Biomedicine', in Robert W. Hahn (ed.), *Intellectual Property Rights in Frontier Industries: Software and Biotechnology*, 2005, 131.

Raymond, E., 'The Magic Cauldron', available at www.catb.org/~esr/writings/magic-cauldron

Stajich, J. et al., 'The Bioperl Toolkit: Perl Modules for the Life Sciences', **12** *Genome Research*, 2002, 1611.

von Hippel, E. and von Krogh, G., 'Editorial: Special Issue on Open Source Software Development', **32** *Research Policy*, 2003, 1149.

16 Several kinds of 'should'

The ethics of open source in life sciences innovation*

Anthony S. Taubman

> What is the matter? Has Protagoras robbed you of anything?
> Yes, indeed he has, Socrates, of the wisdom which he keeps from me.
> But, surely … if you give him money, and make friends with him, he will make you as wise as he is himself.[1]

16.1 A *sui generis* ethical space for life sciences innovation?

Life science innovators work in an ethical space that is distinct from the general run of technology, whether or not they would choose this status. We expect life science innovation to serve such fundamental human needs as health, nutrition and environmental protection, and to deliver its fruits in the forms of proven and effective technologies as widely and equitably as possible. The call for access to the fruits of this innovation is more insistent than for any other technology, because essential human wellbeing – even life itself – is at stake; because a good proportion of the upstream inputs to applied life sciences research are derived from the public sector or from research funded by public or philanthropic sources; and because genetic inputs to research – biodiversity, human tissue, seeds – pose *sui generis* ethical and legal questions. Society's scrutiny over life sciences innovation is therefore more stringent and vigorously debated than the regular run of technology, a scrutiny expressed at the ethical, political and formal regulatory levels.

It follows that in the life sciences especially, intellectual property (IP) law and its practice is typically viewed, from an ethical point of view, as an essentially utilitarian means towards public policy ends, with its worth assessed from a consequentialist and empirical perspective. The

* The present contribution draws in part on the author's presentation, 'Several kinds of "should" in life sciences innovation', Wizards of OS 4, Berlin, 15 September 2006. The paper represents the author's personal views only; does not present views that should be attributed to WIPO, its Secretariat or its Member States.

[1] Plato, Protagoras (translated, Benjamin Jowett, at 310d).

attainment of 'justice' and 'equity' is measured in hard outcomes, and any appeal to 'natural law' underpinnings of IP rights or an inherent sense of entitlement is given an unsympathetic hearing in the busily contested policy arenas of life sciences. Ultimately, in this debate, only public policy outcomes count: the production and effective dissemination of certain concrete public goods. The IP system in the life science is expected to yield knowledge goods that are practically available as proven products and processes (new drugs, crops or uses of biodiversity), and higher level public goods,[2] such as global equity in distribution of these products, and ultimately equity in the enjoyment of the right to life[3] and in adequate health services. Given the strong emphasis on actual access to technologies and on tangible public welfare outcomes, the ethical framework is shaped essentially by the need to address the inherent scarcity of knowledge resources and research capacity (leading to neglected disease burdens and agricultural needs), and to address inequities of access to research outputs; there is less said about the inherent sense of entitlement for the innovator and originator.[4] Where robust and credible incentives for private investment in research and development are recognized as being essential, this is nonetheless argued for broader utilitarian reasons and not because of any natural law entitlement. On the international policy plane, this turn to strong utilitarianism in evaluating the IP system is in part an unwitting consequence of the blending of trade policy and IP regulation though TRIPS. But there are special factors that further accentuate the hard utilitarian demands set for IP in the life sciences. The sense that much is at stake means that perceived failings and shortcomings in the system – any failure to innovate effectively, to address neglected needs, to ensure full and equitable access – attracts sceptical scrutiny and precipitates calls for reform and for new pathways for innovation in public health.

[2] For discussion of higher order public goods in this context, see Antony Taubman, 'Saving the Village: Conserving Jurisprudential Diversity in the International Protection of Traditional Knowledge', in Keith E. Maskus and Jerome H. Reichman (eds.), *International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regime,* 521 (2005).

[3] In 2005, the adult mortality rate (probability per 100,000 of dying between 15 and 60 years) for women ranged from 789 in Zimbabwe to 45 in Japan; life expectancy for males at birth ranged from 39 (Angola) to 79 (several developed countries). (Source: World Health Organization, at www.who.int/healthinfo/statistics/en/).

[4] But contrast traditional knowledge and associated genetic resources for which natural law claims are mingled with calls for historic retribution for misappropriation, and the invocation of higher order public goods in the form of conservation of diversity of biota, of cultures, of jurisprudence.

This search for alternatives to 'IP'[5] in life sciences innovation springs from a critique at three levels: (i) revisiting the inherent legitimacy of the foundational principles of IP law and policy; (ii) assessing how these principles are actually applied in practice at the level of governance and administration; and (iii) gauging the impact of the individual exercise of rights granted under the system. This critical analysis can, indeed, equivocate between these discrete levels, conflating the legal framework with the many and disparate distinct choices made within it. The broad legislative framework itself is critiqued from a hard consequentialist position: it is assessed in terms not of what it aspires to achieve but by its practical impact. But this critique can display a degree of ambivalence: is the essential issue (i) the fact that exclusive rights over new technologies are available in principle under the law; or (ii) a practice of the administrators of the system granting actual patent rights that are inappropriately at odds with these principles, lacking the required attributes of true inventions; or (iii) the manner that individuals and firms apply for, assert and deploy these rights so as, in practice, to yield outcomes at odds with the policy goals of the system (using patents effectively to deny to the public the benefits of valuable new technologies and thwarting valuable innovation) or in tension with society's ethical expectations (e.g. pushing the cost of a diagnostic test beyond the reach of all but the wealthy, or illegitimately profiting from others' investment in research)? Is the root problem the system design, its broad execution or perverse individual choices that conflict with systemic goals? If the critique determines that the essential problem is a mix of all three, how can interventions be calibrated and applied so as to match practical remedies with each facet of the problem? The debate over 'open source' biotechnology is a fascinating case study as it can at times be phrased as a critique of the legitimacy of the formal grant of exclusive rights as such over critical technologies, but as a practical intervention it would appear to reform actual behaviour and actual choices in the deployment of such rights.[6] Could it reform the essential

[5] In this polemical context, 'IP' is often conceived as a distinct innovation system and set of values, rather than – more accurately, in this writer's view – as a precise kind of legal mechanism that can be implemented in radically different ways to construct diverse innovation systems and to express and defend diverse value systems.

[6] The contrast between a policy intervention and the encouragement of preferred forms of exercise of rights is captured well in the preamble of the GNU General Public License Version 3 (29 June 2007), at www.gnu.org/licenses/gpl-3.0.html: 'States should not allow patents to restrict development and use of software on general-purpose computers, but in those that do, we wish to avoid the special danger that patents applied to a free program could make it effectively proprietary. To prevent this, the GPL assures that patents cannot be used to render the program non-free.'

conception of what should be the legitimate bounds of an exclusive right, by influencing actual practice and the effective normative expectations upon right holders?

Precisely because so much is at stake – conceivably, the future well-being of humanity – it is proper for the same ethical and empirical rigour that is applied to the conventional IP system to be applied equally to proposals for the reform, renouncement or replacement of that system: assertion of new modes of innovation that are disruptive or divert resources merits the same ethical scrutiny as the complacent endorsement of the *status quo*. The current necessary, valuable, active debate about how best to optimize innovation processes in the life sciences: how best to draw in and structure the different inputs needed – finance and infrastructure, platform technologies, know-how, regulatory data or product development capacity – and how to ensure equitable dissemination of the fruits of innovation, cannot run the risk of privileging certain abstracted models over a robust and practical assessment of what actually functions, what will deliver.

A priori theoretical preferences range from viewing recognition of intangible property as a bedrock of a sound knowledge economy[7] and as a precondition for the transactions in intangibles that construct a new life sciences product, to acute scepticism about *any* propertisation or legal exclusivities over knowledge goods in the life sciences.[8] Both sets of preferences are argued to be justified by a blend of strictly utilitarian and broader ethical and human rights arguments, often with some equivocation between the two: is public choice to be guided by what is right or by what works, is it right because it works, or does it have to be right (or legitimate) in order to be practically sustainable? In practice, an unexpectedly pluralist spectrum and a supple range of diverse innovation models stretch between these two extremes; while the conceptual dichotomy between the two fuels much debate, the actual working mechanisms that deliver beneficial products typically ply the extensive territory ('policy space') that lies between these two conceptual positions.

[7] See Alexandra C. Horst, International Property Rights Index (IPRI): 2007 Report, at www.InternationalPropertyRightsIndex.org: 'Once a domain mainly considered by the affected inventors and companies themselves, public interest in intellectual property protection has risen substantially, as the vast majority of the world is now affected by its success or failure' (at 8).

[8] E.g. the recasting of intellectual property rights as 'intellectual monopoly privileges' (IMPs), see e.g. Greg Martin, Corinna Sorenson and Thomas Faunce, 'Balancing intellectual monopoly privileges and the need for essential medicines', **3** *Global Health* 4,. 2007 (Published online 2007 June 12. doi: 10.1186/1744–8603–3–4).

The present comment explores the ethical framework for analysing innovation structures in the life sciences to assist in the rational choice of model to support desired innovation and access outcomes, with a particular focus on the conceptual infrastructure for analysis of open source models in the life sciences. This search for rigour is, however, the precise opposite of a sceptical or reactionary appraisal: it is a strategy that aims to shift the search for new models and new structures from an academic inquiry and from an exchange of memes into a practical art: reduction to practice.

The call for open source innovation is at one level a reaction to the observation that the foundational choice in IP policymaking is, at first blush, radically counterintuitive; this is one reason why the patent system in general is subject to a repeated cycle of sceptical review: lawmakers provide for patents in order to induce the production of public knowledge goods, such as new technologies, that would not otherwise be financed and produced, and they do this by a means of structured, systematic exclusions from the public domain. In short, public goods are produced by restricting the public domain. IP management in the life sciences has to reconcile this superficial tension between the exercise of exclusive rights and the promotion of public welfare outcomes, and to ensure that the tension remains only superficial rather than structural: in principle, innovations are excluded from the public domain in order to garner the concentration of resources that is necessary to take an invention entirely through the production pipeline to yield a practically useful product.

In principle, therefore, a utilitarian, objective IP policymaker has to determine what privately-held exclusions from the public domain of otherwise non-excludable knowledge resources are required to harness sufficient private interest to provide for the production of useful public goods that would not otherwise come into existence.[9] But how does the objective policymaker, ideally removed from sectoral bias, in the original position behind a Rawlsian veil of

[9] This is not, of course, by any means the mechanism for harnessing private interest to provide for public goods. There is, for example, a considerable economic literature on the private provision of public goods, considering such phenomena as corporate philanthropy, political campaign donations. See Eduardo Ley, 'On the Private Provision of Public Goods:A Diagrammatic Exposition', **20** *Investigaciones Economicas* 1, 1996, 105–23, at IMF, Washington DC, http://econwpa.wustl.edu/eprints/pe/papers/9503/9503001.abs. See the economic model for non-cooperative provision of public goods in Theodore Bergstrom, Laurence Blume, and Hal Varian, 'Private Provision of Public Goods', **29** *Journal of Public Economics*, 1986 25–49. at http://econwpa.wustl.edu/eprints/pe/papers/9503/9503001.abs.

ignorance,[10] determine what exclusions would be just; or legitimate; or effective; and what blend of hard utilitarianism and more abstract appeal to justice is right? And in setting these formal legal exclusions from the public domain, what assumptions are made about how individual actors will exercise the ensuing exclusive rights? Classical liberal economic analysis[11] (the 'invisible hand')[12] suggests that overall public welfare is unwittingly advanced by the cumulative effect of individual economic actors pursuing their private interests. But can such an analysis be reliably extended to the promotion of welfare through the production of intangible public goods generated by the recognition of private rights under the IP system? Some public goods would result either directly or as externalities from the pursuit of private interest, as the spontaneous ordering of the market and communication through market exchange promotes beneficial investment and innovation. Classically applied to goods and services,[13] this analysis may illuminate the harnessing of private interest to produce intangible knowledge products of benefit to society, offering a systematic utilitarian ethical basis to IP mechanisms. Intangible property, or exclusions from the public domain, can promote the spontaneous order that works for society's overall gain: accepting limitations on commercial use of knowledge through legally crafted exclusions may be the most effective way of producing some public goods.[14] But it would be politically naïve,

[10] John Rawls, *A Theory of Justice*, Harvard University Press, 1971; R.J. Kilcullen, *Rawls: The Original Position,* Macquarie University, 1996, www.humanities.mq.edu.au/Ockham/y64l13.html.

[11] For a brief historical review of these aspects of liberalism, see Steven Horwitz, '*From Smith to Menger to Hayek: Liberalism in the Spontaneous Order Tradition*', **6** *The Indep. Rev.* 1, 2001), at 81.

[12] In Adam Smith's classic formulation: 'by directing that industry in such a manner as its produce may be of the greatest value, he intends only his own gain, and he is in this, as in many other cases, led by an invisible hand to promote an end which was no part of his intention. Nor is it always the worse for the society that it was no part of it. By pursuing his own interest, he frequently promotes that of the society more effectually than when he really intends to promote it.'

[13] With the assumption that intangible knowledge products are not economically significant: note Smith's reference to the intangible or ephemeral product of 'players, opera-singers, opera-dancers, etc.' as producing 'nothing which could afterwards purchase or procure an equal quantity of labour. Like the declamation of the actor, the harangue of the orator, or the tune of the musician, the work of all of them perishes in the very instant of its production.' Smith A., *An Inquiry into The Nature and Causes of the Wealth of Nations*, Henry Frowde (ed.), Oxford Univ. Press, 1909, 1776.

[14] The imposition of an exclusion means that they cease to be true public goods, as these are by definition not excludable, but the disclosure requirements of technology-related IP protection are intended to ensure that protected subject matter passes into the public domain firstly as a public knowledge good (patent information is not, in principle, excludable from the time of its publication), and, through limited term.

ethically obtuse and analytically barren to rely wholly on this mechanism in a laissez-faire manner as the sole means of ensuring the production of public knowledge goods in the life sciences. Precisely tailored exclusions from the public domain are essential to capture and direct private interest towards the production of certain public goods that would otherwise not exist: for instance, this is the rationale, at least, of orphan drugs initiatives and some approaches to protection of test data for pharmaceuticals and agricultural chemicals. But the complexity of the pathway towards a finished product, the need for a broad base of infrastructure and open knowledge, and the distinctive risk patterns of life sciences innovation also entail an exceptional need for public impetus, public policy direction setting and distinct public financing of public goods[15] in such areas as health, agriculture and the environment. One line of argument against exclusive rights and their restrictive exercise is indeed the high level of public funding that goes into the innovation infrastructure and the key upstream technologies in these field. Yet to relinquish altogether the possibility of exclusive rights over such public inputs, waiving any residual say over their application and the distribution of derivative benefits, is itself an expression of confidence in another invisible hand, one that draws enlightened private capital and public researchers together into welfare-enhancing partnerships that invest resources and opportunity cost into the development and delivery of products built from public domain inputs. In some circumstances, at least, the prudent policymaker will retain a reserve possibility of invoking 'private' rights to induce more socially beneficial applications of public-origin technology, and to exert leverage over downstream uses of this technology.

But much hinges on how those private rights are exercised, and by whom they are held: the mere formal recognition that a legal right exists to exclude third parties is only a small part of the overall pattern of knowledge management, since so much depends on who is excluded, and who is included, by those exclusive IP rights, and to what ends, and subject to what conditions. This is perhaps one broad systemic message of the open source paradigm as applied to the life sciences: 'It's not what you got, it's how you use it.'[16]

[15] Samuelson, P. (1954), The Theory of Public Expenditure', **36** *Review of Economics and Statistics*, 386–9.

[16] In this form, apparently written by Eddie Kendricks, 'It's Not What You Got' (single, Motown Records, 1976); but note also the consequentialist, outcome-oriented ethic in an earlier similar lyric: 'T'ain't what you do, it's the way that you do it… That's what gets results'. ('Tain't What You Do (It's The Way That You Do It))', James Young and Sy Oliver), Decca Records, 1939 (Ella Fitzgerald, vocals).

16.2 Analysing options for knowledge management in life sciences innovation

Indeed, actual patterns of life sciences innovation – the life cycles of real products –confute *a priori* assumptions of a fundamental choice between private or public good structures, or between the impetus of exclusive private rights or direct public interest. Actual patterns of ownership and control of patented technology illustrate how the grant and exercise of 'private' rights over IP subject matter need not be solely or even marginally directed towards private interest: it is increasingly inaccurate to conflate the private or exclusive nature of IP rights with the narrow pursuit of private interest. IP management that is solely and explicitly directed towards promoting public interest outcomes can include defensive publication and the pre-emptive creation of a public domain (including by waiving IP rights)[17], but it also includes the judicious deployment of legal exclusions. For instance, an IP-based right to exclude can encourage direct allocation of private resources towards public interest outcomes or leverage access to privately held background technologies for non-profit innovation, in the absence of market incentives.[18] Exclusive rights can be licensed to preclude commercial use of protected materials, to promote non-commercial creative exchange and adaptation.[19] In the life sciences, a right to exclude can be deployed to preserve open access to pre-competitive or upstream inputs to applied or downstream research. Thus the right to exclude can be applied judiciously to safeguard the open quality of a shared innovative domain for agricultural biotechnology (exercising exclusive IP rights to preclude third parties from excluding access to derivative outcomes).[20] In this context, the distinction between an 'open source property right' construed as a 'right

[17] See for example the public domain dedication of the Eldritch Press: 'Eric Eldred hereby releases any creative addition to the literary materials at the Eldritch Pressincluding but not limited to any copyrightable compilation of materials or HTML formattingto the public domain with a Creative Commons Public Domain Dedication.' (at http://creativecommons.org/licenses/publicdomain/eldred/).

[18] Taubman, A. *Practical Management of Public-Private Alliances for Public Health Outcomes in the Developing World: The Lessons of Access Conditions in Research and Development Agreements,* Initiative on Public-Private Partnerships for Health in Global Forum for Health Research, Geneva, 2004. www.ippph.org.

[19] See for example the 'Attribution-NonCommercial-ShareAlike 1.0' draft license at Creative Commons International (UK): 'You may not exercise any of the rights granted to You in Section 3 above in any manner that is primarily intended for or directed towards commercial advantage or monetary compensation.' (at http://creativecommons.org/worldwide/uk/, last visited May 14, 2005).

[20] See for example Biological Open Source License for Genetic Resources Indexing Technologies at www.bios.net/daisy/GRITLicense/750/1170.html.

to distribute' rather than 'a right to exclude'[21] – while perhaps useful and illuminating in a polemical context – cannot be maintained at a foundational or formal level: a 'right to distribute' is either unconditional and unbounded, in which case it is defined by the absence or waiver of the originator's right to exclude; or it is conditional[22] on certain behaviour (such as granting in turn similar rights to distribute) or undertakings, in which case the IP right is exercised to exclude other forms of distribution or other patterns of downstream use. Standards bodies use IP licensing structures to ensure open access to standards while encouraging technology developers to pool their technologies for mutual benefit, such as by defining fair, reasonable and non-discriminatory (FRAND) terms and conditions for licenses.[23] The claim for protection of traditional knowledge is expressed by some proponents, at least, as a collective right or custodial responsibility to prevent illegitimate use of this knowledge, entailing the exercise of rights to exclude third parties in the name of *a* public if not *the* public – i.e. the traditional community which maintains the knowledge according to customary law and practice.[24] Public-sector knowledge management through the assertion of IP rights can be construed as a form of privatisation of public knowledge, or idealised as a

[21] Weber S., *The Success of Open Source*, Harvard University Press, Cambridge, 2004.

[22] See for example GNU General Public License (a free software, not open source license). The Preamble explains: '[t]o protect your rights, we need to prevent others from denying you these rights or asking you to surrender the rights. Therefore, you have certain responsibilities if you distribute copies of the software, or if you modify it: responsibilities to respect the freedom of others. For example, if you distribute copies of such a program, whether gratis or for a fee, you must pass on to the recipients the same freedoms that you received. You must make sure that they, too, receive or can get the source code. And you must show them these terms so they know their rights.' Paragraph 8 provides: 'You may not propagate or modify a covered work except as expressly provided under this License. Any attempt otherwise to propagate or modify it is void, and will automatically terminate your rights under this License.'

[23] Concerning the resolution of conflict between the exclusivity of IP rights and open access to standards in the United Kingdom, 'most standards bodies include procedures that take IPRs into account where a standard is in the process of being drawn up. Each participant is expected to declare at an early stage the IPRs it holds which are (or might be) essential to the draft standard if it were to be adopted. The owner is requested to give an undertaking in writing that it is prepared to grant irrevocable licences on royalty-free or fair, reasonable and non-discriminatory (FRAND) terms and conditions under such IPRs, with a waiver of copyright in documentary material. The standards body also makes sure that the patent in question is endorsed as a 'Licence of Right' at the Patent Office. This ensures that licences under the patent are available to all applicants as of right and that any disagreement of licensing terms is subject to settlement by the Patent Office,' Clarke M, *Standards and Intellectual Property Rights* (2004), at 64.

[24] See Taubman A.S., *Saving the Village*.

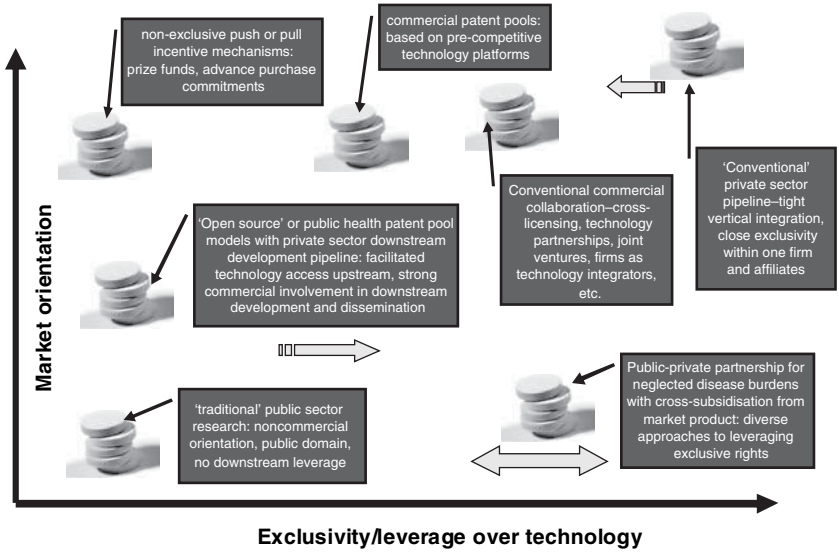

Figure 16.1 Modes of knowledge management in the life sciences

means to maintain collective public-interest control over how public knowledge is developed and applied.

In practice, life sciences innovation practices and structures range across an unexpectedly pluralist spectrum and a supple range of options lying between conceptual extremes. Moving beyond the conventional antinomies of public/private and exclusivity/openness opens a stronger conceptual framework for analysing innovation structures in the life sciences, and in turn assists in the rational choice of model to support desired innovation and access outcomes. Actual development and effective delivery of life sciences products to a target public involve a diverse mix of public, private but part publicly funded, and strictly private inputs; and the cluster of diverse technological inputs that converges on a delivered life sciences output will be governed, licensed and made available in diverse manners. There is rarely a one-to-one correspondence between a patent, or a licensing model, or a genetic input, and an actual complex product such as a new seed or drug, which in its available and functional form will be a convergence of inputs: genetic material, know how, foreground inventions, platform technologies and test data. A hybrid mix of forms of knowledge management is therefore bound to be experienced: Figure 16.1 depicts how innovation structures make use of a range of options between fully

open access and exclusivity, on one axis, and between different levels of engagement with the market on the other. The knowledge management task for the product innovator – whether public or private, or both – boils down to determining what position on this landscape is likely to achieve the practical outcomes desired, recognising that at least some leverage over technology and some engagement with the market will likely be required.

Hence the utilitarian policymaker, operating behind an ethical veil of ignorance (with the aim of remaining disinterested and unbiased so as optimally to promote public welfare) and a technological veil of ignorance (confronted with radical unpredictability and high risk levels as to what research pathway will actually yield desired innovations, when and how), needs to consider how to navigate these options and how to encourage optimal behaviour on the part of innovators, assuming that the intense level of public interest will not, politically, accommodate a *laissez-faire* attitude on the part of those managing the innovation policy and legal framework. Yet *a priori* assumptions about the value of specific models are unlikely to do justice to the complex assemblage of inputs that yield the desired outcome.

16.3 Free *(libre)* and open source as a model for life sciences innovation

The call for open source innovation in the life sciences, by analogy with free (*libre*) or open source software (OSFS), is a striking topical example of the ethical ambivalence that can attach to specific models of knowledge management. 'Open source' is used here as a provisional bookmark for a cluster of conceptually linked innovation structures:[25] in Figure 16.1, the open source model lies towards the left-hand side, ranging up and down the axis of market orientations, as it accepts that a market for derivative products may be a legitimate means of generating the resources and the pathways to bring useful products to the market. It is also a model that entails some limited use of a right to exclude: specifically, the exclusion of those who seek in turn to exclude. But what kind of ethical and prudential guidance might determine the choice of such a mechanism, and determine the specific choice of mechanism within the cluster of possibilities?

[25] The much discussed and conceptually non-trivial distinction between 'open source' and 'free' software is not addressed here, not because it isn't important, but because this paper raises questions that would precede a close discussion of such distinctions in either software or the life sciences. The term open source or free software (OSFS) is therefore used henceforth to refer in general to this cluster of modes of software development.

It's wisest to acknowledge that mixed policy rationales are put forward to argue for an open source approach to life sciences: there is no one ethical argument that holds sway. At times, the rationale can veer towards the logically circular, or at least pose a question-begging justification: a life sciences innovation model may be useful, ethically progressive and worth exploring for the public good, but is it open source enough to earn that epithet? Indeed, given the cultural and social appeal of the open source concept and the somewhat loose invocation of these terms, a valuable – occasionally heated – debate is conducted over what might be termed 'identity preservation' of various forms of OSFS, given the risk that a potent set of ideas and norms can be reduced to a form of social branding, rather than as a significant and distinctive form of innovation structure. On the other hand, there may be features of OSFS software, such as the freedom to 'fork the code'[26] that may be considered essential to a credible migration of the open source meme to the life sciences domain.[27] Yet the objective differences between software coding and breeding plants and formulating medicines – the distinct modes of innovation, of risk and liability management, of identifying a 'kernel' or a 'commons', of regulating and testing technologies – can lead practitioners to challenge 'expectations that one size fits all'.[28] In practice, proponents and analysts of open source models do need to operate at several analytical levels, and the call for open source R&D in the life sciences can be framed variously as:

- a meme – a unit of social evolution[29] – or as a distinct complex or system of memes (a memeplex), conceiving open source as a cultural community,[30] as an evolving innovative culture shaped by certain cultural norms (such as willingness to share improvements);
- a metaphor – the notion of open source in software development offering a general pattern for structuring networks of life sciences researchers, for instance considering access to nucleotide or peptide sequence data as equivalent to free access to source code,[31] and so on;

[26] See, for example, the discussion of the BiOS licence in Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume.

[27] As Hope remarks (Chapter 12 of this volume) this kind of analysis should be 'not mere pedantry, but a question of institutional design.'

[28] Berthels, N. 'Case 8. CAMBIA's Biological Open Source Initiative (BiOS)', Chapter 13 of this volume.

[29] A 'unit of cultural transmission, or a unit of imitation': Richard Dawkins, *The Selfish Gene*, 1976.

[30] Levy S., *Hackers: Heroes of the computer revolution*, New York, 2001, commenting on the sense of the loss of a community that triggered the free software movement.

[31] See The Open Source Definition (Annotated), Version 1.9 (July 24 2006), at www.opensource.org/docs/definition.php.

- more formally, a model or template – open source licensing structures or similar contractual mechanisms granting access on the condition of reciprocal access applied *mutatis mutandis* to life sciences research and development;
- a badge of ethical approval – affirming an inherent ethical value in open source behaviour.

Its attractive brand presence could lead to 'open source' being loosely applied to any kind of life sciences innovation one happens to prefer, provided it falls short of the exclusive exercise of intangible property rights: a badge of approval or commendation for deciding not to exercise rights exclusively. Hence the ethical basis for such advocacy may range from the strictly utilitarian – it just works better – to something approaching an aesthetic of innovation – 'open source' as a kind of hip/geek T-shirt slogan.[32] The open source model could become an end in itself, acquiring an intrinsic ethical or even aesthetic validation. But without denying its social or cultural component, surely the policy rationale for OSFS development is more compelling when phrased in strictly utilitarian terms: it is ultimately 'better' and worth advocating as a mode of innovation when and if it works better for its ostensible objectives, more so than when we approve of it or when it conforms with an abstract model. This suggests that the open source concept would be more productively employed as a *heuristic* for innovation policymakers; advocacy of consciously disruptive models in the life sciences would evolve into a program of harvesting empirical lessons from successful forms of collaborative innovation in the software domain, with a focus on how to make life sciences innovation work better, work more efficiently, and/or work more fairly (in short, 'from concepts to cases').

In describing the practical, heuristic character of open source innovation, for instance, the BiOS FAQ expands: 'people don't just provide solutions; they provide an understanding of how the solution was developed and a way that the solution can be modified to suit other people's needs, and used to develop products. In reality, the concept of open source applies to anything that requires a meeting of innovative minds.' This analysis could be equally applied at a broader level to transferring 'understanding how the solution was developed' from one sector

[32] An analogy may be drawn with the assertion of Creative Commons licences in good faith but for social branding purposes technically at odds with the actual content concerned – which in the author's experience has included Creative Commons licences over fully public domain patent documentation (entailing the effective assertion of copyright) and over text ('available for widescale, free, non-commercial reproduction') protected by technological protection measures through a paid-for password (on file with the author).

of innovation to another. Yet the essential conundrum remains: how to avoid the constraints of a 'naïve expectation that one size fits all',[33] while porting coherent and useful lessons that are 'sector agnostic' to the aid of socially beneficial life sciences research? It is submitted that the preferred analysis should be pragmatic – guided by the practicalities of constructing a functional innovation platform for a given field of technology, and assessed ultimately according to its utilitarian impact.

In establishing an ethical framework for open source in the life sciences, a key consideration, with bioethics and broader utilitarian aspects, has been where to draw the line between the information that should remain freely available (subject to privacy and other ethical concerns from the point of view of the providers or subjects of especially human genetic data)[34], and what should be considered legitimately 'proprietary': what is the upstream material that goes into the pool, and what is a legitimate derivative product that (i) can, ethically, be commercialised by one firm exclusively and (ii) should, pragmatically, be open to exclusive appropriation by a firm as the most effective form of engaging market incentives to bring a downstream product to the public. These broader ethical and more narrow utilitarian considerations converge when the judgement is made that genetic information should intrinsically be considered in the public domain, because of fundamental ethical considerations but also because of the pragmatic assessment that such information should be considered 'pre-competitive' – in other words, ethical and utilitarian concerns led to the view that the provision of raw genetic data shouldn't be a business model in itself. The SNP Consortium, which was formed and funded by major private and public actors in 1999, subsequently delivered some 1.8 million single nucleotide polymorphisms (SNPs) into the public domain.[35] The utilitarian rationale for this pre-competitive collaboration was expressed in utilitarian terms:

> The members of The SNP Consortium will be able to create a commonly accepted SNP map more quickly, and with shared financial risk and less duplication of effort than if each company proceeded on its own … the map that will be constructed will be of greater density and therefore potentially

[33] Berthels, N. 'Case 8. CAMBIA's Biological Open Source Initiative (BiOS)', Chapter 13 of this volume.

[34] The fact that genomic epidemiological research is so far upstream in the pipeline of therapy development has implications for the privacy rights of research participants and for a rigorous definition for prior consent, particularly in resource-poor settings.' (Chokshi D and Kwiatkowski D, 'Ethical Challenges of Genomic Epidemiology in Developing Countries', **1** *Genomics, Society and Policy,* 2005, 1.)

[35] Now accessible at www.ncbi.nlm.nih.gov/SNP/.

greater utility to the pharmaceutical industry than SNP maps currently available.[36]

But competition and the assertion of patent rights were considered legitimate, indeed desirable, for downstream innovations derived from the open SNP data,[37] as a means of delivering useful finished products to the public, building on the pre-competitive substrate. The SNP Consortium itself filed patent applications and obtained a defensive registration as means of leveraging continued open access.[38]

Yet too strict a consequentialist account may end up placing excessive emphasis on short-term outcomes, overlooking the value of investing in technology platforms and information tools such as the SNP map. The SNP map could not of course yield useful medical products in itself and has contributed, for instance, to the International HapMap Project,[39] identifying haplotypes and enabling association studies, which 'will benefit human health by providing an extensive resource that researchers can use to discover the genetic variants involved in disease and individual responses to therapeutic agents. Once such variants have been discovered, researchers can learn much more about the origins of illnesses and about ways to prevent, diagnose, and treat those illnesses,' thus contributing further to a common platform for the ultimate delivery of new treatments, but still an interim step with its utility to be assessed in such terms.

Hence, given the long lead-times, progressive construction of technology platforms, and complex integration of diverse inputs required to yield new life sciences inputs – as well as a healthy experimental need for trial and error – a utilitarian argument may also be made for interventions that open up new pathways and structures for innovation as ends in themselves, even before tangible products are yielded.

It is inherently improbable that any broadly defined mechanism is likely to serve as the optimal, exclusive pathway for all innovation processes within any sector of life sciences, and the invocation of alternative pathways increases the need for a clear framework for assessing these

[36] 'Frequently Asked Questions,' The SNP Consortium, at http://snp.cshl.org/about/faq.shtml, last visited 13 March 2005.

[37] Chokshi D and Kwiatkowski D, at 8.

[38] US patent applications 20060057564, 20030204075 and 20020198371 (all abandoned as applications before grant), and statutory invention registration (SIR) H2,191, June 5, 2007 held by SNP Consortium (the SIR is a registration which 'has the defensive attributes of a patent but does not have the enforceable attributes of a patent', 35 U.S.C. 157).

[39] The International HapMap Consortium, 'The International HapMap Project,' **426** *Nature*, 18 December 2003, 789.

options and for constructing appropriate forms of regulatory intervention to optimize the welfare impact of life sciences research and development. Equally, however, invoking new models for innovation may divert attention towards a relatively abstract discussion about models, and away from fundamental technical obstacles to creating beneficial new products: the view of open source as 'magic pixie dust',[40] that it will in itself yield solutions. When transferring the OSFS meme to life sciences, a key stumbling block is that of false analogising: biotechnology differs fundamentally from software development in key ways, discussed below. Yet several factors may predispose the analyst to a stronger ethical basis for 'open' models in the life sciences than in software: it concerns basic human needs and welfare; public funds account for a significant proportion of research; there are stronger ethical, safety, and environmental concerns, as well as more acute ethical concerns about the obtaining and exercise of *patenting* technology in this domain, including also the cluster of issues concerning equity and prior informed consent for genetic inputs to research, which broaden into a North-South political and trade debate. And there is only one operating system; one can't invent around DNA chemistry nor develop a functional alternative to a gene.

The underlying question, then, is whether 'open source' is a coherent and enabling concept for biotech innovation: is it a badge of approval for behaviour we like, or can the experience of open source software development act as a heuristic for the construction, analysis or retrospective validation of distinct forms of research and development in the life sciences? And if 'open source' or 'free' life sciences innovation can be coherently characterised as a distinct mode, is the rationale for pursuing this mode one of inherent self-interest (it works for the innovator) or a moral duty (it works for society)?

More generally, how to characterise the inducement or the obligation to pursue open source innovation, drawing on the experience (or culture) of open source software development? Some common themes emerge: the notion of collaborative but distributive fashioning of technological platforms for downstream innovation; the contrast between source code and finished products, and between the free use of pre-competitive information and a competitive market for derivative products; an ethic of distributive equity in the share of derivative benefits and resistance to exclusive appropriation of benefits from platform technologies; the goal of freedom to use or operate as against tight structures of vertical or horizontal technological integration, backed by ethical expectations of freedom to use or experiment; and the use of viral licensing techniques

[40] Zawinski J, *Resignation and Postmortem*, 1999 jwz@jwz.org.

to sustain freedoms in derivatives or applications of core technology. In both spheres, the model is driven partly by a meme of a golden age of technological freedom (whether it is open software development, or free exchange of genetic materials such as seeds), contrasted with the rise of the dominant industry behemoth (software giants, seed multinationals), and the appeal to bridge a technological divide (digital or biotechnological), and to democratise the innovation process. In both spheres, too, the boundary between technology user and innovator blurs – what Lessig construes as 'read-write culture'.[41] But, crucially, in each case the open or free innovation structure is technology driven – the rights associated with a 'core' or original or 'platform' technology are asserted to leverage continuing access to derivative uses or adaptations of that technology, which itself is progressively improved. Ultimately, the most robust and persuasive inducement to enter the open source structure will be nothing more abstract than access to useful technology.

Important contrasts between these two fields suggest caution in too immediate an appeal to an OSFS model for the life sciences. First, the research and development dynamic is objectively different, as is the economic and commercial background. And the structure of liability, social responsibility and public interest regulation differ dramatically: 'viral dissemination', 'bug fixing' and the 'blue screen of death'[42] take on dramatic import in the life sciences. A buggy first version of Linux can be benignly released to the hacker community's bazaar[43] for Linus's law[44] to do its therapeutic work on the code, but the release of a buggy open source vaccine or drug could yield a public health crisis: in life

[41] Lessig, The Read-Write Society, Keynote Address, Wizards of OS4, 15 September 2006, at http://wizards-of-os.org/index.php?id=2322

[42] http://bsods.com/.

[43] 'In the cathedral-builder view of programming, bugs and development problems are tricky, insidious, deep phenomena. It takes months of scrutiny by a dedicated few to develop confidence that you've winkled them all out. Thus the long release intervals, and the inevitable disappointment when long-awaited releases are not perfect. In the bazaar view, on the other hand, you assume that bugs are generally shallow phenomena – or, at least, that they turn shallow pretty quickly when exposed to a thousand eager co-developers pounding on every single new release. Accordingly you release often in order to get more corrections, and as a beneficial side effect you have less to lose if an occasional botch gets out the door.' ('Release Early, Release Often' in Raymond E., *The Cathedral and the Bazaar*, Thyrsus Enterprises, <thyrsus.com>, version 3.0 (2000)).

[44] 'Linus [Torvalds] was directly aiming to maximize the number of person-hours thrown at debugging and development, even at the possible cost of instability in the code and user-base burnout if any serious bug proved intractable. Linus was behaving as though he believed something like this: Given a large enough beta-tester and co-developer base, almost every problem will be characterised quickly and the fix obvious to someone. Or, less formally, 'Given enough eyeballs, all bugs are shallow.' I dub this: 'Linus's Law'' (ibid.).

sciences innovation, there is often little clear distinction between management of IP and management of liability. The kind of broad disclaimers typically found in software licensing (open source, free or otherwise) could not be sustained for much life sciences innovation.

If open source licensing indeed pivots on a 'right to distribute',[45] public health and environmental regulation – and diffidence about 'viral dissemination' not only of licensing structures but also of public liability – may inhibit free use and dissemination of life sciences technologies exactly as they close in on offering tangible public welfare – as usable products in the hands of the public. A true 'open source' approach to life sciences innovation may need to address the contentious question of what competitive relationship should exist between the originators and users of test data (such as clinical trial data); a hard open source reading may entail access to competitors' full regulatory dossiers by analogy with 'derived works';[46] as a product moves from the lab bench to the dispensary, the open source design would need to make choices on the economics of clinical trials, not merely proof of concept. It would have to address, too, another distinctive characteristic of life sciences innovation today: the claim for actual property rights or quasi-property rights over non-inventive inputs into the research, in the form of genetic material, or what Kloppenburg termed 'a form of national property'.[47] In short, if the value of the model is to be assessed from a complex ethical framework that links the need to accommodate interests and equities reaches further upstream and downstream than the software model.

Without overplaying such resonances, IP law and practice already offers several tools that could be deployed in open source or free life sciences innovation structures. Past examples exist of the open dissemination of research tools through non-exclusive, accessible licensing; of cross-licensing structures that maintain collective access to improvements; of collective undertakings to maintain free access to genomic information as a 'pre-competitive' foundation for derivative innovation. Patent law requires full enablement disclosure, so that 'source code' – potentially including physical specimens of microorganisms – can't in principle be locked up, but must be available to the researcher; rights to

[45] Weber S., *The Success of Open Source,* Harvard University Press, Cambridge, 2004.

[46] Open Source Definition, para 3: Derived Works: 'The license must allow modifications and derived works, and must allow them to be distributed under the same terms as the license of the original software. Rationale: The mere ability to read source isn't enough to support independent peer review and rapid evolutionary selection. For rapid evolution to happen, people need to be able to experiment with and redistribute modifications.'

[47] Kloppenburg, J., *First the seed: the political economy of plant biotechnology, 1492–2000,* Cambridge: Cambridge University Press, 1988.

research and experiment and the breeder's exception open up derivative uses of protected subject matter; the compulsory cross-licensing provisions of the EU Biotechnology Directive and the law of 'dependent inventions' amount to 'rights to use' patented technology, roughly akin to freedom to use derivative innovations.

These sketchy imprints of the software 'freedoms' or elements of open source even within the existing legislative structure recall the ambivalence about the level of address to policymakers: does the search for reformed innovation structures entail fundamental legislative reform, even treaty renegotiation; or reframing public-policy and public-interest interventions such as research funding and public research policies; or addressing the choices by individual researchers, institutions and firms. At the broadest international level, the objective for IP protection expressed in the WTO TRIPS Agreement poses an ethical and legal challenge: protection of IP 'should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations'. It is difficult to take issue with this statement of a broad objective. Within this legal text, it surely guides the interpreter of the treaty to an inclusive view of public policy interests. But within the broader policy context, is it also a guide to the policymaker – an ethical heuristic? Hence, what kind of specific obligations might this suggest for those actively engaged in structuring the innovation infrastructure? To deliver on this promise for IP protection – and setting aside questions of formal treaty interpretation – there are many ways of construing this 'should': is it ethical in a deontological sense, expressing a duty incumbent on those engaged in protecting IP[48] or in a utilitarian sense, setting a test for legitimacy of policy choices within the TRIPS framework; is it consequentialist, providing a benchmark for the legitimacy of the actual outcomes of policymaking; or is it limited in ethical guidance, being strictly legal in character, establishing a formal obligation on policymakers bound by the treaty; or is it simply aspirational, more apposite for a preamble; or, most tantalising, is it predictive – a statement that the application of well-balanced IP mechanisms, implemented in line with the ensuing detailed standards, will *a fortiori* yield this outcome? In practice, this

[48] Recalling that TRIPS elsewhere views 'protection' in expansive terms as including 'matters affecting the availability, acquisition, scope, maintenance and enforcement of intellectual property rights as well as those matters affecting the use of intellectual property rights specifically addressed [in TRIPS].' (footnote to Article 3).

chapter may conflate into a general test of legitimacy, so flexible as to provide support for many diverse actual dispensations.

Similarly, although the frame of reference is more focused, it remains difficult to pin down a precise ethical basis to support the choice of innovation structures in the life sciences. If it is considered desirable to encourage the adoption of 'open source' or free innovation in the life sciences, what kind of ethical or legal argument applies?

- enlightened self interest: it is good for you, it is a more efficient form of innovation that better serves your objective interests;
- ethical duty: you should behave this way, because it is inherently right to do so: perhaps because you would wish others to offer you the 'four freedoms',[49] and so the Kantian categorical imperative applies;
- strict utilitarian: it yields improved welfare outcomes for society overall;
- legal – you must do it by law, whether or not it is in your real or perceived interests, because of obligations either within IP law (noting the imprints of openness or freedoms found in IP law) or beyond IP law (such as the invocation of human rights or equitable obligations).

Each form of compulsion has been urged for 'open source' or free approaches to life sciences innovation. But does the nature of the 'should' depend on who and where you are? Recall that the essence of IP policymaking is setting what legally defined exclusivities over knowledge resources will advance innovation, fair competition and public welfare, and how those exclusivities should be shaped and governed. Some 'open source' ideas and some freedoms are hard-wired at the legislative level (or at least they can be) – this is at least the spirit of the enabling disclosure, for example, and the term limit on patents (I am not arguing that close congruence exists, not by any means, but identifying limited points of convergence). Individual holders of exclusive rights are also presented with a range of obligations – ethical and legal – and both self interested and altruistic motivations. A complete analysis of a reformed innovation infrastructure in the life sciences would need to consider firstly how to promote the overall goals of innovation policy (broadly, both beneficial innovation and equitable access to the fruits of that innovation) within IP law, as a legal system; and secondly, to promote greater convergence with these goals of the actual outcomes from

[49] By analogy with the freedoms identified by Stallman – the freedom to run a program; the freedom to study how it works through access to the source code; the freedom to redistribute copies; and the freedom to improve and distribute improvements (Stallman R. *The Free Software Definition*, 1996, www.fsf.org/philosophy/free-sw.html).

that system; and third, what modes and structures would most productively draw together providers/users of technologies, including the use of literal or metaphorical open source and free structures, so that their real and perceived interests, and the way those interests are pursued. This would close the ethical gaps between a hard consequentialist account (attaching value only to beneficial outcomes), deontological ethics or the ethics of doing one's duty (so that the ethically approved forms of behaviour do actually yield the desired outcomes), and legally permissible forms of IP and exercise of IP right.

16.4 Concluding comment: situating the hospital and the granary between the cathedral and the bazaar

This discussion aims to illuminate pathways towards practical answers for the following core questions for life sciences policymakers:

(i) Is the only irresistible impetus to 'open source' or free in life sciences ultimately *technological*? Does leverage work essentially because the core (or seed) technology is so good – functionally good or economically attractive – or even effectively indispensable, in the case of unique research tools? Or is it a negative incentive – technology holdings stack up so that practical implementation of proprietary technology is literally unworkable (as occurred in the SNP case)? If the technology is the draw card, then the objective rationale for free/open life sciences may be circular, or recursive: as increasingly valuable technology is placed within this framework, the incentive to use the framework is strengthened. Looking back at the software example, Raymond suggests that a technological seed is essential: '… one cannot code from the ground up in bazaar style. One can test, debug and improve in bazaar style, but it would be very hard to originate a project in bazaar mode. Linus didn't try it. I didn't either. Your nascent developer community needs to have something runnable and testable to play with.'[50]

(ii) Are the hospital and the granary neither 'cathedral' nor 'bazaar'? Although *in silico* and *in vitro* research pathways may cross and merge, the kind of life sciences research and development that moves close to delivering practical products differs in key ways from software development. 'Release early and release often'[51] is unappealing for a new cox-2 inhibitor or glyphosate-resistant seed.

[50] 'Necessary Preconditions for the Bazaar Style' in Raymond E., *The Cathedral and the Bazaar*, Thyrsus Enterprises, <thyrsus.com>, version 3.0 (2000).

[51] 'Release Early, Release Often' in Eric Raymond, *The Cathedral and the Bazaar*.

And this is not merely a regulatory matter: it also concerns different needs for resources, infrastructure, ethical constraints and liability and risk management.

(iii) How to learn from and apply a technology-specific innovation model to a new field? Does one empirically reverse engineer 'open source' or free biotechnology from what has been shown to work in existing life sciences research, and port across models or even license text from the software field, or does one invoke models in the abstract, driven by ethical and broader considerations? If each of these three sources and approaches impels the review process, how does one absorb and integrate these disparate ideas and experiences while continuing to prioritise public interest objectives over particular models?

'Open source' or free research models offer pathways towards democratised innovation – democratised in participation, in its pluralistic directions, and in the distribution of opportunities and benefits. As broad models, they have resonances with long practice in many innovative contexts: many traditional or local technology users have long been read-write innovators. These models touch on issues that are of immediate concern for life science policymakers aiming to advance the public interest: reducing transaction costs for the creation of the bundles of technology and other inputs that define new life sciences products; broadening the scope of innovation to meet neglected needs; and for developing countries especially, strengthening domestic technological capacity and, where sought, technological autonomy and self-reliance.

But the prudent policymaker – with much at stake – will need a stronger objective base to work from, rather than reacting to proprietary models that are aggressively pursued by their principal corporate beneficiaries. Crafting innovation policy is broader in sweep than creating an asylum from monopolistic excesses, which can and should in any case be regulated directly. Open source or free innovation models in the life sciences may be understood and integrated within development strategies inasmuch as they confer systemic benefits. Failure to democratise innovation is not exclusively an artefact of the proprietary nature of rights over technology (system and application software) – the most neglected communities and obvious failures of innovation to deliver are situated where proprietary rights either do not exist or are practically unenforceable. Our natural, polemical tendency to structure debate through polarities might also overshadow the need to understand the complex interplay between proprietary and non-proprietary models of innovation and product development on a broader planning canvas

when looking at the life sciences in the round – basic human needs and the production of public knowledge goods are most unlikely to be met exclusively through proprietary or non-proprietary approaches. The 'open source' debate in the life sciences is therefore valuable in exposing the weakness of this polarisation: exclusive or proprietary rights can be used to leverage access, to promote dissemination, to safeguard downstream use rights: the notion of promoting access through rights that exclude is indeed the underlying paradox of IP law and policy.

Whether and how benefits are obtained in practice depends on how skilfully any model is actually deployed and judiciously adapted, and on skills, resources and infrastructure: no innovation model or licensing structure is magic pixie dust; perhaps the single most damaging step a legal advisor can offer a research project is to reach for her folder of licensing precedents, as a shortcut for an objective appraisal of what broader goals the management of knowledge within the research programme should serve. Any viable open source project in the life sciences is likely to need good core technology and good technologists, clearly an abiding strength of reported open source software projects, and the innovation structure – including its formal legal underpinnings – will be built around what forms of interaction work best for the community of researchers and users (including those users who become sources of incremental innovations). The dissemination and analysis of models and metaphors can, nonetheless, stimulate new innovation practices and structures.

Even so, it is not a compelling need in life sciences innovation simply to construct, analyse and defend new or alternative innovation models for the sake of it; the core policy demands are to enhance, accelerate, decentralise and democratise life sciences innovation, to develop and disseminate more and more diverse useful products to wider groups of beneficiaries, and to reduce barriers to entry for researchers and to broaden the conception of research (for instance so that traditional medicine practitioners are recognised as true research partners in medical R&D[52] and so that the role of farmers in agricultural innovation and crop improvement is more systematically recognized[53]). 'Open

[52] See, for instance, the Indigenous Knowledge Systems policy of the South African government and its application by the Medical Research Council.

[53] Consistent also with the articulation of farmers' rights in the FAO International Treaty on Plant Genetic Resources for Food and Agriculture (Article 9), recognizing 'the enormous contribution that the local and indigenous communities and farmers of all regions of the world, particularly those in the centres of origin and crop diversity, have made and will continue to make for the conservation and development of plant genetic resources which constitute the basis of food and agriculture production throughout the world.'

source' – and any other model – is not an end in itself, but should create pathways to better use of resources to meet more widespread needs. It may help break down illegitimate barriers and overcome poor, overly constricted approaches. But a fully equitable disposition of knowledge goods probably also requires the currently dispossessed acquiring some control afforded by proprietary structures or exclusive rights, to leverage their interests more effectively than purely through moral suasion and the expected benefits of technological diffusion. The open source debate in the life sciences is a reminder that, pragmatically, but also for the best ethical reasons, some degree of leverage over technology – even the use of exclusive rights to exclude overly exclusionary practices so as to protect a commons, or to sustain an enabling technology platform, is necessary.

REFERENCES

Bergstrom, T., Blume, L., and Varian, H., 'Private Provision of Public Goods', **29** *Journal of Public Economics*, 1986, 25–49 (http://econwpa.wustl.edu/eprints/pe/papers/9503/9503001.abs)

Berthels, N. 'Case 8. CAMBIA's Biological Open Source Initiative (BiOS)', Chapter 13 of this volume

Clarke, M., *Standards and Intellectual Property Rights*, 2004

Dawkins, R., *The Selfish Gene*, 1976

Horst, A. C., *International Property Rights Index (IPRI)*, 2007 Report (www.InternationalPropertyRightsIndex.org)

Horwitz, S., 'From Smith to Menger to Hayek: Liberalism in the Spontaneous Order Tradition', **6** *The Indep. Rev.* 1, 2001, 81.

Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume.

The International HapMap Consortium, 'The International HapMap Project', **426** *Nature*, 18 December 2003

Kilcullen, J., *Rawls: The Original Position*, Macquarie University, 1996 (www.humanities.mq.edu.au/Ockham/y64l13.html

Kloppenburg, J., *First the Seed: the Political Economy of Plant Biotechnology 1492–2000*, Cambridge: Cambridge University Press, 1988.

Levy, S., *Hackers: Heroes of the computer revolution*, New York, 2001

Ley, E., 'On the Private Provision of Public Goods: A Diagrammatic Exposition', **20** *Investigaciones Economicas* 1, 1996, 105–23, at IMF, Washington DC, (http://econwpa.wustl.edu/eprints/pe/papers/9503/9503001.abs)

Martin, G., Sorenson, C. and Faunce, T., 'Balancing intellectual monopoly privileges and the need for essential medicines', **3** *Global Health 4*, 2007.

Plato, Protagoras (translated, Benjamin Jowett, at 310d).

Raymond, E., *The Cathedral and the Bazaar,* Thyrsus Enterprises, version 3.0, 2000

Rawls, J., *A Theory of Justice*, Harvard University Press, 1971

Samuelson, P.A., 'The Theory of Public Expenditure', **36** *Review of Economics and Statistics*, 1954, 386–389.

Smith, A., *An Inquiry into The Nature and Causes of the Wealth of Nations*, Henry Frowde ed., Oxford Univ. Press, 1909, 1776

Stallman R., *The Free Software Definition*, 1996 (www.fsf.org/philosophy/free-sw.html)

Taubman, A. *Practical Management of Public-Private Alliances for Public Health Outcomes in the Developing World: The Lessons of Access Conditions in Research and Development Agreements*, Initiative on Public-Private Partnerships for Health in Global Forum for Health Research, Geneva, 2004

'Saving the Village: Conserving Jurisprudential Diversity in the International Protection of Traditional Knowledge', in Keith E. Maskus and Jerome H. Reichman (eds.), *International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regimen*, 2005, 521.

Weber, S. *The Success of Open Source*, Harvard University Press, Cambridge, 2004.

Zawinski, J. *Resignation and Postmortem*. 1999 (jwz@jwz.org).

Part IV

Liability regimes

17 Pathways across the valley of death

Novel intellectual property strategies for accelerated drug discovery

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17.1 Introduction

Most therapeutic interventions produced by pharmaceutical firms take the form of small molecule drugs,[1] which are mass produced at low marginal cost and ingested orally. Drug therapies typically work by affecting the activity of human proteins, known in the industry as targets,[2] that have been implicated in disease pathways. Thus far, medical science has identified safe and effective therapies for only a few hundred of the estimated 3,000 protein targets in the human genome that are potentially susceptible to a drug.[3] Moreover, pharmaceutical

[+] The views expressed here are those of the author and not necessarily of the National Research Council or the National Academies.

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[1] We use the term "small molecule" to distinguish that class of compounds that can alter the activity of DNA or proteins but are not themselves proteins, peptides, or nucleic acids.

[2] Ideally, potential targets would include not only individual proteins but also protein-protein interactions. *See* Arkin, M.R. and Wells, J.A. 'Small-Molecule Inhibitors of Protein-Protein Interactions: Progressing Towards the Dream', 3 *Nature Revs. Drug Discovery* 301 (2004).

[3] Whitty, A. and Gnanasambandam Kumaravel, 'Between a Rock and a Hard Place?', 2 *Nature Chemical Biology* 112, 112 (2006) (giving an estimate of about three hundred proteins); Russ, A.P. and Stefan Lampel, 'The Druggable Genome: An Update', 10 *Drug Discovery Today* 1607 (2005). Under the definition used in this Article, susceptibility to a drug, or "druggability," is defined by whether the protein is capable

firms have encountered major obstacles in producing fundamentally new small molecule drugs, especially those that work against new targets. According to one report, an average of only three drugs that act on novel targets have reached the market annually in recent years.[4]

This highly visible problem has attracted commentary in scholarly articles,[5] government white papers[6] and the popular press.[7] Government agencies, such as the National Institutes of Health,[8] and industry insiders,[9] have also recognized that one of the most serious pitfalls involves the difficulty of moving across the so-called "valley of death" that separates upstream research on promising genes, proteins and biological pathways from downstream drug candidates. For example, an upstream finding that a given protein is differentially expressed in individuals with a particular disease may suggest that the protein merits further investigation. However, much more work (especially medicinal chemistry) is necessary to determine how good a target the protein really is and whether a marketable drug candidate that affects the activity of the protein is likely to be developed.

As industry observers have noted, successfully translating upstream research into potential drugs will require experimentation with new

of binding a chemical compound. This definition does not address the question of whether the binding will yield a result that is biologically useful.

[4] *See* Zambrowicz, B.P. and Arthur T. Sands, 'Knockouts Model the 100 Best-Selling Drugs – Will They Model the Next 100?', 2 *Nature Revs. Drug Discovery* 38, 39 (2003); *see also US* Gov't Accountability Office, New Drug Development: Science, Business, Regulatory, and Intellectual Property Issues Cited as Hampering Drug Development Efforts 1 (2006) [hereinafter *GAO Report*], *available at* www.gao.gov/new.items/d0749.pdf (stating that FDA submissions for new chemical molecules have generally declined since 1995, even though industry research and development increased 147% in inflation-adjusted dollars between 1993 and 2004). New chemical molecules are drugs that differ fundamentally in structure from prior molecules. They are, therefore, the type of drugs that are most likely to be active against new targets (or show substantially increased efficacy against old targets).

[5] *See, e.g.*, Cockburn, I.M., 'The Changing Structure of the Pharmaceutical Industry', *Health Aff.*, Jan–Feb 2004, at 10, 11; Cohen, F.J., 'Macrotrends in Pharmaceutical Innovation', 4 *Nature Revs. Drug Discovery* 78 (2005); Service, R.F., 'Surviving the Blockbuster Syndrome', 203 *Science* 1796 (2004) (discussing low numbers of new chemical entities approved in recent years).

[6] *See, e.g.*, US Food & Drug Admin., Innovation or Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products (2004), *available at* www.fda.gov/oc/initiatives/criticalpath/whitepaper.pdf.

[7] *See, e.g.*, 'Billion Dollar Pills', *The Economist*, 27 January 2007, at 69, 70 ("With its traditional approach, Big Pharma is not coming up with new drugs fast enough to fill its pipeline.").

[8] *See, e.g.*, Austin, C. et al., 'NIH Molecular Libraries Initiative', 306 *Science* 1138 (2004); *see also GAO Report*, above note 4, at 40 (noting importance of "translational medicine" for addressing the drug discovery problem).

[9] *See, e.g.*, Lipinski, C.A., 'The Anti-Intellectual Effects of Intellectual Property', 10 *Current Opinion in Chemical Biology* 380 (2006).

models of R&D.[10] In this article, we propose one such initiative: intensive, large-scale collaboration between academics, who possess unique skills in designing assays that can identify promising targets, and pharmaceutical firms that hold libraries of potentially useful small molecules as trade secrets, making them largely off limits to these same academic scientists.

As we discuss below, conventional patent-based strategies for commercialization of university research, of the type envisioned by statutes like the Bayh-Dole Act of 1980,[11] are unlikely to foster such intensive collaboration. Moreover, while R&D alliances between small biotechnology firms and large pharmaceutical companies can perhaps fill some of the collaboration gap, thus far these vertical alliances have not appreciably stimulated productivity in the area of small molecules.[12] To achieve the goal of inducing more well-trained "eyes" to search chemical space for useful molecules, we need a contract-based platform that makes these molecules broadly available to academic experts without compromising future patents.

The collaborative initiative we propose takes its inspiration from existing horizontal collaborations between pharmaceutical firms, which focus on identifying markers of drug safety and efficacy. However, our proposed effort aims to identify potential drugs that may someday reach the market and generate revenue. We therefore need to define ownership more deliberately than do current collaborations, which focus on information that is generally considered pre-competitive at all stages. Although firms would not bring specific patents to the table *ex ante* (as they do, for example, in most vertical R&D alliances between smaller

[10] *See, e.g.*, DataMonitor, Addressing Pharma's R&D Productivity Crisis: Technical and Strategic Initiatives To Improve Core Drug Discovery Capabilities, www.market-research-report.com/datamonitor/DMHC1960.htm (last visited 2 November 2007) (noting that "[c]ompanies must fundamentally review R&D business models and exploit new strategies for re-establishing core drug discovery expertise").

[11] Bayh-Dole Act of 1980, Pub. L. No. 96–517, 94 Stat. 3015 (codified as amended at 35 U.S.C. §§ 200–212 (2000)).

[12] These alliances have been more successful in increasing productivity in the area of biological macromolecules (a class of specialty drugs known as "biologics") like proteins and large peptides. *See* Cockburn, above note 5, at 12, 14; Service, above note 5, at 1797–8. However, such biologics are expensive to develop and hence quite costly to patients (with prices ranging from thousands to hundreds of thousands of dollars for an annual supply). Moreover, the absence of a generic regime for biologics, see below note 29, means that their prices do not decrease to any meaningful extent even after patents expire. *See, e.g.*, Anand, G., 'As Costs Rise, New Medicines Face Pushback', *Wall St. J.*, 18 September 2007, at A1 (making these points and noting that spending on specialty drugs rose 21% in 2006, as contrasted with 6% for non-generic, non-specialty (e.g., small molecule) drugs); Anand, G., 'Rx for an Industry: As Biotech Drug Prices Surge, US Is Hunting for a Solution', *Wall St. J.*, 28 December 2005, at A1 [hereinafter Anand, 'Rx for an Industry'] (noting that spending on specialty drugs represents 25% of national spending on biopharmaceuticals).

biotechnology firms and larger pharmaceutical companies),[13] future intellectual property rights would nonetheless be suitably allocated among collaborators.[14] Moreover, unlike existing horizontal collaborations that have focused on safety and efficacy issues, our proposed initiative would deliberately integrate academic scientists as a built-in vertical component.

We situate our proposal in the economic literature that has analyzed transaction costs and incomplete contracting in the context of inter-firm R&D alliances.[15] The inter-firm alliance we propose would simultaneously redound to the financial benefit of the pharmaceutical industry and promote the interests of public sector researchers. Most importantly, under our scheme intellectual property would be used creatively to secure efficient pathways across the gap that separates upstream research from downstream products – a gap so economically perilous that it has

[13] Smith, G., 'The Exit Structure of Strategic Alliances', 2005 *U. Ill. L. Rev.* 303, 308 n.29 (noting that in a sample of 125 genomics alliances, 113 involved the licensing of intellectual property by smaller technology firms); *cf.* Lerner, J. and Robert P. Merges, 'The Control of Technological Alliances: An Empirical Analysis of the Biotechnology Industry', **46** *J. Indust. Econ.* 125, 132 (1998) (noting that biotechnology firms with more intellectual property rights exercised more control over the alliance).

[14] *See generally Oliver Hart, Firms, Contracts, and Financial Structure* 29–55 (1995) (discussing the importance of *ex ante* property rights allocation). *Ex ante*, the information at issue in our proposal is not patentable. Boilerplate patent law does not allow patents on biochemical inventions of unknown function. *See* Utility Examination Guidelines, 66 Fed. Reg. 1092, 1097–99 (5 January 2001).

[15] *See, e.g.*, Majewski, S. and Dean V. Williamson, 'Incomplete Contracting and the Structure of R&D Joint Venture Contracts', in *Intellectual Property and Entrepreneurship* 201 (Libecap, G.D., ed., 2004) (arguing that the allocation of property rights in innovation generated by R&D partners is an important part of contract design, particularly in patent sensitive industries like the biopharmaceutical industry); Sampson, R., 'The Cost of Misaligned Governance in R&D Alliances', **20** *J.L. Econ. & Org.* 484 (2004) (finding that alliance governance based on transaction cost arguments substantially improves collaborative benefits). The economic literature on incomplete contracting grows out of the literature on transaction cost economics (TCE). Both literatures emphasize the *ex ante* and *ex post* transaction cost challenges that managing uncertain future conditions poses for efficient contracting. Unlike the TCE literature, however, the property rights strand of the incomplete contracting literature tends to stress the role of *ex ante* property rights allocation. A related literature discusses how the availability of statutory intellectual property rights (typically patent rights) in modular information defines the boundaries of the firm and may also facilitate inter-firm market transactions. *See, e.g.*, Arora, A. et al., *Markets for Technology: The Economics of Innovation and Corporate Strategy* (2001); Arora, A. and Robert P. Merges, 'Specialized Supply Firms, Property Rights and Firm Boundaries', **13** *Indus. & Corp. Change* 451 (2004); Burk, D.L. and Brett H. McDonnell, 'The Goldilocks Hypothesis: Balancing Intellectual Property Rights at the Boundary of the Firm', 2007 *U. Ill. L. Rev.* 575. This literature is not as directly relevant to our proposal, as we do not purport to alter the statutory standards by which patent rights are granted or propose new statutory rights.

earned the "valley of death" moniker.[16] If these arrangements generated a larger number of efficacious drugs, the public at large would become the ultimate beneficiary.

In Section 17.2, we frame the problem and describe some alternative efforts, existing and proposed, to accelerate drug development. In Section 17.3, we examine several new pharmaceutical industry collaborations that provide some precedent for our proposed collaboration. In Section 17.4, we set out our proposed multi-firm collaboration model. In Section 17.5, we discuss the perspectives of various stakeholders (e.g. pharmaceutical companies, academic researchers, non-profit funders), with a view toward finding common ground on which to develop the proposed public-private partnership. We also discuss the possibility of single firm public–private partnerships, which could represent a desirable option if a comparison of pharmaceutical firm libraries showed substantial overlap among them. We conclude by considering briefly antitrust concerns as well as the broader implications of the collaborative framework we construct for small molecule libraries.

17.2 Framing the problem

Biomedical research in the pharmaceutical industry mainly focuses on small molecule chemical compounds. In contrast with proteins or other biologics, small molecule chemicals are usually mass produced at low marginal cost and are taken orally.[17] Many pharmaceutical firms own collections, or "libraries," of hundreds of thousands of small molecules that they have either synthesized internally or have purchased from outside vendors. Because the functional attributes of these molecules have not generally been studied in any depth, they typically do not meet even the relatively lax standards for patentability currently applied by the courts.[18] To protect their investment, firms impose a strict regime of trade secrecy.

In order to test the molecules for biological activity pertaining to disease processes, pharmaceutical firms must screen them against interesting

[16] Although we focus here on translation of biological research into small molecule drugs, the term "valley of death" is widely used to describe difficulties of market translation across different fields of scientific endeavour. *See, e.g.*, *Comm. on Accelerating Tech Transition, Nat'l Research Council, Accelerating Technology Transition: Bridging the Valley of Death for Materials and Processes in Defense Systems* (2004).

[17] The systemic bioavailability of small molecules tends to be greater as well. Depending on their construction, small molecules may simply diffuse through tissues, whereas proteins must be transported.

[18] *See generally In re* Brana, 51 F.3d 1560, 1565–68 (Fed. Cir. 1995) (finding the patentability requirement of utility met where molecule in question had shown cancer-fighting properties in a mouse model).

proteins. The experimental protocol under which a target protein is screened is known as an "assay". For the past few decades, pharmaceutical firms have been using high-throughput screening (HTS)[19] of small molecule libraries against assays containing target proteins to identify promising compounds that may lead to patentable drugs. HTS allows researchers to examine the interaction between the subject of the assay and all of the many thousands of small molecules housed in a single library in only a few hours, which vastly increases the scope of potentially useful information available to scientists. However, despite explosive growth in genomic and proteomic information about potential targets, and increasing levels of R&D spending,[20] results of the HTS approach have thus far been disappointing. As noted earlier, the production of drugs that work against new targets has been particularly difficult.[21]

The pharmaceutical firms' failure to find new drugs has been accompanied by a significant decline in sales revenues on existing drugs. Large pharmaceutical firms have typically generated very high sales revenues (and profits) through patents on so-called "blockbuster drugs" that they can market to large population segments. Prominent examples of blockbuster drugs include cholesterol-lowering agents, anti-hypertensives and antidepressants. But patents on many blockbusters are now expiring.[22] Moreover, insurers are becoming reluctant to pay high prices for so-called "me-too" drugs – new products that represent mere incremental improvements over existing molecules.[23] In order to maintain

[19] *See* Bleicher, K.H. et al., 'Hit and Lead Generation: Beyond High-Throughput Screening', **2** *Nature Revs. Drug Discovery* 369 (2003); Walters, W.P. and Mark Namchuk, 'Designing Screens: How To Make Your Hits a Hit', **2** *Nature Revs. Drug Discovery* 259 (2003). The initial mechanical problem presented by high-throughput screening of thousands of chemical compounds was solved by the use of robotic devices. Current state-of-the-art scanners use robotics to test more than one million compounds per day against various assays. *See* Vogel, G., 'NIH Gears Up for Chemical Genomics', **304** *Science* 1728 (2004).

[20] *See GAO Report*, above note 4.

[21] *See* above note 4 and accompanying text; *see also* Bleicher, above note 19, at 370 ("[D]espite the massive growth in screening compound numbers over the past fifteen–twenty years, no corresponding increase in successfully launched new chemical entities has resulted."). *See generally* US Food & Drug Admin., above note 6.

[22] *See* Smith, A., 'Generic Drug Flood Headed Our Way', *CNN Money*, 3 August 2005, http://money.cnn.com/2005/08/03/news/fortune500/generic/ (quoting drug industry analyst Andrew Forman of W.R. Hambrecht & Co. for the proposition that $100 billion worth of brand name drugs will lose patent protection between 2006 and 2010).

[23] In 2005, 68% of employers who provided insurance reported using tiered programs of co-payment to encourage the purchase of inexpensive pharmaceuticals (either generics or brand name drugs on which discounts had been negotiated). Blumenthal, D., 'Employer-Sponsored Insurance – Riding the Health Care Tiger', **355** *New Eng. J. Med.* 195, 199 (2006). Historically, the market signals sent to pharmaceutical firms have been less than efficient. Not only have health care payers generally been reluctant

profitability, pharmaceutical firms must produce fundamentally new molecules that address new targets and thus represent substantial improvements over existing treatment.

Dearth of drugs against new targets

Although the genome is estimated to contain at least 3,000 druggable targets, only a few hundred proteins are fully validated[24] in the sense that they are shown to be biologically interesting and also susceptible to regulation by metabolically accessible, non-toxic drugs. Despite the infusion of new information about possible targets, some pharmaceutical companies continue to focus on this group of a few hundred, already validated targets. While this strategy may indicate excessive risk-aversion, the fact that health insurance companies were once willing to pay high prices for me-too drugs remains a factor. Validating new targets is also more risky and complex now than in the past. Many observers believe most of the "low hanging fruit" – that is, targets that can be readily modulated by well-tolerated, simple chemicals – has been found. This tendency to focus on a small number of known targets means that insufficient research has been undertaken on new targets.[25]

A number of discovery-oriented pharmaceutical firms continue to engage in target validation using in-house biological and chemical expertise. So do some small biotechnology firms. For the latter, patents on new targets can serve as the basis for both arms-length licensing and more vertically integrated R&D alliances with pharmaceutical firms. One empirical study indicates that biotechnology and pharmaceutical firms formed more than 1,000 such two-firm alliances between 1993 and 2000.[26] Despite these alliances, which may be responsible for a

to use cost-effectiveness analysis in determining coverage, but the information necessary for determining cost-effectiveness – a public good – has been undersupplied. Avorn, J., 'Sending Pharma Better Signals', **309** *Science* 669 (2005). However, this situation may be changing. *See ibid.* Moreover, at least in some cases, incremental improvements may not even be patentable. *See, e.g.*, *Pfizer v. Apotex*, 480 F.3d 1348 (Fed. Cir. 2007) (holding that a new salt form of an existing chemical compound was not patentable).

[24] *See* Whitty and Kumaravel, above note 3.

[25] *See, e.g.*, Cockburn, above note 5, at 12. It is theoretically possible that the low-hanging fruit that has already been found represents the sum total of biological targets on which research is justified as an economic matter. In other words, the costs of doing further research may exceed the health benefits achieved by any new drugs that might be found. There is little evidence to back this hypothesis, however.

[26] Higgins, M.J., *The Allocation of Control Rights in Pharmaceutical Alliances* (Soc. Sci. Research Network, Working Paper No. 918980, 2006), *available at* http://ssrn.com/abstract=918980 (describing an empirical study using data from Recombinant Capital, a California-based biotechnology consulting firm). For a discussion of such

growing pool of therapeutics that are biological macromolecules,[27] very few new small molecule drugs have emerged.[28] Given escalating health care expenditures, this dearth of cost-effective small molecules, which (unlike biologics) can be made at low marginal cost after relevant patents expire,[29] is particularly unfortunate.

Moreover, while biotechnology firms could previously use early stage patents to secure venture capital funding or form vertical alliances, such patents no longer guarantee either funding or an alliance. Industry analysts have recently emphasized the biomedical "funding gap" resulting from the increasing reluctance of venture capital and pharmaceutical firms to invest far upstream.[30]

The failure of efforts to fill the small molecule pipeline may prove to be a transient phenomenon, particularly if the integration of information technology accelerates drug development efforts. However, despite optimistic predictions in the past,[31] information technology has not yet yielded significant efficiencies. This failure makes experimentation with supplementary approaches imperative.

Another candidate for undertaking financially risky target validation is academia. Indeed, a key economic argument for public funding of science is that the private sector will tend to undersupply research with uncertain commercial potential.[32] Even though it may need some assistance in identifying which targets are most likely to bind drug-like molecules, the academic sector generally possesses the combination of

licensing and alliance activity at one of its historical spikes (around 2000–1) see Rai, A.K., 'Fostering Cumulative Innovation in the Biopharmaceutical Industry', **16** *Berkeley Tech. L.J.* 813, 815–18 (2001).

[27] *See* Anand, *Rx for an Industry*, above note 12 (noting the 25% market share now held by specialty drugs, primarily biologics).

[28] *See GAO Report*, above note 4.

[29] Currently, there is no generic biologics regime. Moreover, even if a generic biologics regime were established, bioequivalence is likely to be harder to prove in the context of biologics than in the context of small molecules. In any given case, the FDA may require clinical trials to demonstrate comparable safety and efficacy. This will create a barrier to entry for generic competitors. *See* Grabowski, H. et al., 'Entry and Competition in Generic Biologics', **28** *Managerial & Decision Econ.* 439 (2007).

[30] *See, e.g.*, Klausner, A., 'Mind the (Biomedical Funding) Gap', **23** *Nature Biotechnology* 1217 (2005) (tracking the history of funding for research, and noting the reluctance of venture capital firms to fund upstream biomedical ventures).

[31] One of the authors of this Article previously made some optimistic predictions in this regard. Rai, A.K., 'The Information Revolution Reaches Pharmaceuticals: Balancing Innovation Incentives, Cost, and Access in the Post-Genomics Era', 2001 *U. Ill. L. Rev.* 173.

[32] *See* Arrow, K., 'Economic Welfare and the Allocation of Resources for Invention', in Nelson, R.R. (ed.), *The Rate and Direction of Inventive Activity* 609 (1962) (discussing problems of uncertainty, indivisibility, and lack of appropriability involved in the production of information).

skills needed for assay development.[33] But most academics have lacked systematic access to high-throughput screening and to the small molecule libraries necessary for comprehensive target validation. Instead, academics who desire access to small molecules in a pharmaceutical firm's library must negotiate terms of access and the corresponding intellectual property considerations on an ad hoc basis. Knowledgeable observers have long suggested that the transaction costs associated with these individualized negotiations constitute a significant barrier.[34]

A recent survey of 414 academic scientists by John Walsh, Charlene Cho and Wesley Cohen provides some evidence of the magnitude of these costs. In general, academic scientists report that negotiations between industry and academia concerning materials are likely to take longer, and cause more delay, than negotiations within academia: 35% of such negotiations require more than a month (as contrasted with 21% of negotiations with university suppliers) and 16% of such negotiations result in a research delay of over one month (as contrasted with 6% of academic negotiations).[35] Where the material in question is a drug, the transaction becomes particularly arduous. All other factors being equal, an academic's request for a drug (whether from industry or from another academic) was one-twelfth as likely to be fulfilled as requests for other materials.[36]

Strains in academic–industry negotiations concerning drug-related materials should come as no surprise. Such negotiations would typically become an option only in cases where the firm's research on a drug compound had progressed to the point of disclosure through publication (and associated patenting).[37] Disclosure would serve to alert the academic researcher that a firm had discovered a promising compound. At that stage, much would be known about the drug compound, which would make the resulting transactions of relatively high value. The firm would probably demand significant compensation for transferring the drug. In

[33] *See* Ivinson, A.J., Letter to the Editor, 'University Investment in Drug Discovery', **310** *Science* 777 (2005) (contending that academics have been underutilized in drug research and discovery).

[34] *See* Lipinski, above note 9, at 382 (discussing individualized negotiations between principal investigators and pharmaceutical firms).

[35] Walsh, J.P. et al., 'Where Excludability Matters: Material Versus Intellectual Property in Academic Biomedical Research', **36** *Research Policy* 1184, 1185–7 (2007).

[36] *Ibid.* at 1190–1. When reporting this statistic, the authors do not control for whether the supplier is an academic or is in industry. Thus it is not possible to determine whether requests for drugs were less likely to be fulfilled by industry suppliers than academic suppliers.

[37] *Cf.* Lipinski, above note 9, at 381 (discussing circumstances where a firm refers to a compound in a peer reviewed publication). In order to preserve commercial value, the firm would presumably allow publications about the compound only after a relevant patent application had been filed.

fact, empirical data indicates that 70% of agreements involving the transfer of drugs to academics include reach-through rights on improvements.[38]

At some point, industry requests for reach-through rights in patented drugs may become routine. As matters currently stand, however, academics and university technology transfer officers remain uncertain about the appropriate use of such rights,[39] and their uncertainty can lead to impasse. The fact that 70% of agreements to transfer drugs to academics also include some restrictions on publication[40] no doubt exacerbates difficulties in negotiation.

Of course, information could flow in the opposite direction. Firms do monitor academic publications to determine whether researchers are working on promising targets. In some cases they successfully form partnerships with the academics in question.[41] But surmounting difficulties in negotiation across the academic–industry divide appears challenging in this context as well. In the survey by Walsh and his colleagues, academic respondents admitted to failing to fulfil 31% of requests for materials from industry (as contrasted with only 6% from other academics).[42]

Attempts to bridge the public–private divide

More standardized legal documentation is one obvious mechanism for reducing transaction costs in transfers of drug-related materials between the private sector and academics. In general, standardized contracts can produce positive externalities that reduce transaction costs for users,[43] and efforts in this direction could be helpful. However, because the transactions in question are likely to be of high value,

[38] Walsh et al., above note 35, at 1193. A reach-through royalty is an industry term that refers to a royalty that extends beyond the licensed item to products made using the licensed item.

[39] *See* Eisenberg, R.S., 'Bargaining Over the Transfer of Proprietary Research Tools', in Dreyfuss, R. et al., (eds.), *Expanding the Boundaries of Intellectual Property* 223 (2001). It is also noteworthy that while academics often ignore patents on research materials and make the materials in-house if they have the ability to do so, drug patents represent a prominent exception. *See* Walsh et al., above note 35, at 1192. In the case of drugs, *both* lack of in-house expertise and patents represent barriers to use. *Id.*

[40] Walsh et al., above note 35, at 1193.

[41] Telephone Interview with Roses, A., Senior Vice President of Pharmacogenetics, GlaxoSmithKline, in Research Triangle Park, N.C. (18 April 2006) [hereinafter Roses Interview] (discussing partnerships that firms sometimes form upon reading of interesting work by academic researchers).

[42] Walsh et al., above note 35, at 1191.

[43] *See* Kahan, M. and Michael Klausner, 'Standardization and Innovation in Corporate Contracting (or "The Economics of Boilerplate")', **83** *Va. L. Rev.* 713, 720–30 (1997) (discussing learning benefits conferred on later users and "network benefits" conferred on contemporaneous users).

full standardization will be difficult to achieve, or even affirmatively undesirable. Significant benefits may accrue from some level of customization. Moreover, the creation of standardized agreements represents a collective action problem.[44] Given the divergent perspectives of academia and the private sector, solving this problem may not be straightforward.[45]

Even if standardized agreements were successfully created and implemented, the universe of transactions would be limited to those circumstances in which significant work had already been carried out. Drug discovery might be accelerated, but only to a limited extent. To put the point another way, the problem is only partly one of transaction costs in instances where transactions might currently occur. More fundamentally, under the existing regime, insufficient numbers of transactions – specifically, screens of potentially interesting assays against large volumes of small molecules – occur in the first instance.

A more comprehensive response to the valley-of-death problem is the Molecular Libraries Initiative (MLI), undertaken by the National Institutes of Health (NIH) several years ago.[46] Although the purposes of the MLI go beyond target validation, one key goal is to use public funding to advance research on targets to a stage that would elicit industry interest. The MLI reflects NIH's recognition of three key technological changes: first, that recent research in genomics (e.g., the Human Genome Project) has produced many new potential drug targets; second, that enormous increases in high-throughput screening power make the screening of hundreds of thousands of molecules a day possible for academic centres; and third, that academic centres now have the capacity to efficiently synthesize large numbers of chemical molecules.[47]

The MLI has created a "Molecular Libraries Small Molecule Repository" at the San Francisco facilities of Discovery Partners

[44] *Ibid.* at 736–40 (discussing "coordination" problems).

[45] In some cases, implementation of standardized agreements can also represent a collective action problem. *See* Rai, A.K. and Rebecca S. Eisenberg, 'Bayh-Dole Reform and the Progress of Biomedicine', **66** *Law & Contemp. Probs.* 289, 306 (2003) (discussing failure of collective action in university implementation of the standardized Uniform Biological Materials Transfer Agreement).

[46] *See generally* Austin et al., above note 8 (describing the background and goals of the MLI).

[47] *See* Nat'l Insts. Health, Overview, Molecular Libraries and Imaging, http://nihroadmap. nih.gov/molecularlibraries/ (last visited 30 October 2007). In addition to the MLI, various individual public institutions offer some HTS capability. For a list, see Nwaka, S. and Alan Hudson, 'Innovative Lead Discovery Strategies for Tropical Diseases', **5** *Nature Revs. Drug Discovery* 941, 947 (2006). However, the MLI is the most ambitious effort.

International.[48] It has been paying, and will continue to pay, academic researchers with expertise in medicinal chemistry to generate molecules to populate this public domain repository.[49] Currently, the repository contains about 100,000 small molecules (some of which may duplicate molecules held in pharmaceutical firm libraries). This repository consists of four molecular classes: "specialty sets," including compounds with known biological activity, such as drugs and toxins; natural products; "targeted libraries" for specific, high-profile proteins; and diversity compounds.[50] Ten academic centres have received funding to use this repository to perform high-throughput screening on assays submitted by the research community.[51]

The assays pertinent to this effort encompass more than simply proteins that are potential drug targets.[52] As NIH recognizes, small molecules available in the public domain for all researchers are likely to be extremely valuable as research tools that will further basic understanding of biological pathways not necessarily related to direct drug development. Nevertheless, one of NIH's goals is to encourage target validation, so as to narrow the gap between academic outputs and commercial investment and produce more breakthrough drugs.[53]

In assessing the more directed goal of generating validated targets, it is important to recognize that the molecules in the public repository are likely to be of lower quality (in terms of target specificity, metabolic attributes, toxicity and other relevant features) than those held by pharmaceutical firms. Although academics and the public sector more generally are beginning to achieve some expertise in medicinal chemistry,[54] they still do not possess the level of expertise available in

[48] Molecular Libraries Initiative, General Information, http://mli.nih.gov/mlsmr/general-information (last visited 30 October 2007).

[49] Ibid.

[50] NIH Molecular Libraries, A Roadmap Initiative, MLSMR Project, http://mlsmr.glpg.com/ MLSMR_HomePage/identify.html (last visited 30 October 2007). Targeted libraries include modulators of prominent protein families, such as proteases, kinases, ion channel proteins, and nuclear receptor sets. Diversity compounds include all other compounds. *Ibid.*

[51] Nat'l Insts. Health, New Paradigm Will Help Identify Leads for Drug Discovery, www.nih.gov/news/pr/july2006/nhgri-24.htm (last visited 30 October 2007).

[52] Other assays will include "protein-protein interactions, splicing events, and diverse cellular and even organismal phenotypes." Austin et al., above note 8, at 1139.

[53] *Ibid.* at 1138 (noting goal of target validation).

[54] Thus, it appears that the NIH Chemical Genomics Centre, which is part of the MLI, has identified three classes of molecules that might be useful in treating Gaucher's disease and is currently working on optimizing their activity and reducing toxicity. *See* Press Release, Nat'l Insts. Health, Novel Approach Targets an Inherited Disorder: NIH Chemical Genomics Centre Jumpstarts Drug Development in Public Sector (23 July 2007), *available at* www.genome.gov/2552214. In addition, according to

the pharmaceutical industry. This handicap may make the MLI target validation goal harder to attain. More comprehensive validation may await confirmation by a private firm's screening against a more "drug-like" molecule in its own library.

One might argue that private firms should be willing to undertake this additional work. Under the default rules of the Bayh-Dole Act of 1980 (which gave universities broad discretion to secure patents on federally funded research),[55] as well as NIH rules specific to the MLI program,[56] universities may patent targets or associated assays. Thus, following the conventional vision of Bayh-Dole,[57] a private firm might hedge the risk involved in this additional work by obtaining an exclusive license to the patented target or assay. However, given venture capitalists' current reluctance to invest in relatively early-stage patents,[58] these exclusive licenses may not suffice.

In any event, experimentation with another alternative – direct screening of academic assays against a pool of the small molecule libraries held by pharmaceutical firms – would eliminate some unnecessary intermediate work and could also reduce the transaction costs associated with licensing targets. To the extent that such a pool encompassed distinct contributions from several firms,[59] it might contain considerably more molecules than the current group of 100,000 held in the public-domain repository.

In sum, the impasse in genomic science presents the following underlying characteristics. First, too few qualified researchers are able to use screening assays against the small molecule libraries held as trade secrets by discovery-oriented pharmaceutical firms.[60] In particular, academic scientists with the talent to design assays lack access to these libraries. Second, to the extent that the libraries held by individual, discovery-oriented

Centre director Chris Austin, the Centre's specific use of quantitative high-throughput screening techniques, which allows chemical compounds to be tested at different concentrations, is likely to reduce false positives and false negatives. *Ibid.*

[55] Bayh-Dole Act of 1980, Pub. L. No. 96–517, 94 Stat. 3015 (codified as amended at 35 U.S.C. §§ 200–212 (2000)).

[56] *See* NIH MLSCN Project Team Position on Data Sharing and IP in the MLSCN Program (15 October 2005) (on file with authors).

[57] *See, e.g.*, Eisenberg, R.S., 'Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research', **82** *Va. L. Rev.* 1663, 1698–9 (1996) (discussing motivations behind the Bayh-Dole Act); Rai, A.K., 'Regulating Scientific Research, Intellectual Property Rights and the Norms of Science', **94** *Nw. U. L. Rev.* 77, 95–7 (1999).

[58] *See* above text accompanying notes 30.

[59] For a discussion of questions regarding overlap in molecular library contents see below.

[60] Our research suggests that pharmaceutical firms may conduct fewer than one hundred screens per year against their whole library. *See* Roses Interview, above note 41.

pharmaceutical firms differ from each other, it would be advantageous for academics to conduct screening assays against a pool that contains portions of all the libraries held by discovery-oriented firms.[61]

If such a pool were created, it is unlikely that pharmaceutical firms would contribute molecules about which they already possessed significant information (let alone molecules they considered potential lead compounds). Even so, a pool that included some substantial subset of pharmaceutical firms' compounds – for example, "diversity" compounds about which little was known – could prove extremely useful.

17.3 Models for multi-firm, public–private collaboration

As a supplement to current approaches such as the MLI and to possible future efforts, including standardized contracts, we suggest a novel, large-scale public-private model. This collaborative approach would draw upon some recent experimentation that pharmaceutical firms are already conducting in this area. Moreover, it would respond to the advice that analysts have been giving the pharmaceutical industry for years – that it must "fundamentally review [its] R&D business models".[62] In this Section, we describe inter-firm, public–private collaborations in the areas of safety and efficacy upon which our proposed approach would draw. Section 17.4 describes our proposed collaboration in detail.

Existing collaborations on toxicity and efficacy

Until recently, pharmaceutical companies paid insufficient attention to optimizing particular characteristics of small molecules, such as toxicity and "pharmacokinetics" (i.e., absorption, diffusion, metabolism and excretion), which are important for drug safety and efficacy in the human body.[63] For example, firms sometimes designated a "lead" compound, and assembled a full team around it, solely because the compound had shown significant activity (affinity and selectivity) in a high-throughput laboratory screen against an assay containing a target protein.[64] Thus, firms were making a substantial investment without

[61] Molecule libraries held by firms that do not seek to discover new targets would be much less useful, as those libraries would primarily contain molecules that work against existing, already validated targets.

[62] DataMonitor, above note 10.

[63] *See GAO Report*, above note 4, at 87 (finding that failure rates in human clinical trials based on lack of safety or efficacy were 82% in the 1996–9 period and 91% in the 2000–3 period).

[64] Bleicher et al., above note 19, at 370 ("It was not uncommon for a single [hit] compound to be considered a 'lead' structure.").

any good information about how the body would respond to the potential drug. In recent years, analysts have recognized that the lack of early attention to pharmacokinetic and toxicity-related characteristics of proposed small molecules was a factor in the growing number of pipeline failures, including costly failures at late stages of clinical testing or even after FDA approval for commercial marketing.[65]

Pharmaceutical firms have worked diligently to address this problem. As an initial matter, they purged their libraries of molecules that are likely to be "grit" – for example, molecules that are non-selective inhibitors of many different targets or that have well-known pharmacokinetic or toxicological liabilities.[66] Firms are also enhancing the quality of their libraries with the help of specialized suppliers of small molecules. Moreover, prior to selecting lead compounds for optimization, pharmaceutical firms have been supplementing high-throughput screening with another stage of focused inquiry into properties necessary for safety and efficacy in the human body.[67]

The pharmaceutical industry is also advancing safety and efficacy goals by means of public–private collaborative partnerships. Specifically, in establishing at least two such consortia, firms have recognized that an optimal level of inquiry into safety or efficacy may require knowledge not contained within the boundaries of a single firm. To the extent that any participating pharmaceutical firm finds standard, early biological signs (also known as biomarkers) of drug toxicity or efficacy, all the other firms in the consortium could use this information for a variety of efficiency-enhancing functions.

For example, biomarkers might help to provide expedited preclinical drug safety evaluation as well as early indicators of clinical safety and efficacy.[68] They could also be used to troubleshoot compounds that fail preclinical drug safety testing.[69] Whenever the Food and Drug Administration approved a particular biomarker as a reliable indicator of safety or efficacy for a variety of drugs, it might become an industry standard around which all competing firms could converge.

[65] *Ibid.*

[66] Telephone Interview with Roses, A., Senior Vice President of Pharmacogenetics, GlaxoSmithKline, in Research Triangle Park, N.C. (19 December 2006) (on file with authors). *See also* Lipinski, above note 9, at 381 (discussing the use of the Lipinski "rule of 5" to filter out compounds that are unlikely to be absorbed orally).

[67] *See* Hopkins, A.L., Michael J. Witty and Solomon Nwaka, 'Mission Possible', **449** *Nature* 166, 168 fig. (2007) (discussing steps such as cell-based or animal model testing).

[68] *See, e.g.*, Toxicogenomic Cross-Validation Consortium Agreement § 2.1 (20 January 2006) (on file with authors) [hereinafter Consortium Agreement] (discussing the use of "safety biomarkers" for expediting preclinical and clinical drug development).

[69] *See* i*bid.* § 2.1(c) (discussing such troubleshooting).

As the National Academy of Sciences noted in a recent report endorsing horizontal biomarker consortia, these "precompetitive projects (most likely unrelated to a particular drug) would be enabling to the field".[70]

In one recently formed collaboration, the Predictive Safety Testing Consortium (PSTC), all of the major pharmaceutical firms have committed to sharing internally-developed laboratory methods that predict the safety of new treatments.[71] They have also committed to performing validation experiments on laboratory methods developed by other consortium members.[72] As a result, under the PSTC, experts from multiple firms work on sequential phases of the same project to develop tests of drug safety.

The PSTC agreement relies heavily on a non-profit, trusted intermediary, Critical Path, of which the FDA is a founding member. Critical Path is responsible for consortium management. For example, it collects membership fees from pharmaceutical firm participants, coordinates the selection of research projects and (with the assistance of an advisory committee composed of Critical Path and pharmaceutical firm representatives) manages the flow of any confidential information.[73] If the PSTC advisory committee deems it appropriate to seek patents on technology generated by the consortium, Critical Path will own the patent rights.[74]

While the PSTC focuses on tests for safety, the recently-formed Biomarkers Consortium aims to encompass research that identifies

[70] Nat'l Acad. of Scis., Cancer Biomarkers: The Promises and Challenges of Improving Detection and Treatment 6 (2007), *available at* http://books.nap.edu/catalog/11892.html.

[71] Consortium Agreement, above note 68, § 3.2 (stating that members "must be willing and able to contribute one or more nominated exploratory Safety Biomarkers or other information or Materials for use in Consortium research activities"). Note that the Predictive Safety Testing Consortium was formerly known as the Toxicogenomic Cross-Validation Consortium.

[72] *See ibid.* (stating that members must "perform validation work with respect to one or more Safety Biomarkers … and have the capability to cross-validate Safety Biomarkers").

[73] *See ibid.* §§ 5.2, 6.1 (discussing various aspects of Critical Path's management role).

[74] *See ibid.* § 8.2(a) (noting the role of the advisory committee in determining whether to pursue formal patent rights); *id.* § 8.2(b) (stating that "[e]ach Member performing any activities under a Research Project hereby assigns to C-Path all of such Member's right, title, and interest in and to any and all Consortium Technology"). The PSTC recently submitted twenty-three proposed biomarkers that could be used to identify kidney toxicity in preclinical animal testing. *See* Toner, B., 'Predictive Safety Testing Consortium Submits First Biomarkers to FDA for Qualification', *Genome Web Daily News*, 21 June 2007, www.genomeweb.com/issues/news/140703–1.htm. It is unclear whether any patent rights have been sought.

good biomarkers of both drug safety and efficacy.[75] Like the PSTC, the Biomarkers Consortium includes all of the major pharmaceutical firms, and it allows scientists at competing firms to contribute their expertise to the development of specific biomarkers. As with the PSTC, public sector agencies – most prominently the non-profit Foundation for the NIH, which manages public–private partnerships for NIH – play a major role in selecting research projects and in managing the flow of funding.[76]

Research on biomarkers will ultimately yield products, such as safety assays, that are beneficial to multiple pharmaceutical firms, but are unlikely to represent a core product for any firm. For this and other reasons, both of these consortia require *ex ante* commitments to relatively liberal licensing agreements for any intellectual property their common efforts may generate.

In the case of the PSTC, members agree that the objective of the consortium is to achieve "broad public dissemination of the results of the research and development projects conducted pursuant to this Agreement".[77] Patents are to be sought only in cases where the advisory committee determines that they would promote dissemination of discoveries.[78] Moreover, Critical Path is obligated to license any patents it may own to all comers on commercially reasonable terms.[79]

In contrast with the PSTC, the Biomarkers Consortium does not assign intellectual property rights to a trusted intermediary. Rather, inventorship is governed by the default rules of US law, and ownership is defined by the policies of the inventor's employer.[80] Nonetheless, for all new data and inventions arising out of a particular project, all participants that have an ownership interest in the intellectual property generated must grant to all other participants a "non-exclusive, remuneration-free license".[81]

[75] Press Release, Foundation for the NIH, Public-Private Partnership Forms the Biomarkers Consortium To Advance the Science of Personalized Medicine (5 October 2006), *available at* www.fnih.org/news/TBC_Press_Release.shtml (noting that "the FDA can use biomarkers to determine whether drugs can safely and effectively treat disease"). The Biomarkers Consortium also plans to identify biomarkers for early disease detection. *See ibid.* That research goal is not directly relevant here.

[76] *See* Found. for the NIH, The Biomarkers Consortium, Two-Phased Project Approval Process: Concept Clearance and Project Plan Approval 3 (2006), *available at* http://test.fnih.org/Biomarkers%20Consortium/Project_Clearance.pdf (showing a flowchart that details responsibilities of the FNIH Board). While the PSTC funds its research projects from membership fees, the Biomarkers Consortium agreement requires the Foundation for the NIH to seek specific funding for each new project. I*bid.*

[77] Consortium Agreement, above note 68, § 8.2(a). [78] *See ibid.* [79] *Ibid.* § 8.3(b).

[80] Found. for the NIH, The Biomarkers Consortium, General Intellectual Property and Data Sharing Principles 5 (2006), *available at* http://test.fnih.org/Biomarkers%20Consortium/IP_Policies.pdf.

[81] *Id.*

Expanding the collaborative approach

The formation of collaborative horizontal partnerships to address safety and efficacy raises the question of whether other, somewhat analogous, but more ambitious forms of collaboration could successfully address problems of translation. Specifically, we ask whether large-scale collaboration might improve translation by the academic sector of large volumes of upstream biological information into "validated targets" and potential drug candidates that would be of interest to industry. Like safety and efficacy, translation arguably entails further improvement of relatively undifferentiated trade secret information held by multiple firms. This improvement process may be greatly enhanced through evaluation by multiple parties.

Like the PSTC and the Biomarkers Consortium, our proposed partnership would use a trusted intermediary to facilitate firm participation. Additionally, like the Biomarkers Consortium, it could use the lure of public funding to stimulate greater participation by the private sector. Unlike these other consortia, however, our partnership would produce outputs – potential drug candidates – that engender fierce inter-firm competition. Thus, while the PSTC does not link inventive contribution and ownership, our proposal would maintain a tight link between the two. Additionally, whereas the PSTC and the Biomarkers Consortium mandate relatively liberal licensing practices, our proposal would have no such mandate.

In our proposed partnership, the trusted intermediary would necessarily play a more vigorous role in handling confidential information. As discussed further in the next Section, the intermediary would itself conduct the high-throughput screening of the pharmaceutical firms' molecules against assays contributed by academics. It would thus be the only party to the collaboration that possessed full knowledge of all of the assays and molecules that academics and pharmaceutical firms, respectively, had contributed.

By merging academic talent in assay design with the high-quality but underutilized research resource represented by the pharmaceutical firms' libraries, our proposed public–private partnership aims to help the parties traverse the valley of death that currently impedes research on drugs that address new targets. As contrasted with the alternative of complete vertical integration – for example, subsidizing discovery-oriented pharmaceutical firms to hire academics with assay design skills – the public–private partnership we envision would allow assay designers access not simply to one firm's library but instead to a larger, pooled library consisting of small molecule collections that

a number of firms had contributed. Unlike complete vertical integration, a public–private collaboration would not require academics to change career paths, which would make it more likely to succeed. Pharmaceutical companies contributing portions of their libraries might still be subsidized to the extent that the trusted intermediary consented, at least initially, to bear some of the costs associated with establishing the pool and of providing academic researchers relevant grants.

Pharmaceutical firms that contributed compounds to the pool would profit directly from any commercial drug that emerged from molecules they contributed. As we discuss in the next Section, ordinary patent rules would deliver this result. Additionally, participating firms might find it in their interest to allow those who contributed molecules to the pool to receive a small share of the patentee's profits when one or more of their molecules fell within a subset of initially promising molecules identified by the screening process. In the latter instance, profit would be derived from a predetermined royalty stream to the contributing firms under an automatic license, as discussed below.

17.4 Proposed multi-firm partnership

In this Section, we outline the institutional framework and intellectual property strategies that could help stakeholders in both the private and public sectors to make better and more productive use of the aggregate stock of small molecules available for high-throughput screening. These proposals attempt to bridge the gap between patents and the public domain, which is currently regulated only by the application of trade secret law (or actual secrecy), to the private sector's large hoards of small molecules.

The ultimate objectives of our approach are to:

1) Create a research regime in which qualified public-sector participants explore a larger and higher quality pool of molecules than is currently possible.
2) Design a contractually constructed framework in which publicly funded university research could identify potential lead compounds without compromising patents on those compounds.
3) Administer this voluntarily adopted framework within a public–private partnership that would more effectively translate upstream research into truly innovative therapeutic advances, thereby contributing to overall public health.

Threshold question of overlap

An initial question regarding pool formation concerns possible overlap among molecules that participating firms may contribute. If, for example, it turned out that molecules contributed by different firms were substantially identical, then there would be little reason to pool the molecules. In that case, a model of multiple public–private partnerships, each built around contracts with a single firm, would become preferable. This alternative model is discussed in Subsection 'Single firm public–private partnerships' below.

Because libraries are held by firms as trade secrets, the amount of overlap among them is currently unknown. More important for present purposes, it is unclear whether the molecules actually selected and contributed by participating firms would overlap. Even if we postulate that most firms would contribute so-called "diversity" molecules (because these were the molecules about which they had little specific information), the extent of overlap between the various firms' diversity molecules remains unknown. A trusted intermediary accordingly would need access to structural data on a confidential basis in order to determine the degree of overlap. It could then release this information (in suitably anonymized fashion) to participating firms.

For example, in a situation where three firms had contributed molecular libraries, the intermediary might reveal that, of the total number of molecules contributed, about 20% were duplicates owned by two firms and 10% by three firms. At that point, the participating firms would determine whether the degree of overlap was sufficiently small to justify going forward. If the firms decided to proceed, the pooled molecules would already have been collated and any instances of duplication identified. This collation would, in turn, eliminate duplicative screening.

Two-tiered regime

Central to our proposed multi-firm partnership is a two-tiered system. At Tier 1, both academic external researchers and the participating companies could be viewed as operating behind a "veil of ignorance".[82] Although the researcher might possess some information about a potentially interesting assay, and the participating companies might hold some basic information about the molecules they contributed, information on both sides would be relatively inchoate and precompetitive in nature.

[82] *Cf.* Rawls, J., *A Theory of Justice* (1971).

Equally important, only the trusted intermediary would know about the full set of assays and molecules existing at Tier 1. Individual academic researchers and contributing firms would remain unaware of contributions by any other parties. In contrast, research activities conducted at Tier 2, under the custom-made contractual arrangements described below, would necessarily have moved beyond this veil of ignorance.

The trusted intermediary would host the pool and assume responsibilities for its day-to-day management and administration. The intermediary would also certify and perhaps fund the public-sector academics allowed to explore the molecules held in the pool. Additional financial guarantees from participating universities might become necessary in order to assure pharmaceutical firms that contractual obligations regarding nondisclosure were respected.

Tier 1: Behind the veil of ignorance

At the first tier of the partnership, researchers in approved academic institutions (that is, institutions that had signed nondisclosure agreements and perhaps put up a bond to guard against misappropriation) would contribute assays. The trusted intermediary would then run these assays against the pooled collection of small molecules made available by participating firms. All molecules contributed to the pool would be tagged with a marker that tracked their corporate origin. The trusted intermediary would, however, code these markers so that researchers receiving information on "hits" resulting from high-throughput screening would not know the pharmaceutical firm owner of the molecules they were using.

Successful high-throughput screening of these molecules would likely identify a subset of molecules as "hits" – in other words, molecules that showed significant activity against the target in question and could lead to new drug candidates. The academic who contributed the assay would receive coded results showing levels of activity for the relevant molecules, and the firms would receive some information as well. This Tier 1 information would be released in a structured way, in order to best facilitate the formation of an academic–pharmaceutical partnership for further target validation and drug development.

Prior to being told that one or more of the molecules it had contributed represented a hit, the firm could withdraw a molecule at any point. In order to forestall opportunistic behavior, however, once the trusted intermediary informed the firm that one of its molecules represented a hit, that molecule could not be withdrawn. On the contrary, after a hit, the contributing firm would have an obligation to provide

relevant structural information to the academic via the intermediary.[83] Standardized licenses governing first-tier access would forbid information disclosure or misappropriation.

For its part, the academic laboratory and associated university (communicating through the intermediary) would provide the firms that owned hit molecules with a general statement of the methodology used to develop its target. However, in order to maintain its bargaining position despite the absence of a patent,[84] the academic institution would not identify that target.[85] Therefore, at this point, the academic scientist would know the chemical structure of a number of compounds that showed activity against the target, while the pharmaceutical firm(s) would know that one or more molecules from their libraries had presented interesting research possibilities.

The public-sector scientist, with the assistance of the trusted intermediary, would attempt to determine which firm had the combination of hit molecules most likely to yield a successful drug. The decision would presumably be based on an assessment of liabilities and assets associated with the structures in question. Through the trusted intermediary, a firm could also, if it so desired, share with the scientist on a confidential basis any additional information that it might have. Presumably, it would do so in order to entice the scientist into a second-tier partnership.

A complication in the process would arise if one or more of the chosen firm's hit molecules were duplicates of molecules owned by another firm. In all likelihood, co-ownership of even one molecule should remain a relatively rare occurrence because, as discussed earlier, if molecules contributed by different firms overlapped significantly, there would be little reason to move forward with a multi-firm pool.

In the event of co-ownership, there are several options worth considering, and one to be avoided. The latter is the default route of future *patent* co-ownership (e.g. co-ownership of a patent on a potential lead compound that emerged from the co-owned molecule). Patent law

[83] For purposes of collation and determining overlap, the firm would already have provided this structural information to the intermediary. As discussed further in the illustrative example below, structural information is probably the primary information the firm would have. In particular, firms would be unlikely to contribute to the pool molecules about which they had significant positive information.

[84] University participants in the partnership would be barred from seeking patents on assays or targets prior to participation in the screening program. See below.

[85] For further discussion of the university perspective, as well as the perspectives of other stakeholders, see below.

encourages strategic behavior on the part of co-owners by allowing each one to "make, use, offer to sell, or sell the patented invention… without the consent of and without accounting to the other owners".[86] Although this default approach has the virtue of facilitating licensing (because the consent of only one co-owner is needed), it also means that disagreement between co-owners undermines the existence of an effective patent monopoly. Under our current system of R&D financing, monopoly rights on drugs are critical for hedging the risk associated with the long and complex pre-clinical and clinical development process.[87]

The simplest solution would allow the researcher to continue with the firm he or she had chosen, notwithstanding co-ownership of one or more hits. This option would be particularly useful if (as seems likely, given that the threshold inquiry would presumably have found relatively little overlap in contributions) only one or two molecules out of the chosen firm's set of hits were co-owned. The co-owner might then be entitled to royalty-based compensation if the molecule in question led to a marketable drug, but it would have avoided the cost and risk of follow-on work.

In the rare case where all (or most) of the relevant molecules were co-owned, the co-owning firms could set up a separate joint venture that would hold future patent rights. In order to avoid antitrust concerns in cases where the joint venture occupied a large share of the relevant research space, one of the firms could remain a silent partner that simply held a pre-determined equity stake in the joint venture. Importantly, the initial framework agreement would specify the alternatives available in situations of dual ownership so as to rule out the possibility of co-ownership of patents.

As noted earlier,[88] it appears that some pharmaceutical firms have already formed public–private partnerships with academic researchers

[86] *See* 35 U.S.C. § 262 (2000). *See generally* Merges, R.P. and Lawrence A. Locke, 'Co-Ownership of Patents: A Comparative and Economics View', **72** *J. Pat. & Trademark Off. Soc'y* 586 (1990) (discussing possibilities for opportunistic behaviour created by the law of co-ownership).

[87] *See, e.g.*, Cohen, W.M. et al., 'Protecting Their Intellectual Assets: Appropriability Conditions and Why US Manufacturing Firms Patent (or Not)', (Nat'l Bureau of Econ. Research, Working Paper No. 7552, 2000), *available at* www.nber.org/papers/w7552; *cf.* Lewis, T.R., Jerome H. Reichman and Anthony D. So, 'The Case for Public Funding and Public Oversight of Clinical Trials', *Economists' Voice*, Jan. 2007, www.bepress.com/ev/vol4/iss1/art3/ (arguing that clinical trials should be treated as a public good).

[88] *See* above note 41 and accompanying text.

whose published work indicates that they are working on interesting targets. They have done so, however, on a limited, ad hoc basis. Our first tier public–private partnership would provide a standardized platform for the systematic formation of many more second tier relationships than currently exist. Not only would the basis for forming such relationships be put in place, but with routine access to a pool of high-quality small molecule libraries guaranteed, one would also expect the public sector to develop many more validated targets that would be of interest to pharmaceutical companies.

Essentially, firms would be outsourcing assay development and target validation to individual academics who are well placed to do this work, but who would otherwise be difficult to integrate into the firm vertically as employees.[89] As contrasted with vertical integration, a public–private partnership would allow assay developers to run their assays against a broad array of molecules held by multiple firms.

Tier 2: Beyond the veil of ignorance

Once the academic had chosen a prospective partner, second-tier negotiations would commence. Because the terms of such second-tier partnerships are likely to vary quite substantially depending on the type of target at issue, we do not propose standard-form agreements for this tier. Presumably, the negotiated contract enabling Tier 2 research would further specify the expected relations of the parties during the drug development phase, and the distribution of expected royalties from patented lead compounds. Assuming the drug development process proved successful, and the patented drug passed clinical trials and entered the stream of commerce, the patent owner (i.e., the pharmaceutical firm) would obtain patent rents exactly as occurs at present.

A possible complication could arise, however, if the scientist and the pharmaceutical firm could not successfully conclude a second-tier agreement. In that case, we would propose that the scientist retain the opportunity to negotiate with the owners of other molecules that had represented hits at Tier 1. The information obtained by the academic in the negotiations with the first firm would, of course, remain subject to confidentiality and non-disclosure agreements.

[89] *Cf.* Munos, B., 'Can Open-Source R&D Reinvigorate Drug Research?', **5** *Nature Revs. Drug Discovery* 723, 723 (2006) (discussing the outsourcing of drug research-related laboratory and clinical studies "to institutions with the requisite capacity through the help of matchmaking software").

If a Tier 2 partnership was formed and *subsequently* dissolved, the magnitude of potential inter-firm information leakage could become sufficiently great as to rule out allowing the scientist to negotiate with other firms. In any event, the framework agreement for the partnership would have to provide for both of these contingencies.

An important question to be addressed in the Tier 2 agreement would concern the timing of any eventual publication by the academic. Although we do not propose standard form agreements at Tier 2, the framework agreement should ensure that the academic can publish his or her findings as soon as appropriate arrangements for patentability had been made. This would represent an improvement over the current situation, where the available empirical evidence indicates that corporate sponsors sometimes require academics to withhold data well beyond the time necessary to file a patent.[90]

Option of a contractually constructed liability regime[91]

In addition to the structure outlined above, participating firms might also agree on a supplementary system of royalties that would govern compensation to any firm that had provided structural information about its molecules to a researcher deciding among promising "hits." In other words, firms would be contracting into a subsidiary set of "take and pay rules", or liability rules, rather than relying entirely on exclusive property rights.[92] As a historical matter, liability rules have always modulated between exclusive property rights, on the one hand, and the public domain, on the other.[93] In modern times, codified liability regimes that provide *ex ante* entitlements to compensation for certain uses (but not necessarily a right to exclude others from use) have been

[90] *See, e.g.*, Blumenthal, D. et al., 'Relationships Between Academic Institutions and Industry in the Life Sciences – An Industry Study', **334** *New Eng. J. Med.* 368, 371 (1996) (finding that 56% of corporate sponsors report that research results are sometimes kept confidential longer than the time required to file a patent).

[91] The term "contractually-constructed liability regime" is drawn from Reichman, J.H. and Paul F. Uhlir, 'A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment', **66** *Law & Contemp. Probs.* 315 (2003).

[92] The classic reference is, of course, Calabresi, G. and Douglas Melamed, 'Property Rules, Liability Rules, and Inalienability: One View of the Cathedral', **85** *Harv. L. Rev.* 1089 (1972); *see also* Merges, R., 'Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations', **84** *Cal. L. Rev.* 1293 (1996).

[93] *See, e.g.*, Reichman, J.H., 'Saving the Patent Law from Itself: Informal Remarks Concerning the Systemic Problems Affecting Developed Intellectual Property Regimes', in Kieff, F.S. (ed.), *Perspectives on Properties of the Human Genome Project* 289 (2003).

adopted in some intellectual property systems,[94] and in at least one international treaty.[95]

One feature of liability rules is that, even in the absence of legislative fiat, they may be voluntarily adopted whenever stakeholders seek to obtain a private ordering with outcomes that differ from what the default rules of intellectual property law might otherwise provide.[96] For example, various commentators have discussed patent pools as an example of contractually constructed liability rules.[97] Similarly, contractually constructed liability rules are sometimes used by patent holders as a mechanism for generating revenue from background property rights. (Indeed, proponents of the "one monopoly profit" thesis would argue that patent holders should generally be indifferent between using liability rules and exploiting their monopoly exclusively.)[98] When Stanford University famously made its Cohen-Boyer patent on DNA manipulation techniques available to all users willing to pay specified royalties under a non-exclusive license,

[94] *See, e.g.*, Reichman, J.H., 'Charting the Collapse of the Patent-Copyright Dichotomy', **13** *Cardozo Arts & Ent. L.J.* 475, 504–20 (1995) (stressing the need for a new intellectual property paradigm based on liability rules for cumulative and sequential innovation); Reichman, J.H., 'Legal Hybrids Between the Patent and Copyright Paradigms', **94** *Colum. L. Rev.* 2432, 2477 (1994) (discussing an Italian regime protecting construction designs and technical drawings); *ibid.* at 2480 (discussing the British Design Law of 1988, since repealed by the E.U. Design Regulation); *see also* Merges, above note 92, at 1308–9 (discussing 17 U.S.C. § 115, a liability regime for sound recordings of copyrighted musical works).

[95] F.A.O. Res 3/2001, International Treaty on Plant Genetic Resources for Food and Agriculture, 3 November 2001, www.fao.org/ag/cgrfa/itpgr.htm (imposing a compensatory liability regime on those who make commercial applications derived from public-domain seeds).

[96] *See* Reichman, J.H., 'Of Green Tulips and Legal Kudzu: Repackaging Rights in Subpatentable Innovation', **53** *Vand. L. Rev.* 1743 (2000); *see also* Reichman, J.H. and Tracy Lewis, 'Using Liability Rules To Stimulate Innovation in Developing Countries: Application to Traditional Knowledge', in Maskus, K.E. and Jerome H. Reichman (eds.), *International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regime* 337 (2005).

[97] *See, e.g.*, Merges, above note 92, at 1340–52. As Merges discusses, the typical patent pool involves multiple firms agreeing voluntarily to refrain from exercising their rights to exclude. Instead of asserting patent rights, firms contribute the rights to a package license that is available on reasonable terms either to participants in the pool or to all comers. I*bid.* In recent years, the pooling of patents around information technology industry standards has become quite common. *See, e.g.*, Shapiro, C., 'Navigating the Patent Thicket: Cross-Licenses, Patent Pools, and Standard Setting', in Jaffe, A. et al. (eds.), **1** *Innovation Policy and the Economy* 119, 2001.

[98] For an excellent discussion of the implications of the "one monopoly profit" thesis for platform technologies, and of situations where the thesis might not apply, see Farrell, J. and Philip Weiser, 'Modularity, Vertical Integration, and Open Access Policies: Towards a Convergency of Antitrust and Regulation in the Internet Age', **17** *Harv. J.L. & Tech.* 85, 104, 105–19 (2003).

it voluntarily converted the exclusive rights conferred by its patent to a liability regime.[99]

As discussed further below,[100] we believe the possibility of a liability rule payment could induce greater participation by pharmaceutical firms. This compensatory liability payment (say, on the order of 3–5%) would become available to firms if any of their molecules fell within the class of promising hits at the initial stage of high-throughput screening. Firms would accordingly benefit from income streams not only in circumstances where they actually undertook the expensive and risky follow-on work that led to a patented marketable drug, but also if they contributed a small amount (in the form of structural information on a hit) to upstream work. In this manner, firms could, to some extent, mitigate the overall risks of drug development.[101]

The framework agreement for our proposed partnership would spell out any *ex ante* liability rule entitlements that the participating firms had agreed to adopt. The intermediary would also collect and share data concerning the impact of the liability regime as a cost-sharing and risk-reducing technique over time. However, in the event that such obligations triggered antitrust difficulties or deterred participation (perhaps because firms doing the follow-on work resisted the liability rule as an unacceptable reach-through royalty),[102] they remain an optional feature of our proposal.

Adding new participants

The public–private partnership we propose would be most likely to succeed if the founding members were firms with robust libraries that continued to be active in the search for new targets. At the same time, it would be inopportune, counterproductive, and possibly illegal as a matter of antitrust law to foreclose the possibility that other firms might join the pool. The pool members would thus be well advised to organize from the outset the conditions of future membership.

Because of the manner in which the pool would be structured – specifically, the fact that private-firm researchers would not have any

[99] For a discussion of the Cohen-Boyer licensing strategy, see Rai and Eisenberg, above note 45, at 300.

[100] See below.

[101] We also believe that the innovation-related benefits of a liability rule scheme (in terms of inducing participation in the pool) are sufficiently large that a small royalty paid to competitors should not be deemed to violate antitrust law. See below.

[102] See above note 38.

access to the small molecule pool and that even access by academic researchers at Tier 1 would be restricted to information about potentially promising hits – adding additional members should be relatively straightforward. New members and their contributions would be protected by the same nondisclosure agreements as pre-existing members. Similarly, hit molecules contributed by new members would be treated in the same manner as hit molecules contributed by founding members.

Notably, existing consortia, such as the PSTC, explicitly provide for the addition of new members. Under the PSTC framework agreement, new members that can contribute to biomarker validation and pay membership fees are allowed into the consortium as a matter of course.[103]

An illustrative example

Consider the following stylized example of the manner in which our proposed public–private partnership would work.[104] Many researchers believe that Alzheimer's disease is caused by the accumulation of short protein fragments that are formed when certain precursor proteins (known as amyloid precursor proteins) break down.[105] An Alzheimer's researcher (Researcher A) in University B determines that a previously unknown protein (protein C) appears to be centrally involved in the breakdown of amyloid precursor proteins. She creates an assay designed to test whether a small molecule binds to protein C ("protein C binding assay").

Researcher A (and her employer, University B) have previously complied with all the requirements for participation in the screening pool. She and her university have signed the relevant non-disclosure agreements and have posted the bond necessary to reinforce the pertinent non-disclosure rules. Thus, she is eligible to submit her assay to the trusted intermediary who will screen it against the aggregate collection of molecules that Companies 1, 2, and 3 have contributed to the pool.

The trusted intermediary will have previously compared the structure of the molecules submitted by these companies and presumably

[103] Consortium Agreement, above note 68, § 3.3.

[104] Note that although the facts in this example are generally based on accurate scientific information, they are intended for illustrative purposes only.

[105] See, *e.g.*, Marchesi, V.T., 'An Alternative Interpretation of the Amyloid Hypothesis with Regard to the Pathogenesis of Alzheimer's Disease', **102** *Proc. Nat'l Acad. Sci.* 9093, 9093 (2005).

found only a small amount of overlap (e.g., only 10% of molecules were owned by two firms and 1% were owned by three firms). Based on this small amount of overlap, the companies had decided to go forward with the pool.

The trusted intermediary proceeds to screen the combined molecule libraries of all three companies against the protein C binding assay. The intermediary then gives the results, which include the raw data generated in the experiment, to Researcher A. In consultation with the trusted intermediary, Researcher A determines that there is a group of seven molecules that show significant activity and might lead to promising new drugs. The trusted intermediary informs A that these molecules are owned by Companies 1 and 3 – Company 1 owns three of the molecules, and Company 3 owns the other four.

At this point, the trusted intermediary also informs Companies 1 and 3 that they have molecules that represent hits, but the companies do not learn that they are hits on protein C specifically. Companies 1 and 3 can no longer withdraw the relevant molecules from the pool, and they must provide Researcher A with information about the structures of the hit molecules. Researcher A and the trusted intermediary analyze the structures they have been given and the results of the assay, and on that basis decide that Researcher A and University B should attempt to negotiate a Tier 2 agreement with Company 3. If an agreement is reached with Company 3, and subsequently results in a new drug, Company 1 may be entitled to a 3–5% royalty as provided for in the framework agreement. If the negotiations with Company 3 fail, Researcher A and University B have the option of negotiating with Company 1.

In the more complex case where one or a few of the molecules in Company 3's set of hits is also owned by another company (say Company 2), the decision-making process would be governed by the rules upon which the stakeholders had previously agreed. For example, the framework agreement might provide that in most cases, Researcher A could simply continue working with Company 3, while Company 2 might become entitled to some predetermined compensation but would not participate in, or bear any risk associated with, downstream research. In the rare case that the relevant molecules were all co-owned, the framework agreement might enable Companies 2 and 3 to form a joint venture that owned any resulting patent rights.[106]

[106] The possibility of using joint ventures in downstream work on a set of promising molecules drawn from different sources would depend on the attitude of the relevant antitrust authorities. We discuss the antitrust implications of these options below.

If this and similar ventures were to succeed, the framework agreement would have maximized opportunities to generate new drugs by multiplying the number of assays that were screened against an expanded chemical space. In this manner, our model would enable complex and risky research that might not otherwise have occurred under existing arrangements. More importantly, it could enable and greatly increase the likelihood of breakthrough therapeutic results on significant diseases.

Single firm public–private partnerships

As previously observed, even if the trusted intermediary determined that the molecules that firms had contributed overlapped substantially, it would still be in the firms' interest to undertake some sort of collaborative approach. In that case, however, a better approach might rely on one or more single firm public–private partnerships. A single-firm partnership would give academic researchers the opportunity to screen their assays against that portion of the firm's library that the firm chose to make available.

Single firm public–private partnerships would not require the level of organizational infrastructure required by a broader pooling approach. A willing firm might simply invite interested academic researchers to submit assays, which it would then screen in-house against some subset of compounds within its proprietary library. However, a trusted intermediary might remain useful in this context, especially if it could assist the firms in identifying potential academic research participants and their associated institutions.

For example, in the context of tropical diseases targets, it appears that the World Health Organization's (WHO) Tropical Disease Network has organized a consortium of researchers who are interested in screening their targets against pharmaceutical firm libraries. Three firms – Pfizer, Merck Serono and Chemtura – are now allowing this "TDR Compound Evaluation Network" to submit targets for in-house screening against a subset of the firms' respective chemical libraries.[107] The trusted intermediary might also help to fund the academic scientists, guard against misappropriation of unpatented results by participants in the partnership, and set the conditions of eventual publication of research results.

Because the private side of the partnership would, at any given time, be limited to a single firm, there would be no need for a two-tiered

[107] Hopkins, Witty and Nwaka, above note 67, at 169.

regime. Rather, qualified academics would simply submit assays to the firm in question. If and when a particular screening assay yielded a group of hits, the academic and the firm would then negotiate the terms of a public–private development partnership. As with the multi-firm partnership, the private firm would be free to withdraw molecules from the screening process up to the point when the molecule yielded a hit.

In the event that screening against the library of a given firm yielded no interesting hits, the academic investigator might want to submit the assay to other firms that had made a subset of their libraries available. However, because anonymity could not be preserved in a single-firm arrangement, "sequential" screening would depend on the first firm's willingness to permit it.

17.5 Analyzing the collaboration: stakeholder incentives and tradeoffs

Having outlined the basic principles of our two-tiered proposal, we turn to a detailed discussion of the incentives that would induce stakeholders to enter into such an arrangement. We also briefly discuss salient antitrust issues pertinent to our proposal.

Firms' perspective

Pharmaceutical firms stand to gain a great deal, and lose little, through participation in our proposal. Current efforts to generate truly novel drugs are failing. Our proposal would leverage the expertise of publicly funded researchers in a manner that redounds to the benefit of the pharmaceutical industry as a whole while limiting aggregate costs and generating considerable efficiencies in the upstream research process.

Firms will be concerned about the risk that potentially important trade secret information (specifically, molecular structure and the fact that a particular molecule shows activity against an assay) might leak over to competitors. For this reason, only academic researchers should be allowed access to such information. Those researchers who identified a promising molecule would be deterred from misappropriation not only by contractual obligations and required bonding, but also by their need to partner with the firm contributing the most promising molecule in order to commercialize the research results.

By contrast, allowing private-sector researchers entry into the pool would create undue risk of misappropriation and industrial espionage. Fear of such misappropriation might deter firms from entering the pool in the first instance. Alternatively, firms might be tempted to contribute

only "bad" molecules. Indeed, fear of misappropriation is so great that various efforts to foster even a limited amount of inter-firm information exchange about molecular library contents in the past have foundered on the inability of firms to sufficiently disguise or mask information about molecular structure.[108] Restricting participation to academic scientists – a prominent feature of our proposal – should prove attractive from the firms' perspective.

Moreover, even with respect to academic researchers, access to molecules would remain quite limited. The trusted intermediary would conduct the high-throughput screening on submitted assays. At Tier 1, academic researchers would receive results (and accompanying structural information) only with respect to molecules that represented hits. In exchange for this information, firms would be rewarded with the possibility of a collaboration as well as a potential royalty even if their firm was not chosen to undertake downstream development.

However, leakage of some structural information between firms might occur in certain circumstances, namely, when an assay revealed hit molecules from two different firms. If an academic moved on to a Tier 2 collaboration with one firm, there is some concern that he might inappropriately use information about the other firm's molecule(s). Similarly, if Tier 2 negotiations with one firm fell through, the researcher might take information derived from those negotiations into conversations with a second firm.

To forestall these possibilities, the framework agreement for the partnership should explicitly prohibit researchers from using information derived from one firm in their dealings with another firm. Enforcement of such a provision might prove difficult, however. Thus, the firm that was not chosen might be best rewarded for the risk of some level of leakage through the contractually constructed liability scheme discussed above.[109]

Academic researchers' perspective

Researchers, and their universities, should be motivated to participate in the collaboration through financial incentives and the potential for groundbreaking discoveries. If academic researchers succeeded in

[108] See Wilson, E.K., 'Is Safe Exchange of Data Possible? Modelers in Need of Proprietary Compounds Seek Ways To Share Information, But Not Structure', *Chemical & Engineering News*, 25 April 2005, at 24, *available at* http://pubs.acs.org/cen/science/83/8317sci1.html (describing efforts to enable "safe exchange" of chemical structures).

[109] See above.

validating a target, they, and their universities, would find themselves in a strong position to negotiate a favorable Tier 2 agreement with one of the companies contributing hit molecules.

The academics would bring to the table their substantial knowledge of the assay and target, and the pharmaceutical firm would bring its information concerning the relevant molecule, its expertise in medicinal chemistry, as well as all of its downstream development resources. If the resulting partnership yielded a commercially successful drug, the researcher and his university would secure a share of the revenues.[110] They would also secure a reputational gain through eventual publication of the breakthrough research.

In our view, these financial and reputational benefits to the public research community should help to offset delays in publication that participating firms might deem necessary to protect commercially valuable information. Specifically, as noted earlier, the researcher exploring chemical space at Tier 1 would have to sign a nondisclosure agreement with respect to any structural data on molecules that he or she received.[111] Additionally, at Tier 2, the researcher must be willing to forego publication of commercially valuable information until relevant patents (e.g. on promising lead compounds) had been filed.

The ultimate financial benefits should also mitigate certain limitations on university patenting that are likely corollaries of our proposed public–private partnership. Under current law, universities are entitled to seek intermediate patents on validated targets. In the proposed collaboration, universities would forgo such patents in exchange for a transactional commitment at Tier 2 by the pharmaceutical company to a revenue stream from any drug that was ultimately developed. This revenue stream would recognize the significant research contribution of the university and its researcher.

[110] Note that this is a different claim from the argument that technology *licensing* (e.g., patent licensing) is likely to bring in substantial revenue. As many observers have noted, university patent licensing generally involves upstream technology with uncertain payoffs and therefore revenues are typically quite small. Only in the relatively unusual circumstance where the university sells rights to a drug is the revenue payoff substantial. *See, e.g.*, Press Release, Emory University, Gilead Science and Royalty Pharma Announces $525 Million Agreement with Emory University To Purchase Royalty Interest for Emtricitabine (18 July 2005), *available at* www.news.emory.edu/ Releases/emtri/ (describing payment of $525 million for sale of royalty rights to anti-AIDS drug). Our proposal similarly would involve partnerships dealing with end-product drugs; therefore, revenue payoffs could be substantial.

[111] See above.

Perspective of the trusted intermediary

In order for the proposed public–private partnership to take off, the trusted intermediary would probably have to provide some seed funding. Specifically, the intermediary might, at least initially, bear the cost of funding researchers to develop assays, of conducting high-throughput screening, and of general pool administration. However, once the concept of pooling small molecule libraries had proved to be scientifically and economically viable, the firms themselves should be willing to subsidize many, if not all, of the activities in the collaboration.

If the trusted intermediary were the NIH, or an NIH-funded proxy, our proposal could be seen as complementary to its Molecular Libraries Initiative. While the MLI is likely to prove very useful in advancing basic knowledge about biological pathways, lack of access to small molecule libraries held by pharmaceutical firms may limit its success in target validation. At a minimum, the MLI will not typically result in potential lead compounds. More generally, two of the three themes highlighted in the current NIH Roadmap for Medical Research – encouraging "new pathways for discovery" and supporting "research teams of the future",[112] (including interdisciplinary work and public–private partnerships) – are specifically promoted by the terms of our proposal.

The pharmaceutical companies could, of course, foot the bill for the entire initiative and establish their own trusted intermediary. We believe, however, that participation of a public entity remains desirable, even if the operation were totally funded by the private sector. For example, the presence of a public-sector player would greatly simplify relations with academia and add a layer of indirect enforcement of non-disclosure rules that would reassure the participating firms. Likewise, a public sector presence would reinforce the academic scientists' expectations that the public interest in shared research results would ultimately be respected, without compromising either side's intellectual property rights. Finally, the presence of a public-sector player would greatly facilitate negotiations between the trusted intermediary and the antitrust authorities over time.

Antitrust concerns and the public interest

If successful, our proposal would necessarily entail some level of collaboration between firms that represent a significant percentage of the

[112] Nat'l Insts. of Health, NIH Roadmap for Research (2006), http://nihroadmap.nih.gov/ pdf/NIHRoadmap-FactSheet-Aug06.pdf.

pharmaceutical industry. For the most part, only limited inter-firm R&D coordination or exchange of information would occur – largely confined to contexts where complementary assets had to be deployed in order to maximize research potential. Thus, we believe that our proposal should pass muster from the standpoint of both normative economic analysis and antitrust doctrine.

The question of whether a competitive or concentrated (perhaps even monopolistic) market structure best promotes innovation has long been mooted in the economic literature. Joseph Schumpeter famously argued that concentration promotes risky innovation by allowing firms to limit diffusion of knowledge to competitors and thus appropriate more fully the benefits of their innovative efforts.[113] In contrast, Kenneth Arrow and others have asserted that monopoly power can dull incentives to innovate, particularly in situations where a new product would displace a product already produced by the monopolist.[114]

As antitrust doctrine has expanded its focus beyond end product markets, it too has examined the relationship between competition and innovation. Influenced by Arrow's work, in the mid-1990s the Federal Trade Commission (FTC) and the Antitrust Division of the Department of Justice (DOJ) adopted an "innovation markets" analysis, which looks at competition in the R&D processes that produce end products.[115] Under innovation markets analysis, a joint venture, licensing agreement, or merger is suspect if it unduly limits the number of competing innovators and yields no offsetting innovation-related efficiencies.

Although innovation markets analysis might imply a relatively strict review of R&D collaborations, the DOJ and FTC have emphasized how difficult it is to define an innovation market.[116] In practice, the overriding focus in most cases is not market definition but whether the collaboration is likely to accelerate or slow the pace at which R&D

[113] See Schumpeter, J.A., *Capitalism, Socialism and Democracy* 81–106 (1942).

[114] See, *e.g.*, Arrow, above note 32. For a summary of these arguments, see Rai, above note 26, at 824–5.

[115] Dep't of Justice & Fed. Trade Comm'n, Antitrust Guidelines for the Licensing of Intellectual Property § 3.2.3 (1995) [hereinafter DOJ, Intellectual Property], available at www.usdoj.gov/atr/public/guidelines/0558.htm (defining innovation markets); see also Dep't of Justice & Fed. Trade Comm'n, Antitrust Guidelines for Collaborations Among Competitors § 3.32(c) (2000) [hereinafter DOJ, Collaboration], available at www.ftc.gov/os/2000/04/ftcdojguidelines.pdf (discussing innovation markets).

[116] "The Agencies will delineate an innovation market only when the capabilities to engage in the relevant research and development can be associated with specialized assets or characteristics of specific firms." DOJ, Intellectual Property, above note 115, § 3.2.3; see also DOJ, Collaboration, above note 115, § 3.32(c).

efforts are pursued.[117] The agencies specifically recognize that "[t]hrough the combination of complementary assets, technology, or know how, an R&D collaboration may enable participants more quickly or more efficiently to research and develop new or improved goods".[118]

In the case of our proposed collaboration, the reality that R&D on new drug targets is very expensive and risky should make antitrust authorities more disposed towards a Schumpeterian perspective on the resulting pharmaceutical innovation. Nonetheless, two aspects of our model might concern antitrust regulators. First, the optional liability rule scheme we have proposed might be seen as a reach-through royalty that dulled incentives on the part of the firm enjoying the royalty to innovate independently. However, we think it is unlikely that a small royalty stream would significantly affect such incentives. The situation where no one works on a molecule that modulates a new target is much more likely. Indeed, it is the status quo.

The second antitrust difficulty might involve the situation where co-ownership of molecules required a substantial compensatory royalty or even a joint venture. In both cases, the argument in favor of allowing collaboration would rest on the fact that the assets in question were co-owned and therefore complementary.

To address antitrust concerns expeditiously, we would propose that the initial framework agreement expressly address questions of co-ownership (and, if desired, liability rules), and that this agreement be vetted by the antitrust authorities before any collaborative work began. The PSTC framework agreement provides an instructive example. It contains an "antitrust statement" that limits inter-firm sharing of information to that necessary for purposes of biomarker validation and allows consortium members to pursue independent biomarker validation projects.[119] We would envision a similar statement addressing antitrust concerns in our framework agreement.

17.6 Conclusion: broader implications of the collaborative approach

In developing our proposal for greater access to small molecule libraries, we have drawn upon models of inter-firm collaboration that the pharmaceutical industry is currently using for biomarkers. However, our approach is designed to work in settings different from the creation

[117] DOJ, Collaboration, above note 115, § 3.31(a). [118] Ibid.
[119] See Consortium Agreement, above note 68, at exhibit A.

of biomarker standards, where rights in collaborative outputs must be tightly protected.

For example, a similar approach may be useful in advanced materials engineering research. Such research represents a context where inter-firm transfer of inchoate and unpatented, but nonetheless valuable, information is desirable.[120] Contract-based exchange can be implemented so long as the connection between the inchoate information put in *ex ante* and the codified, differentiated information that emerges *ex post* is reasonably clear. The presence of a trusted intermediary that polices contract breaches and prevents undesirable spillovers is also important.

Our proposal attempts to embody all the features that are likely to facilitate contract-based exchanges of pre-patentable, but nonetheless valuable, information. If academics and pharmaceutical firms are interested in truly innovative drug discovery, they should experiment with this effort to forge new and viable pathways across what has hitherto proved to be a largely impassable valley of death.

REFERENCES

Anand, G., 'As Costs Rise, New Medicines Face Pushback', **18** *Wall St. J.*, September 2007, A1.

'Rx for an Industry: As Biotech Drug Prices Surge, US Is Hunting for a Solution', **28** *Wall St. J.*, December 2005, A1.

Arkin, M. R. and James A. Wells, 'Small-Molecule Inhibitors of Protein-Protein Interactions: Progressing Towards the Dream', **3** *Nature Revs. Drug Discovery*, 2004, 301–17.

Arora, A. et al., *Markets for Technology: The Economics of Innovation and Corporate Strategy*, 2001, 338.

and Robert P. Merges, 'Specialized Supply Firms, Property Rights and Firm Boundaries', **13** *Indus. & Corp. Change*, 2004, 451–75.

Arrow, K., 'Economic Welfare and the Allocation of Resources for Invention', in R. R. Nelson (ed.), *The Rate and Direction of Inventive Activity*, 1962, 674.

Austin, C., L. S. Brady, T. R. Insel, and F. S. Collins, 'NIH Molecular Libraries Initiative', **306** *Science*, 2004, 1138–9.

Avorn, J., 'Sending Pharma Better Signals', **309** *Science*, 2005, 669

Bayh-Dole Act of 1980, Pub. L. No. 96–517, 94 Stat. 3015, codified as amended at 35 U.S.C. §§ 200–212 (2000).

'Billion Dollar Pills', *The Economist*, **27** January 2007, 71–3.

[120] Professor Rajan, K., Iowa State University, Presentation at the University of Tokyo Conference on Designing Global Information Commons for Innovation in Frontier Sciences (8 November 2007) (conference notes on file with authors).

Bleicher, K. H. et al., 'Hit and Lead Generation: Beyond High-Throughput Screening', **2** *Nature Revs. Drug Discovery*, 2003, 369–78.

Blumenthal, D., 'Employer-Sponsored Insurance – Riding the Health Care Tiger', **355** *New Eng. J. Med.*, 2006, 195–202.

Blumenthal, D. et al., 'Relationships Between Academic Institutions and Industry in the Life Sciences – An Industry Study', **334** *New Eng. J. Med.*, 1996, 368–73.

Brana, 51 F.3d 1560, 1565–68 (Fed. Cir. 1995)

Burk, D. L. and Brett H. McDonnell, 'The Goldilocks Hypothesis: Balancing Intellectual Property Rights at the Boundary of the Firm', *U. Ill. L. Rev.*, 2007, 575–636.

Calabresi, G. and Douglas Melamed, 'Property Rules, Liability Rules, and Inalienability: One View of the Cathedral', **85** *Harv. L. Rev.*, 1972, 1089–1128.

Cockburn, I. M., 'The Changing Structure of the Pharmaceutical Industry', *Health Aff.*, Jan–Feb 2004, 10–22.

Cohen, F. J., 'Macrotrends in Pharmaceutical Innovation', **4** *Nature Revs. Drug Discovery*, 2005, 78–84.

Cohen, W. M. et al., 'Protecting Their Intellectual Assets: Appropriability Conditions and Why US Manufacturing Firms Patent (or Not)', Nat'l Bureau of Econ. Research, Working Paper No. 7552, 2000, *available at* www.nber.org/papers/w7552

Cohen, W. M. *Comm. on Accelerating Tech Transition, Nat'l Research Council, Accelerating Technology Transition: Bridging the Valley of Death for Materials and Processes in Defense Systems* (2004), 68.

DataMonitor, Addressing Pharma's R&D Productivity Crisis: Technical and Strategic Initiatives To Improve Core Drug Discovery Capabilities, www.market-research-report.com/datamonitor/DMHC1960.htm

Dep't of Justice & Fed. Trade Comm'n, Antitrust Guidelines for the Licensing of Intellectual Property § 3.2.3 (1995), *available at* www.usdoj.gov/atr/public/guidelines/0558.htm

Dep't of Justice & Fed. Trade Comm'n, Antitrust Guidelines for Collaborations Among Competitors § 3.32(c) (2000), *available at* www.ftc.gov/os/2000/04/ftcdojguidelines.pdf

Eisenberg, R. S., 'Bargaining Over the Transfer of Proprietary Research Tools', in R. C. Dreyfuss et al, (eds.), *Expanding the Boundaries of Intellectual Property*, 2001, 496.

'Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research', **82** *Va. L. Rev.*, 1996, 1663–1727.

Emory University, Gilead Science and Royalty Pharma Announces $525 Million Agreement with Emory University To Purchase Royalty Interest for Emtricitabine, 18 July 2005, *available at* www.news.emory.edu/Releases/emtri/

F.A.O. Res 3/2001, International Treaty on Plant Genetic Resources for Food and Agriculture, 3 November 2001, www.fao.org/ag/cgrfa/itpgr.htm

Farrell, J. and Philip Weiser, 'Modularity, Vertical Integration, and Open Access Policies: Towards a Convergency of Antitrust and Regulation in the Internet Age', **17** *Harv. J.L. & Tech.*, 2003, 85–134.

Found. for the NIH, The Biomarkers Consortium, Two-Phased Project Approval Process: Concept Clearance and Project Plan Approval 3 (2006), *available at* http://test.fnih.org/Biomarkers%20Consortium/Project_Clearance.pdf

Found. for the NIH, The Biomarkers Consortium, General Intellectual Property and Data Sharing Principles 5 (2006), *available at* http://test.fnih.org/Biomarkers%20Consortium/IP_Policies.pdf

Foundation for the NIH, Public-Private Partnership Forms the Biomarkers Consortium To Advance the Science of Personalized Medicine, 5 October 2006, *available at* www.fnih.org/news/TBC_Press_Release.shtml

Grabowski, H. et al., 'Entry and Competition in Generic Biologics', **28** *Managerial & Decision Econ.*, 2007, 439–451.

Higgins, M.J., *The Allocation of Control Rights in Pharmaceutical Alliances*, Soc. Sci. Research Network, Working Paper No. 918980, 2006, *available at* http://ssrn.com/abstract=918980

Hopkins, A.L., Michael J. Witty and Solomon Nwaka, 'Mission Possible', **449** *Nature*, 168 fig., 2007, 166–9.

Ivinson, A.J., Letter to the Editor, 'University Investment in Drug Discovery', **310** *Science*, 2005, 777

Kahan, M. and Michael Klausner, 'Standardization and Innovation in Corporate Contracting (or "The Economics of Boilerplate")', **83** *Va. L. Rev.*, 1997, 713–70.

Klausner, A., 'Mind the (Biomedical Funding) Gap', **23** *Nature Biotechnology*, 2005, 1217–8.

Lerner, J. and Robert P. Merges, 'The Control of Technological Alliances: An Empirical Analysis of the Biotechnology Industry', **46** *J. Indust. Econ.*, 1998, 125–56

Lewis, T.R., Jerome H. Reichman and Anthony D. So, 'The Case for Public Funding and Public Oversight of Clinical Trials', *Economists' Voice*, Jan. 2007, www.bepress.com/ev/vol4/iss1/art3/

Lipinski, C.A., 'The Anti-Intellectual Effects of Intellectual Property', **10** *Current Opinion in Chemical Biology*, 2006, 380–3.

Majewski, S. and Dean V. Williamson, 'Incomplete Contracting and the Structure of R&D Joint Venture Contracts', in G.D. Libecap (ed.), *Intellectual Property and Entrepreneurship*, 2004, 304.

Marchesi, V.T., 'An Alternative Interpretation of the Amyloid Hypothesis with Regard to the Pathogenesis of Alzheimer's Disease', **102** *Proc. Nat'l Acad. Sci.*, 2005, 9093–8.

Merges, R., 'Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations', **84** *Cal. L. Rev.*, 1996, 1293–1393.

Merges, R.P. and Lawrence A. Locke, 'Co-Ownership of Patents: A Comparative and Economics View', **72** *J. Pat. & Trademark Off. Soc'y*, 1990, 586–99.

Molecular Libraries Initiative, General Information, http://mli.nih.gov/mlsmr/general-information (last visited 30 October 2007)

Munos, B., 'Can Open-Source R&D Reinvigorate Drug Research?', **5** *Nature Revs. Drug Discovery*, 2006, 723–9.

Nat'l Acad. of Scis., Cancer Biomarkers: The Promises and Challenges of Improving Detection and Treatment 6, 2007, *available at* http://books.nap.edu/catalog/11892.html

Nat'l Insts. Health, New Paradigm Will Help Identify Leads for Drug Discovery, www.nih.gov/news/pr/july2006/nhgri-24.htm (last visited 30 October 2007)

Nat'l Insts. Health, Novel Approach Targets an Inherited Disorder: NIH Chemical Genomics Centre Jumpstarts Drug Development in Public Sector, 23 July 2007, *available at* www.genome.gov/2552214

Nat'l Insts. Health, Overview, Molecular Libraries and Imaging, http://nihroadmap.nih.gov/molecularlibraries/ (last visited 30 October 2007)

Nat'l Insts. of Health, NIH Roadmap for Research, 2006, http://nihroadmap.nih.gov/pdf/NIHRoadmap-FactSheet-Aug06.pdf

NIH Mlscn Project Team Position on Data Sharing and IP in the MLSCN Program (15 October 2005)

Nih Molecular Libraries, A Roadmap Initiative, MLSMR Project, http://mlsmr.glpg.com/MLSMR_HomePage/identify.html (last visited 30 October 2007)

Nwaka, S. and Alan Hudson, 'Innovative Lead Discovery Strategies for Tropical Diseases', **5** *Nature Revs. Drug Discovery*, 2006, 941–55.

Oliver Hart, Firms, Contracts, and Financial Structure, 1995, 240 p.

Pfizer v. Apotex, 480 F.3d 1348 (Fed. Cir. 2007)

Rai, A.K., 'Fostering Cumulative Innovation in the Biopharmaceutical Industry', **16** *Berkeley Tech. L.J.*, 2001, 813–53.

'Regulating Scientific Research, Intellectual Property Rights and the Norms of Science', **94** *Nw. U. L. Rev.*, 1999, 77–152.

'The Information Revolution Reaches Pharmaceuticals: Balancing Innovation Incentives, Cost, and Access in the Post-Genomics Era', *U. Ill. L. Rev.*, 2001, 173–210.

Rai, A.K. and Rebecca S. Eisenberg, 'Bayh-Dole Reform and the Progress of Biomedicine', **66** *Law & Contemp. Probs.*, 2003, 289–314.

Professor Rajan, K., Iowa State University, Presentation at the University of Tokyo Conference on Designing Global Information Commons for Innovation in Frontier Sciences, 8 November 2007.

Rawls, J., *A Theory of Justice*, 1971, 607.

Reichman, J.H., 'Charting the Collapse of the Patent-Copyright Dichotomy', **13** *Cardozo Arts & Ent. L.J.*, 1995, 475–520.

'Legal Hybrids Between the Patent and Copyright Paradigms', **94** *Colum. L. Rev.*, 1994, 2432–558.

'Of Green Tulips and Legal Kudzu: Repackaging Rights in Subpatentable Innovation', **53** *Vand. L. Rev.*, 2000, 1743–98.

Reichman, J.H., 'Saving the Patent Law from Itself: Informal Remarks Concerning the Systemic Problems Affecting Developed Intellectual Property Regimes', in F.S. Kieff (ed.), *Perspectives on Properties of the Human Genome Project*, 2003, 538.

Reichman, J.H. and Paul F. Uhlir, 'A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment', **66** *Law & Contemp. Probs.*, 2003, 315–462.

Reichman, J.H. and Tracy Lewis, 'Using Liability Rules To Stimulate Innovation in Developing Countries: Application to Traditional Knowledge', in K.E. Maskus and J. Reichman (eds.), *International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regime*, 2005, 952.

Roses, A., Senior Vice President of Pharmacogenetics, GlaxoSmithKline, in Research Triangle Park, N.C., 18 April 2006.

Senior Vice President of Pharmacogenetics, GlaxoSmithKline, in Research Triangle Park, N.C., 19 December 2006.

Russ, A.P. and Stefan Lampel, 'The Druggable Genome: An Update', **10** *Drug Discovery Today*, 2005, 1607–10.

Sampson, R., 'The Cost of Misaligned Governance in R&D Alliances', **20** *J.L. Econ. & Org.*, 2004, 484–526.

Schumpeter, J.A., *Capitalism, Socialism and Democracy*, 1942, 38.

Service, R.F., 'Surviving the Blockbuster Syndrome', **203** *Science*, 2004, 1796–9.

Shapiro, C., 'Navigating the Patent Thicket: Cross-Licenses, Patent Pools, and Standard Setting', in A. Jaffe et al (eds.), 1 *Innovation Policy and the Economy*, 2001, 300.

Smith, A., 'Generic Drug Flood Headed Our Way', *CNN Money*, **3** August 2005, http://money.cnn.com/2005/08/03/news/fortune500/generic/

D. Smith G., 'The Exit Structure of Strategic Alliances', *U. Ill. L. Rev.*, 2005, 303–18.

Toner, B., 'Predictive Safety Testing Consortium Submits First Biomarkers to FDA for Qualification', *Genome Web Daily News*, 21 June 2007, www.genomeweb.com/issues/news/140703–1.htm

Toxicogenomic Cross-Validation Consortium Agreement § 2.1 (20 January 2006)

U.S. Food & Drug Admin., Innovation or Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products, 2004, *available at* www.fda.gov/oc/initiatives/criticalpath/whitepaper.pdf

U.S. Gov't Accountability Office, New Drug Development: Science, Business, Regulatory, and Intellectual Property Issues Cited as Hampering Drug Development Efforts 1, 2006, *available at* www.gao.gov/new.items/d0749.pdf

U.S. Gov't *Utility Examination Guidelines*, 66 Fed. Reg. 1092, 1097–99 (5 January 2001).

Vogel, G., 'NIH Gears Up for Chemical Genomics', **304** *Science*, 2004, 1728.

Walsh, J. P. et al., 'Where Excludability Matters: Material Versus Intellectual Property in Academic Biomedical Research', **36** *Research Policy*, 2007, 1184–1203.

Walters, W. P. and Mark Namchuk, 'Designing Screens: How To Make Your Hits a Hit', **2** *Nature Revs. Drug Discovery*, 2003, 259–66.

Whitty, A. and Gnanasambandam Kumaravel, 'Between a Rock and a Hard Place?', **8** *Nature Chemical Biology*, 2006, 112–18.

Wilson, E. K., 'Is Safe Exchange of Data Possible? Modelers in Need of Proprietary Compounds Seek Ways to Share Information, But Not Structure', *Chemical & Engineering News*, **25** April 2005, at 24, *available at* http://pubs.acs.org/cen/science/83/8317sci1.html

Zambrowicz, B. P. and Arthur T. Sands, 'Knockouts Model the 100 Best-Selling Drugs – Will They Model the Next 100?', **2** *Nature Revs. Drug Discovery*, 2003, 38–51.

18 Case 10. The International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA)

The Standard Material Transfer Agreement as implementation of a limited compensatory liability regime

Victoria Henson-Apollonio

18.1 Introduction

Exchange of crop germplasm, usually in the form of seeds, is essential to obtain new sources of disease and pest resistance, improved nutritional characteristics and other desirable and necessary traits, in the breeding of crops grown to provide food for the sustenance of humanity. Historically, seeds, as well as slips and tubers for propagation have been carried by travellers of all sorts – farmers, explorers and adventurers – to share with crop breeders who eagerly await new inputs as they attempt to provide seeds and plant materials that fit the current needs of local farmers. Farmers and other breeders of crop varieties have always depended upon exchange of seeds as a reservoir of inherited characteristics as the history of every domesticated crop shows. Breeding pedigrees of spring bread wheats, for example, have shown that up to 4,500 different parental combinations, involving the contributions of 3,800–4,000 original parents, were used to produce one variety of wheat that was released in India.[1] Although wheat originated from the fertile crescent of Mesopotamia ~7500BC, modern varieties contain materials obtained from all over the globe.[2] The breeding of

[1] Cassady, K., Fowler, C., Heisey, P.W., and Smale, M., 2001. Benefits from giving and receiving genetic resources: the case of wheat, **127** *Plant Genetic Resources (PGR) Newsletter*, 1–10 using data from Smale and McBride, 1996.

[2] According to Day Rubenstein, K., Heisey, P., Shoemaker, R., Sullivan, J., and Frisvold, G. 2005. 'Crop Genetic Resources: An Economic Appraisal', Economic Information Bulletin No. (EIB2) 47, USDA: "Furthermore, useful landraces of some crops have been found in parts of the world other than those in which they were originally domesticated. For example, wheat landraces found in the pedigrees of many modern wheat

existing materials with newly obtained genetic stocks ensures that planting materials for next year's crops contain a complement of genetic alleles (choices) that provide farmers with planting varieties resulting in the best possible yields of desirable crops.

18.2 Collection of germplasm

Collections of germplasm – seed banks, also called gene banks – have been set up by national and international institutions to house international collections of plant germplasm that can be distributed to crop breeders upon request.[3] Together the Alliance Centers of the Consultative Group on International Agricultural Research (CGIAR) house the world's largest *ex situ* collection of seeds and germplasm material of crop plants in the world.[4] Center scientists are involved in the conservation, characterization, breeding and distribution of germplasm to users throughout the world and thus fill the role of a central element in the global seed bank system.[5] Accordingly, the Centers have been involved in providing policy advice, both at the national and the international level to ensure that seed exchange can continue, in light of developments such as the Convention on Biological Diversity (CBD). With a heightened awareness of the national heritage that biological genetic diversity can represent for a country, the transactional costs of collecting seeds of local crop varieties have become much higher and seed exchange has come to a standstill in many areas of the world.

18.3 Exchange of germplasm

To address this issue, the Food and Agriculture (FAO) of the United Nations (UN), in conjunction with member countries as well as the CGIAR, worked to negotiate a treaty that would facilitate the exchange of crop germplasm for food and agricultural uses. The final text of the International Treaty on Plant Genetic Resources for Food and

varieties have come from every continent except Antarctica." Heisey has indicated that "Landraces are usually varieties developed in traditional agriculture by many years of farmer selection. They are not the result of planned crosses between two distinct breeding lines." (Heisy, P., 2002). 'International Wheat Breeding and Future Wheat Productivity in Developing Countries', in *Wheat Yearbook*/WHS-2002/March 2002. 24–33).

[3] Collections of germplasm may include seeds, tubers, plantlets, and perhaps in the future even individual genes and thus the original name may be replaced by "gene bank".

[4] Information about this collection is available at http://singer.grinfo.net.

[5] Reynolds, M.P. and Borlaug, N.E., 2006. Centenary Review: Impacts of Breeding on International Collaborative Wheat Improvement, **144** *Journal of Agricultural Science* Number, 3–17.

Agriculture (IT-PRGFA) was adopted by a conference of FAO on 3 November 2001. The importance of this treaty can be appreciated by the fact that none of the 167 FAO-Commission on Genetic Resources for Food and Agriculture-member countries voted against this approval, which culminated seven years of negotiations over the exchange of crop germplasm materials. The Treaty's main provisions promote the recognition of farmers' efforts in conservation of PGRFA and their sustainable use, through promoting farmer's rights. In addition, it sets up a Multilateral System, (MLS) of Access and Benefit-Sharing, for facilitated exchange of germplasm among member countries of the treaty as well as international seed banks, such as the CGIAR genebanks. Initially the MLS will apply to a list of about sixty-five food crops and forages. The MLS will provide facilitated access to PGRFA for research, breeding and education; benefit-sharing arrangements; a funding strategy; and agreement on terms of access to important collections managed by international agricultural research centers. The means of implementation of the ITPGRFA is through a standard material transfer agreement (SMTA) that was approved by the First Meeting of the Governing Body, held in Madrid 12–16 June 2006.[6] The CGIAR Centers placed their collections in a trust created by the treaty, by signing agreements with FAO on behalf of the Governing Body of the ITPGRFA in October of 2006 and began using the SMTA to implement the transaction for distribution of germplasm in January 2007.

Compensatory liability regimes have been proposed by several authors as a way to minimize transaction costs in sharing resources in general[7] and to specifically facilitate access and benefit sharing with regard to genetic resources.[8] Such regimes have been described as "take and pay",[9] wherein materials or property is taken with the resulting liability to pay for what is taken. The SMTA, which is a private contract between the provider of the germplasm and the recipient, incorporates a mandatory scheme of compensatory liability upon the commercialization of seed or crop germplasm products, *when such product is unavailable*

[6] Text of the ITPGRFA and the SMTA can be found at the website: www.planttreaty.org. Background documents related to the negotiations leading to the SMTA can be found at www.fao.org/AG/cgrfa/gb1.htm.

[7] See Rai, A.K., Reichman, J.H., Uhlir, P.F. and Crossman, C., 'Pathways Across the Valley of Death: Novel Intellectual Property Strategies for Accelerated Drug Discovery', Chapter 17 of this volume.

[8] Okediji, R, 2005, 'Access and Benefit-sharing and the ABS and the Interface with Existing IP Systems: Limits and Opportunities', *in* Interface International Expert Workshop on Access to Genetic Resources and Benefit Sharing: Record of Discussion, Cuernavaca, Mexico, October 24–27, 2004. CONABIO and Environment Canada, Mexico.

[9] Calabresi and Melamed, 1972, as cited in Rai et al., Chapter 17 of this volume.

for further breeding.[10] Annex 2, of the SMTA states that "If a recipient, its affiliates, contractors, licensees, and lessees, commercializes a product or products, then the recipient shall pay one point-one percent (1.1%) of the sales of the product or products less thirty percent (30%)." The payments are to be made into a trust account, established by the Governing Body of the Treaty as a mechanism for sharing the monetary benefits generated by use of germplasm from the MLS. Although some, such as Okediji (2005) have admonished that such contractual arrangements should guarantee benefit-sharing at an earlier stages rather than at the royalty-bearing or commercialization stage, the negotiations were not able to attain such conditions. And, in reality, because of the length of time that it takes for breeding and testing material, as well as seed multiplication, this compensation will likely happen several years after material is accessed and then usually only if the particular product is protected by a form of license or intellectual property rights (such as a utility patent protection) that specifically excludes the recipient of the material from using the product as a parent in future breeding schemes. However, the SMTA also includes a voluntary, *ex ante* system, Annex 3, the 'Alternative Payments' scheme whereby a recipient can opt, *at the time the material is accessed*, to promise to pay a fee on the sales of any product that are plant genetic resources for food and agriculture where any material has been accessed that is of the same species at a rate of 0.5% of the sales of any product derived from such plant genetic resources. In other words the voluntary system is independent of whether or not the product is available without restriction. (This voluntary option is also called the "African Proposal", as it was brought to the negotiating table by the African group.[11])

18.4 Concluding remark: "Watch this space"

Because use of the SMTA is so recent, there is little data available yet to indicate the effect of this compensatory scheme – either with regards to facilitation of the exchange of germplasm, in general or in its effect on the collection of monies resulting from commercialization. However,

[10] The exact text from the SMTA is as follows: "6.7 In the case that the Recipient commercializes a Product that is a Plant Genetic Resource for Food and Agriculture and that incorporates Material as referred to in Article 3 of this Agreement, and where such Product is not available without restriction to others for further research and breeding, the Recipient shall pay a fixed percentage of the Sales of the commercialized Product into the mechanism established by the Governing Body for this purpose, in accordance with *Annex 2* to this Agreement.

[11] Declaration of Bern, Available at the URL: www.evb.ch/cm_data/ABS_under_the_ITPGR_engl_2_2_2.pdf.

the excitement and the increase in overall positive outlook of crop breeders worldwide, signal that the signing of the ITPGRFA, the coming into force of the treaty and the successful negotiation of the SMTA bode well for enhanced exchanged of material in crop improvement strategies for the future.

REFERENCES

Cassady, K., Fowler, C., Heisey, P.W., and Smale, M., 2001, 'Benefits from Giving and Receiving Genetic Resources: the Case of Wheat', **127** *Plant Genetic Resources (PGR) Newsletter*, 1–10.

Day Rubenstein, K., Heisey, P., Shoemaker, R., Sullivan, J., and Frisvold, G., 2005, 'Crop Genetic Resources: An Economic Appraisal', Economic Information Bulletin No. (EIB2) 47, USDA.

Heisy, P., 2002, 'International Wheat Breeding and Future Wheat Productivity in Developing Countries', in *Wheat Yearbook*/WHS-2002/ March 2002, 24–33.

Okediji, R, 2005, 'Access and Benefit-sharing and the ABS and the Interface with Existing IP Systems: Limits and Opportunities', *in* Interface International Expert Workshop on Access to Genetic Resources and Benefit Sharing: Record of Discussion, Cuernavaca, Mexico, 24–27 October, 2004. CONABIO and Environment Canada, Mexico.

Rai, A.K., Reichman, J.H., Uhlir, P.F. and Crossman, C., 'Pathways Across the Valley of Death: Novel Intellectual Property Strategies for Accelerated Drug Discovery', Chapter 17 of this volume.

Reynolds, M.P. and Borlaug, N.E., 2006, 'Centenary Review: Impacts of Breeding on International Collaborative Wheat Improvement, **144** *Journal of Agricultural Science*, 3–17.

Smale, M. and T. McBride 1996, 'Understanding global trends in the use of wheat diversity and international flows of wheat genetic resources', Part 1 of *CIMMYT 1995/96 World Wheat Facts and Trends: Understanding Global Trends in the Use of Wheat Diversity and International Flows of Wheat Genetic Resources*. Mexico, D.F.: CIMMYT.

19 Critical analysis: property rules, liability rules and molecular futures

Bargaining in the shadow of the cathedral

Dan L. Burk

19.1 Introduction

The chapters in this volume on pharmaceutical development and on the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPRGFA) are oriented toward the use of liability rules to promote innovation. Each describes an attempt to re-align the incentives of innovators by structuring a set of contractual options that will overcome the barriers to investment. In response to the formidable barriers to development of viable pharmaceuticals from private libraries of receptors and ligands, Rai et al. propose the creation of a private molecular "semi-commons" of pooled molecules from which promising drug targets could be tested, and for which a contributor would be paid if a viable product resulted.[1] In a similar vein, Henson-Apollonio reports on the structure of the ITPRGFA, which allows use of genetic resources with the guarantee of a royalty if a contributor's variety is used.[2]

A common feature of these systems is a type of conscription mechanism that permits a participant in the system to use intellectual property (IP) without a direct negotiation with the IP owner. Users of an asset are required to pay for their use of the asset; they cannot be refused use of that asset but they control the decision whether to take the asset or not. In other words, owners of the asset have a right to payment, but not a right to exclude. Following the nomenclature developed in the famous Calebresi and Melamed article on 'Property Rules, Liability Rules, and Inalienability: One View of the Cathedral', we dub such

[1] Rai, A.K., Reichman, J.H., Uhlir, P.F. and Crossman, C., 'Pathways across the valley of death: novel intellectual property strategies for accelerated drug discovery', Chapter 17 of this volume.

[2] Henson-Apollonio, V., 'Case 10. The International Treaty on Plant Genetic Resources for Food and Agriculture: the Standard Material Transfer Agreement as implementation of a limited compensatory liability regime', Chapter 18 of this volume.

payment regimes as 'liability rules' as opposed to regimes of exclusivity, or 'property rules'.[3]

Yet the incentive structure of these systems employs liability rules with a particular structure, in very particular circumstances. The Rai et al. proposal contemplates a two-stage process of agreement to testing, then the option of payment or further collaboration, depending upon the outcome of such testing. In describing the proposal of Rai and her co-authors, I use the term *option* advisedly, indeed deliberately, as it has economic meaning beyond its colloquial usage to designate a particular type of contract employed in futures markets. One might say that the proposal attempts to construct a type of futures market in molecular options, facilitating trading under the scientific uncertainty of matches between receptors and ligands. And although it may not be immediately obvious, the liability rules schema of the ITPRGFA shares the same features of institutional design.

In this comment, I shall attempt to set in context the characteristics of such liability regimes, particularly the incentive choices that might guide us to choose them or to reject them. In that effort, I draw heavily upon the recent literature analyzing property and liability rules from the standpoint of options and information theory. I begin by briefly reviewing the structure of liability rules and their relationship to the property rules that typically characterize the IP regime. I then turn to the literature analyzing asset entitlements as options, including the very nascent literature on IP and real options. I conclude with some observations regarding the allocative choices that we might make in a proposal like that of Rai et al., including some possibilities not considered in their paper. My goal in all of this is to situate the ITPRGFA and the Rai et al. proposal within both the landscape of property theory and the existing literature.

19.2 Liability in the cathedral

Although we commonly use the term "property" to refer to intellectual and tangible assets, it is exceptionally rare in practice to find a pure property regime in the sense of exclusivity. Property rules are typically subject to a host of exceptions. Easements, takings, compulsory licenses of various sorts tend to overlay and modify property rights, whether in real or IP.[4] Similarly, pure liability regimes are exceptionally rare;

[3] Calabresi, G. and Melamed, A.D., 'Property Rules, Liability Rules, and Inalienability: One View of the Cathedral', **85** *Harvard Law Review*, 1972, 1089.

[4] Burk, D., 'Muddy Rules for Cyberspace', **21** *Cardozo Law Review*, 1999, 121.

non-consensual uses are typically limited in time or space, triggered by certain events, subject to some type of reservation or control by the holder of the asset. Property owners typically have the right to exclude all but certain defined classes of users under particular circumstances. Asset owners seldom have complete control over the disposal of the asset, but compulsory licensees seldom have complete freedom as to use.

Recognizing that assets are almost always subject to mixed regimes of exclusive rights and compulsory licensing leads inevitably to a second insight about entitlements: that entitlements to an asset are rarely unified, complete packages; they are more often split among two or more stakeholders. Familiar divisions of entitlements include physical or temporal or situational divisions. A less immediately obvious division under liability rules is a relational division. Liability rules are by definition not exclusive; one party has a right to take, the other has the right to be paid for the taking. Such divided entitlements mean that the different stakeholders must deal with one another in some fashion; they are tied together by their shared rights to the asset.[5]

Additionally, the criteria by which either a property or a liability regime is applied to an asset may differ. The application of either property or liability regimes may be determined by clear, *ex ante* rules, or it may be determined *ex post*, after a taking, according to flexible standards.[6] The type of legal imperative under which assets are allocated also has implications for the relationships between claimants. The more vague or muddy entitlement criteria are, the more multiple stakeholders will be required to deal with one another, as it will be less clear where one entitlement begins and another ends, or when and how new sets of entitlements might be triggered. Thus the type of legal imperative under which allocations are determined may also be considered as a partition of asset entitlements.[7]

In previous work I have attempted to map the conceptual space defined by these entitlement parameters.[8] I have argued that a useful visualization of allocation regimes can be plotted along the dimensions of property vs. liability, divided vs. complete, and rules vs. standards entitlements. Each of these dimensions constitutes a separate continuum rather than a binary choice of entitlements, and a given property allocation will have characteristics along each of these dimensions; it may be a liability regime with clear, complete entitlements, or

[5] Rose, C., 'The Shadow of the Cathedral', **106** *Yale Law Review*, 1997, 2175.
[6] Rose, C., 'Crystals and Mud in Property Law', **40** *Stanford Law Review*, 1988, 577.
[7] Johnston, J.S., Bargaining Under Rules Versus Standards, **11** *Journal of Law, Economics and Organizations*, 1995, 256.
[8] Burk, 'Muddy Rules'.

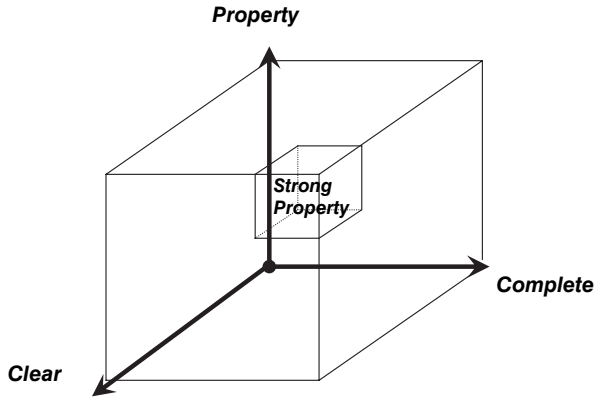

Figure 19.1 Possible entitlements in property law

an exclusive property regime with muddy, divided entitlements, or any of myriad other combinations in the three. If each of these continua is viewed as an axis in a coordinate system, a space of possible property entitlements is mapped, each point within that space representing a different combination of entitlement parameters (as shown in Figure 19.1).

The point of this illustration is that there is a broad range of possible entitlements in property law. The law and commentary on IP are filled with comparisons to the law of tangible property, and typically to the law of real property. These comparisons are frequently not merely uni-dimensional, but a-dimensional; they contemplate a single point in the property regime space that I have mapped out, ignoring the continuum of possible rules and allocations, assuming or asserting that property, by definition, can only constitute the prototypical Blackstonian "sole and despotic" control over a particular good. As I have argued elsewhere, this Blackstonian prototype is an idealized fiction, and often an ideological fiction.[9] The law of real property in fact has never contemplated a regime of pure exclusivity, but instead incorporates a range of allocative regimes under a variety of labels: easements, takings, nuisance and so on. And indeed, there is an important additional set of dimensions to property allocations that we have not yet considered.

[9] Burk, D., 'Legal Consequences of the Cyberspatial Metaphor' in Consalvo, M., et al. (eds.) *Internet Research Annual Volume 1: Selected Papers From the Association of Internet Researchers Conferences 2000–2002*, New York, Peter Lang.

19.3 Real options in the cathedral

I have so far said little about the placement of allocations between different claimants to the asset. And it is this question of vesting, even more than the nomenclature of liability and property, to which the Calabresi and Melamed article owes its fame. The prototypical negotiation or dispute over an asset contemplates at least two parties to a transfer, although there could well be more. But no matter the absolute number of claimants, there will be at least two classes of claimants to the asset, one of which will hold the entitlement in a given instance and one of which will not. Calabresi and Melamed recognized that as between the two classes of claimants, entitlements may be reciprocal.

A given entitlement can be assigned to either of the classes of claimants. An exclusive entitlement, a property right, could be vested in either of the claimants to an asset – in the case of judicial remedies, issuing an injunction effectively allows the asset owner to exclude others from the asset, while denying the injunction effectively allows the user to take control of the asset. Similarly, a liability rule, a right to be paid, could be vested in either claimant. The asset user might be allowed to take the asset in return for payment to the asset owner, or the asset owner might be allowed to reclaim the asset upon payment to the user for the value of the asset. This reciprocity produces a set of four possible rules, allocating the rights in the asset either exclusively to one party or the other, or under a liability regime to one party or the other.

But the four reciprocal possibilities of the Calabresi/Melamed schema do not define the entire universe of rights assignments. Commentators relatively quickly realized that the incentive structure of liability rules is equivalent to that of a "call" option in futures markets.[10] In the language of options contracts, a call is the right to purchase an asset at a pre-defined price. The contractual price set for the transfer is known as the exercise price. Liability rules, like call options, obligate the owner of the asset to a transfer of all or part of the rights in an asset for a predetermined price. At the time the transfer is required, neither the price nor the transfer may necessarily be desired by the asset owner, but the transfer is imposed anyway. In the case of bargained-for options, the transfer occurs due to an earlier agreement; in the case of liability rules,

[10] Morris, M., 'The Structure of Entitlements', **78** *Cornell Law Review*, 1993, 440; Krier, J. and Schawb, S., 'Property Rules and Liability Rules: The Cathedral in Another Light', **70** *NYU Law Review*, 1995, 440.

the transfer may occur due to an agreement or due to the operation of other law, such as a statute.

Liability regimes are of particular use in situations of bilateral monopoly, that is, where the parties can only deal with one another. In the presence of property rules, such situations are expected to produce "holdout" problems, where each party acts strategically to capture all or most of the value of an exchange. Because of the exclusive nature of the property regime, the rights holder can prevent any beneficial use of an asset except on his terms, but the other party may refuse those terms. This may result in a bargaining impasse, where no exchange occurs. The impasse may be especially acute where the valuations of the parties create a large bargaining range, making agreement on a price for exchange prohibitively difficult. The asset goes inefficiently unused as a result.

Liability rules break the impasse by allowing one of the parties to take the asset without the permission of the other party. But of course such a taking will occur only if the party taking the asset is willing to pay the royalty set for the asset. Analyzed under option theory, we may say that the option holder will only exercise the option when his private valuation is higher than the strike price. On average, this is expected to produce efficient returns.[11] Importantly, this occurs because the liability structure harnesses the parties' private information about valuation. It may be difficult to get parties who are behaving strategically to reveal their private valuations, but they can be prompted to act on those valuations under a liability system.

The recognition that liability rules operate as call options raises the possibility that another type of option, the put option, may also be present in the cathedral of asset allocations.[12] A "put" is the right to sell an asset at a pre-defined price. Each type of option contemplates an asset transfer, the terms of which were agreed upon and memorialized in the contract at some previous time. The party subject to the call or the put may no longer necessarily desire the transaction, or may no longer desire the transaction at the exercise price, but is contractually obligated to the transfer anyway. Thus, call options effectively confer the right to force a sale to the option holder; put options effectively confer the right to force a purchase from the option holder.

As I have suggested above, liability rules or call options are well known in the law of real property and chattels, in the form of easements,

[11] Kaplow, L. and Shavell, S., 'Property Rules Versus Liability Rules: An Economic Analysis', **109** *Harvard Law Review*, 1996, 713.

[12] Ayres, I. 'Protecting Property with Puts', **32** *Valparaiso University Law Review*, 1998, 793.

claims of nuisance, and so on. Put options are somewhat more rare in the law, but allocations of rights with the features of a put do occur. Ayres has identified a number of situation in which judicial remedies provide for put-type property allocations.[13] Typically these involve an election of remedies by the asset owner, either to recover taken property or to be paid the value of the asset. These remedies parallel put options in that the asset owner, rather than the taker, has the election whether to be paid for the taken asset – in effect, to force a sale of the asset whether or not the taker would prefer that outcome to returning the asset. The striking feature of such put options is that they not only create a divided entitlement that will harness the private information of the parties, as a call option would do, but they provide the entitlement holder with more than the value of the asset. The holder of the put is entitled to the value of the asset plus the value of the put, which has an independent worth.

The independent value of the put derives from value of flexibility under future uncertainty. A critical feature of both types of options is the allocation of choice. The choice as to whether the transfer will occur lies with the option holder. Thus options will have a two-stage allocative and temporal structure. In the first stage, the option holder is given, or decides whether to acquire the option. In the second, later stage, the option holder decides whether to exercise the option. The second-stage, future choice to give up an asset and require payment for an asset, or to take an asset and pay for it at the exercise price, has present value, quite literally the value of keeping one's options open until the future situation becomes more certain.

19.4 Options in IP law

I have argued that if one is to make analogies between IP and tangible property, then the full range of allocative systems in tangible property ought to be part of such an analogy, not the idealized view of exclusivity that some commentators would selectively import into the consideration of IP. Options analysis has become well established in the law of real property and chattels, and so by my argument deserves consideration in regard to IP as well. Do such options exist in the law of IP? In particular, given the theme of this volume, do they exist in patents and related systems of proprietary rights? And if they do not, should they?

[13] Ayres, 'Protecting Property', 800.

The first place to look for options, particularly call options, in IP, is where there are functioning liability rules, as we have seen that liability rules function like call options. Liability rules in IP are most often associated with copyright: for example with the compulsory licensing schemes for music, or with user privileges and exceptions like fair use, that are essentially a compulsory license at a zero royalty.[14]

But in the US, patents are largely devoid of formal liability rules. Compulsory licenses in the US statute itself are quite rare, limited to a handful of provisions governing civilian nuclear technology, certain particulate emissions technologies, or medical procedures.[15] In other countries, compulsory licensing for many types of patentable subject matter were fairly common, but such liability systems have been limited by the requirements of the WTO TRIPs Agreement. Prior user rights, which are available in many countries but are limited in the US, are also effectively a type of compulsory license at a zero royalty.

But the fact that liability rules act as "call" options does not mean that all call options are liability rules. Carroll has noted that the patent system effectively includes call-type options in the maintenance fees required to keep a patent in force. Patents lapse without payment of these fees.[16] Patent holders have in essence an option to buy the next increment of patent protection, at a set price, by paying the fee.

Call options on patents can also be created by courts. In the US, liability regimes are occasionally created as judge-made law, in the context of remedies to infringement suits. Courts have in a very few instances denied injunctive relief to patent holders in favor of monetary damages, effectively creating a compulsory license for that patent, at a royalty determined by the court.[17] Such cases have typically involved patents drawn to essential technologies – such as municipal sewage treatment – that would precipitate a public health crisis if enjoined. Preliminary injunctive relief requires such consideration of the public interest, and the Supreme Court has recently re-emphasized that permanent injunctions are subject to equitable considerations.[18] So the door remains open for purely monetary remedies, but denying a patent holder the right to exclude will likely remain unusual.

In addition, Hausman et al. have employed the methodology of options analysis in critiquing the effects of certain patent infringement

[14] 17 USC §§ 107, 110, 115. [15] 35 USC §§ 287, 2183; 42 USC § 7608.

[16] Carroll, M., 'One for All: The Problem of Uniformity Cost in Intellectual Property Law', Villanova Law/Public Policy Research Paper No. 2005–17, October 11, 2005, http://papers.ssrn.com/sol3/papers.cfm?abstract_id=820308

[17] *City of Milwaukee* v. *Activated Sludge*, 69 F.2d 577 (7th Cir. 1934).

[18] *eBay, Inc.* v. *MercExchange*, L.L.C., 126 S. Ct. 733 (2005).

decisions by the US Court of Appeals for the Federal Circuit regarding lot profit damages.[19] In recent cases, the Federal Circuit has held that if a non-infringing technology was hypothetically available to an accused infringer, then lost profit damages are unavailable to the patent holder, because the infringer could have substituted the non-infringing technology, sold the same output, and reaped the same profits. This holding effectively confers on the alleged infringer an option on patent damages in situations where a substitute to the patented technology was hypothetically available. If the alleged infringer chooses to use the patented technology, and the patent is held valid or uninfringed in an enforcement action, then the alleged infringer pays nothing. If the patent is found to be valid and infringed, the infringing company can switch to a non-infringing technology and pay damages equal to a reasonable royalty, essentially what the infringer would have paid for a license initially.

This approach to patent damages shows how the decision whether to infringe or not can be modelled in the familiar two-stage option. The alleged infringer initially decides in the first stage whether to use the patented technology; if a lawsuit ensues and the patent is held valid, then the accused infringer can switch to the substitute technology and pay a reasonable royalty. This means the accused infringer can effectively defer the costs of adopting the substitute technology until after the patent validity has been litigated – after uncertainties have been resolved. The option to wait and decide whether to adopt the substitute technology after uncertainties are resolved has value that accrues to the infringer since the cost of acquiring the option is no more than the infringer would have paid for a license to the patented technology anyway.

Despite the movement toward analysis of call options in patent law, virtually nothing has been said to date about put options in patent law. If call options are rare in the patent system, put options are even rarer – although this should come as no surprise, given that they are relatively rare in the law of real property and chattels as well. But the US patent system does include at least one put mechanism, in the form of the Statutory Invention Registration (SIR), which allows inventors to publish enabling descriptions of an invention without receiving a patent, placing the invention into the public domain.[20] This is effectively a put

[19] Hausman, J., et. al. 'Patent Damages and Real Options: How Judicial Characterization of Non-Infringing Alternatives Reduces Incentives to Innovate', **22** *Berkeley Technology Law Journal*, 2007, 825.

[20] 35 USC § 157.

at an exercise price of zero – the holder of the technology can essentially require the public to take the invention, electing not to hold it as a trade secret or pursue a patent.

19.5 Contracting into options

Although recognizable liability rules may be sparse in the law of IP, the kind of analyses performed by Carroll and by Hausman et al. demonstrates how options theory may be useful in assessing legal incentives to innovation. The liability systems considered here require us to go a step further, as they contemplate arrangements beyond existing statutes or judicial remedies. Both the ITPRGFA as described by Henson-Appollonio and the "semi-commons" pooling arrangement proposed by Rai et al. may be viewed as attempts to set up an exchange, in the institutional sense of that word. We are familiar with other more obvious exchange institutions; with securities exchanges directed toward the trading of stocks and other financial instruments; or with commodities exchanges, directed toward the trading of foodstuffs or raw materials. Such exchanges set the rules and parameters for trade between parties that ostensibly wish to exchange real or financial assets.

But it is critical to understand that such institutions are in fact contract exchanges, where the primary goods traded are promises to deliver certain properties at a certain price. Such promises may be current, intended for immediate execution, or they may be options intended for execution at some later date. It is not in fact securities or commodities that change hands in such exchanges; they are the basis for the promises, but it is the exchange of promises that is the point of the institution. Moreover, the exchange of contracts is subject to contract; traders in a given exchange contractually agree to certain rules governing buying and selling within the exchange. These contracts structure the transaction environment; in effect they lower the transaction costs for trading, and create a contractually defined marketplace.

The ITPRGFA and small-molecule proposal contemplate the same arrangement: defining a marketplace according to certain contractually agreed upon rules, in order to lower the transaction costs for trades. This is especially striking in the case of the Rai et al. proposal: it is not merely information about biological and chemical molecules that is exchanged within their contractual marketplace, it is a set of promises, as to what may be done, what price will be paid and under what conditions, that is exchanged within their pooling arrangement. The standardized exchange structure is necessary due to the high transaction

costs first, of bargaining under uncertainty regarding the receptor/ligand combinations tested; and second, strategic behaviours of the parties who hold physical title to the molecular pairs.

Additionally, the agreements within the shelter of the exchange structure are drafted under uncertainty, contemplating different outcomes depending on the results of testing. Uncertainty dictates the contingent nature of such promises; the parties may or may not exercise their contractual options depending on the outcome of test results that cannot be known at the time the contract is drafted. We have seen that options are desirable to harness the private information of parties to a bargain. The proposal of Rai et al. facilitates information exchange in the physical sense that certain molecules will be found to react optimally with certain targets. But this is intertwined with information forcing regarding the parties' valuation of the asset, or their willingness to pay for the asset. Private valuation is of course profoundly affected by information about the asset, in this case chemical and physiological information that is privately held by each of the parties and unavailable to the other.

Call options are well suited to such bargaining under future uncertainty, but we have seen that they are not the only tool available to facilitate innovative exchange where the parties stand in bilateral monopoly, and bilateral monopolies characterize the small molecule market place – one party holds materials, and information about materials, that will physically interact with materials held by the other. The possibility of adding put options to the suite of property entitlements in this situation is particularly interesting for the Rai et al. pharmaceutical research proposal. Ayres has noted that under *ex ante* conditions, put options can increase a rights holder's expected payoff from bargaining above that which would be expected under a pure property regime, without reducing what the other party to the bargain would expect.[21] That is to say, when assessing the parties' expected payoff before they acquire information about the value of the resource they hold, puts can raise the level of payoff a party expects from an exchange.

This means that put options may be an attractive mechanism to employ where it is desirable to encourage investment in the resource held by the rights holder. If at the time of investing, the holder of a put option does not know her expected value, she does know that the put will have at least the value of the property. And, because the put gives the holder the entitlement plus the value of the put, the holder should be willing to invest up to the level of the larger expected payoff. Given

[21] Ayres, 'Protecting Property', 805.

that the problem Rai et al. address is precisely a problem about *ex ante* investment, about deciding what to invest before the value of a small molecule compound is known, puts may be appropriate to consider.

19.6 Conclusion

I have argued that the liability systems found in the ITPRGFA and the pharmaceutical testing proposal of Rai et al. can be viewed as establishing essentially a type of commodities exchange, which in turn suggests that these systems may be fruitfully analyzed by application of option analysis. The chapters to which this comment is directed contemplate liability regimes for IP exchange, but the place of liability rules in the cathedral of asset entitlements can only be understood by reference to the place of other regimes in the cathedral. Option analysis provides an excellent window through which to view these relationships. While there has been to date relatively little application of option analysis to IP, the sizeable body of literature applying option analysis to real property suggests the range of entitlement allocations that might be contemplated. In the present context, option analysis clarifies the structure of the liability regimes discussed in the previous chapters, and suggests additional arrangements, such as "put" rules, that might be worth exploring.

I have directed my comments to discussion of the ITPRGFA and the pharmaceutical development proposal, but of course a similar view could be taken of virtually all the species of "clearinghouse" mechanisms reviewed in this volume. Virtually all of them attempt to create exchange environments via contractual structures aimed at lowering transaction costs. Previous commentary on patent pools, performance societies and the other mechanisms in this volume have suggested that if property rights are granted, clearinghouse mechanisms through a process of "contracting into liability rules".[22] Yet the transaction costs of such contracts may be substantial, deterring such exchanges from forming. Transactions costs of contracting can be significantly lowered by the availability of standardized contracts, which is in essence what institutional exchanges provide.[23] Such a "nexus of contracts" has been identified as providing a lower cost transaction environment than

[22] Merges, R., 'Contracting Into Liability Rules: Intellectual Property Rights and Collective Rights Organizations,' **84** *California Law Review*, 1996, 1293.

[23] Hillman, R. and Rachlinsky, J., 'Standard-Form Contracting in the Electronic Age', **77** *NYU Law Review*, 2002, 429.

open market transactions.[24] Once established, the rules of institutional exchanges may in essence allow asset owners to "contract into contracting into liability rules". And once within the shelter of an institutional structure, the diversity of possible rights allocations provides a rich diversity of option structures to prompt investment and exchange.

REFERENCES

Ayres, I. 'Protecting Property with Puts', **32** *Valparaiso University Law Review*, 1998, 793.

Burk, D., 'Muddy Rules for Cyberspace', **21** *Cardozo Law Review*, 1999, 121.

Burk, D., 'Legal Consequences of the Cyberspatial Metaphor', in Consalvo, M., et al. (eds.) *Internet Research Annual Volume 1: Selected Papers From the Association of Internet Researchers Conferences 2000–2002*, New York, Peter Lang.

Burk, D. and McDonnell, B., 'The Goldilocks Hypothesis: Balancing Intellectual Property Rights at the Boundary of the Firm', 2006 *University of Illinois Law Review*, 2006, 275.

Calabresi, G. and Melamed, A. D., 'Property Rules, Liability Rules, and Inalienability: One View of the Cathedral', **85** *Harvard Law Review*, 1972, 1089.

Carroll, M., 'One for All: The Problem of Uniformity Cost in Intellectual Property Law', Villanova Law/Public Policy Research Paper No. 2005–17, October 11, 2005, http://papers.ssrn.com/sol3/papers.cfm?abstract_id=820308

Hauseman, J. et. al., 'Patent Damages and Real Options: How Judicial Characterization of Non-Infringing Alternatives Reduces Incentives to Innovate', **22** *Berkeley Technology Law Journal*, 2007, 825.

Henson-Apollonio, V., 'Case 10. The International Treaty on Plant Genetic Resources for Food and Agriculture: the Standard Material Transfer Agreement as implementation of a limited compensatory liability regime', Chapter 18 of this volume

Hillman, R. and Rachlinsky, J., 'Standard-Form Contracting in the Electronic Age', **77** *NYU Law Review*, 2002, 429.

Johnston, J. S., 'Bargaining Under Rules Versus Standards', **11** *Journal of Law, Economics and Organizations*, 1995, 256.

Kaplow, L. and Shavell, S., 'Property Rules Versus Liability Rules: An Economic Analysis', **109** *Harvard Law Review*, 1996, 713.

Krier, J. and Schawb, S., 'Property Rules and Liability Rules: The Cathedral in Another Light', **70** *NYU Law Review*, 1995, 440.

Merges, R., 'Contracting Into Liability Rules: Intellectual Property Rights and Collective Rights Organizations', **84** *California Law Review*, 1996, 1293.

[24] Burk, D. and McDonnell, B., 'The Goldilocks Hypothesis: Balancing Intellectual Property Rights at the Boundary of the Firm', **2006** *University of Illinois Law Review*, 2006, 275.

Morris, M., 'The Structure of Entitlements', **78** *Cornell Law Review*, 1993, 440.
Rai, A. K., Reichman, J. H., Uhlir, P. F. and Crossman, C., 'Pathways across the valley of death: novel intellectual property strategies for accelerated drug discovery', Chapter 17 of this volume
Rose, C., 'The Shadow of the Cathedral', **106** *Yale Law Review*, 1997, 2175.
'Crystals and Mud in Property Law', **40** *Stanford Law Review*, 1988, 577

Part V

Different perspectives

20 Gene patents: from discovery to invention

A geneticist's view

Gert Matthijs and Gert-Jan B. Van Ommen

20.1 Introduction

At the start of the 1990s, gene patents were already well engrained in the field of biochemistry and cell biology. Typically, they were targeted at specific, well-described and credible applications, ranging from receptor proteins useful for drug entry to sweetening proteins to replace sugar. The advent of gene cloning per se, in the preceding two decades, had not made an impact as a dramatic departure from existing patent practice. The major onslaught of large-scale, high-throughput automated sequencing, however, precipitated an intense debate on intellectual property (IP) issues, associated with the identification of our genetic heritage. As early as 1991, HUGO organised an expert workshop on this topic in Munich. This led to a first 'HUGO position statement on cDNA patents' (1992),[1] noting that patenting DNA segments of unknown function was unjustified as these were mere discoveries, and that this practice would stifle upstream research. It was proposed to restrict patents to genes or other DNA elements of which the function was elucidated.

The issue of gene patents materialised in earnest in the genome community in 1992, when J. Craig Venter, then employed by the US National Institute of Health (NIH), after internal NIH consideration and stimulated by its director Bernadine Healey, submitted patent applications for 2,000 so-called ESTs (expressed sequence tags, short randomly cloned cDNA segments), on the basis that if they would not be protected this might cause missed future commercialisation possibilities. The scientific community reacted with profound and widespread dismay. The patenting of snippets of protein-coding DNA, based on their putative function as coding for segments of the myriad proteins of the human body, but with as yet undisclosed, hypothetical functionality, was widely condemned as heralding an IP blockade of

[1] HUGO position statement on cDNA patents (1992) (see www.hugo-international.org/PDFs/Position Statement on cDNAs Patents 1992.pdf.)

unprecedented scope which would severely hamper free exchange of pre-competitive knowledge. These events, as well as the major industrial involvement, caused the issue to be revisited at HUGO's 'International Genome Summit', held in January 1994 in Houston. This summit brought together for the first time representatives of funding agencies and governments of most countries sponsoring genome research, with key specialists in the molecular, technical, clinical, ethical and legal fields. This ultimately resulted in the 'HUGO Statement on Patenting of DNA sequences', released in April 1995 in HUGO's regular publication 'Genome Digest'.[2] The statement argued, amongst other points, that sequence data should be immediately and publicly disseminated without restrictions on its use, and that future patent rules, rather than rewarding routine discoveries, should provide protection for the much more intellectually challenging work of determining biological function and application of the gene sequences.

The NIH patent applications were eventually not maintained, but meanwhile the next, much larger-scale endeavour of the same nature, targeting 100,000 ESTs, had gotten under way, by the company Human Genome Sciences (HGS), established by Venter, who had by then left NIH and founded The Institute for Genome Research (TIGR), and William Haseltine, who licensed the rights exclusively to a pharma company SmithKline Beecham. This eventually led to about a hundred patents, of a quite broad nature. In a densely packed room at the fall 1994 Genome Meeting in Washington, a consortium of academic institutions led by Washington University and funded by Merck&Co, arguing that industries and academia were not in the business of collecting patents on unclear genome segments, but in that of developing drugs, announced a counter-move by pledging to rapidly generate 300,000 ESTs in one year and make them publicly available. By November 1995, this single project alone had generated 200,000 of the 270,000 EST sequences then present in the dbEST database[3] at the National Centre for BioInformatics (NCBI) in the US, mirrored at the European Centre for BioInformatics (EBI) in the UK. This early treasure trove of publicly available genomic coding data greatly stimulated positional cloning and functional analysis worldwide, as witnessed by its attracting more than 12,000 inloggers in one year. Its project-based nature, as well as the joint public–private involvement stood model for the later human

[2] HUGO Statement on Patenting of DNA sequences (1995) (see www.hugo-international.org/PDFs/Statement on Patenting of DNA Sequences 1997.pdf.)

[3] dbEST is a division of GenBank that contains sequence data and other information on 'single-pass' cDNA sequences or 'Expressed Sequence Tags', from a number of organisms (see www.ncbi.nlm.nih.gov/dbEST/). Also see **4** *Nature Genetics,* 1993, 332–3.

genome project and the Single Nucleotide Polymorphism (SNP) and Hapmap[4] consortia. Indeed, it is ironic that, of all bodies, it was the major US public research institution NIH which was at the root of the early gene patenting furore, while, in contrast, it was an industry-led group which sparked the first collective action to rapidly move hotly debated IP matter into the public domain.

In these and subsequent statements, like that of July 1997, reiterating viewpoints in the light of advancing insights, that of October 2000, commenting on the EU Biotechnology Directive[5] and that of 2003 on the altering field in relation to the extensive generation of large-scale genomics data, HUGO has continued to seek a balance between advancement of health research and protection by IP. Basically, from early 1992 onwards, it has envisaged the course from discovery to invention as a stepwise process of gradually added inventive contributions, starting with the discovery of anonymous DNA sequences without attributed function, and crossing the trajectory via gene fragments, entire genes with unknown function, to sequences with known function, including genes, control elements and mutations in disease, to end with diagnostic tests and ultimately, therapies. Unlike for the development of therapy, where few will challenge the importance of IP protection, the role and format of IP protection for diagnostic tests in genetics is still contentious and intensively debated even today.

20.2 From publish *or* perish to publish *and* perish: the European dilemma

There are significant differences between the patenting systems in the world. When concentrating on the aspects directly impinging on the scientific process, by far the most important difference is the presence or absence of a so-called 'grace period'. This is a given amount of time during which publication of scientific results by scientist-inventors does not damage the novelty of their own invention. The US and many other countries have a one-year grace period in which authors

[4] The goal of the International HapMap Project is to develop a haplotype map of the human genome, the HapMap, which will describe the common patterns of human DNA sequence variation. The HapMap is expected to be a key resource for researchers to use to find genes affecting health, disease, and responses to drugs and environmental factors. The information produced by the Project will be made freely available. The Project is a collaboration among scientists in Japan, the UK, Canada, China, Nigeria, and the US (see www.hapmap.org.).

[5] HUGO statement on patenting of DNA sequences, in particular in response to the European Biotechnology Directive (2000) (see www.hugo-international.org/PDFs/Statement on Patenting of DNA Sequences 2000.pdf).

of scientific papers, or their university's valorisation institutions, can still seek patent protection for competitively published findings, while Japan and a few other countries have a half-year grace period. In contrast, in the European patenting system there is no such grace period. Any data made public prior to patent filing are fully novelty-damaging, also to the inventors themselves. While in industrial circles in Europe this arrangement has quite strong support, as it essentially forces their research scientists to be very reticent and keen on taking out patents; this comes at the price of greatly widening the gap between industrial and academic research. Even while today there is much more attention for protection of commercially viable ideas, the measure of research is still the publication and citation in high-impact journals. This is what generates scientists the best chances to get their grants funded or renewed and the most attractive jobs. Thus, the scientists in Europe are at a fundamental disadvantage relative to their US colleagues. While the latter can place maximal efforts on making rapid progress and publish as fast as possible in the best possible journal, their European competitors have either to give up on IP protection and go for the gold as well, or enter a parallel procedure in their institutions, or with industrial parties, to negotiate for the necessary agreements, funds and patent attorney support. Consequently, in the European academic world the patenting process has long had the ring of complexity and is hard to reconcile with competitive frontline research. Even while today major European academic institutions are beginning to be well-versed in dealing with this, it is far from widely resolved as a conception of the past. In our view, as long as this inequality is not fundamentally resolved the process of IP protection will continue to be perceived by the average scientist in European academic institutions as cumbersome, and a necessary but annoying evil at best. Aside from the direct effects on scientific research, this attitude also hampers the easy transfer of top scientists between academia and industry as it creates a big perceptional difference to which people have to 'readjust'. Thus, European industry would be much better served by adopting a grace period like most other countries, thus removing this perception gap and creating a much more level playing field, both scientifically and in the innovation arena.

20.3 Discovery or invention: monogenic vs. multifactorial genes

The discussion about the role of IP protection, and its importance or suitability, has gained impact by the recent breakthroughs of 'Genome-Wide Association Studies' (GWAS), driven by the high-throughput

SNP studies and the 'next-generation' sequencing possibilities. In the days of the discovery of the major genes for monogenic disease, frequent or rare, there was at least no doubt about the predictive value of the disease-associated disease variants, and thus of the clinical benefit of applying gene-based diagnosis. In contrast, the discovery of predictive factors in multifactorial disease – besides a long time coming – is a slow and gradual process. Often the first to appear are a variety of associations and failures to replicate, in both of which cases it is often not clear, even after the fact, who is right, due to varying disease definitions and – even in large cohorts – the luck of the draw. This may lead to finding a confirmed risk (or protective) factor in a cohort which would only have a 20% power to detect it, or, conversely, not finding it in a cohort with an 80% detection power. This said, definitely 2007 has been the year in which the GWAS got under way, and in which most of the earlier scepticism about the feasibility of the approach has been refuted.[6]

But in terms of drug development, this is only the start of the agony: years of painstaking validation often will have to follow, reported in papers which in all but the high-profile cases have a hard time to get published and thus recognised in the public domain. This in turn, is only the beginning of the elucidation of the biological pathways involved. So the risk taken with the investment in drug development at the time of the initial risk/protective factor discovery is truly immense. As a consequence, more and more voices are proclaiming that this entire stage should be seen as a pre-competitive phase, in which the joint parties have more to gain by access to each others 'proprietary' (but ill-defined) findings than by each one embarking on its own, at best tame, goose chase.

What, in these cases, with patent applications? Clearly, many of the currently studied disorders, like diabetes, obesity, heart or neurological disease, cancer, or arthritis, are very frequent and amongst the severest plagues of the worlds' gluttony regions today. So the reward of actually developing a working drug – even a reliable diagnostic or, better yet, a good prognostic tool – would be enormous. Thus, in the field of common disorders there may be a case for considering diagnostic patents provided these are linked to better targeting therapy, so-called 'theranostics'. On the other hand, we are still far away from 'big markets': the actual prognostic power of even the clearest of confirmed diabetes discoveries today is still very modest. We are dealing with risk increases of 1.1 to 1.3, i.e. people which have these risk factors are only

[6] See Van Ommen G.J.B., 'Popper Revisited: GWAS Here, Last Year', **16** *Eur J Hum Genet.*, 2008, 1–2 and references therein.

at a 10–30% increased risk, while moving more and eating less would reduce the risks several fold, for both the risk- and the non-risk groups. 'No problem: safety in numbers', may the market optimists say, considering that people having five or more of those risk factors do in fact have far greater risks. The sceptics – often geneticists who know how these calculations work – will then counter that finding these people – the ones with high clinical benefit – comes at a price: multiplying risk equally reduces the number of people at this risk. So, yes, we will find high-risk people, but no more than 1–2% of all people likely to develop these diseases.

The good news is that there is a big market for these tests – already exploited on the Internet. The bad news is that nearly all tests now on offer have only a tiny chance to correctly predict disease, and a much greater chance that, in case of a borne-out positive prediction, the disease is not due to the factor in question, while for a negative prediction the chance to still develop the disease is almost unchanged.[7] Thus, the term 'hot air' is not very far from these 'early adopter' products, and this bubble will soon burst, when the public comes to realise this. At the cost of its confidence in later, better products! So one should hope that this part of the common disease risk factor market is not the focus of serious investment by large enterprises.

More plausibly, and more sensibly, today's discoveries will track the path to new, unforeseen, biology, and lead to better, more mechanistic understanding. This is a more rational way to get to sound therapeutic and preventive innovations. Once again, however, we reiterate that in this model the current discoveries are but tools for further research, so it still remains doubtful what the utility is of IP protection in this very upstream stage.

20.4 Diagnostic tests and patents

Diagnostic tests are used to detect pathogenic mutations in genes responsible for inherited and acquired genetic disorders. The invention of the Polymerase Chain Reaction (PCR), back in 1985, and the rapid pace at which novel genetic defects have been identified since 'positional cloning' came of age in the early 1990s, have greatly increased the possibilities for genetic diagnosis. Over the past two decades, the number of diagnostic tests has steadily increased.

[7] Hunter D.J., Khoury M.J. and Drazen J.M., 'Letting the Genome out of the Bottle – Will We Get Our Wish?', **358** *N Engl J Med.*, 2008, 105–7; van Ommen and Cornel, 2008.

Patenting

Once a link between a disease and a genetic defect (mutation) has been established, a diagnostic test can relatively easily be developed. Most laboratories use a combination of different methods: from 'home-brew' detection methods and commercial kits, to high-throughput mutation scanning platforms and direct sequencing.

Patents on diagnostic tests based on DNA sequences have been criticised, both in the genetics community and by the public at large. The inventions are usually based on the disclosure of a link between a mutation and a disease. One serious problem with such diagnostic gene patents stems from the fact that it is impossible to 'invent around', i.e. to invent an alternative test that would not require the gene sequence or gene product. Thus, the patent holder effectively holds a monopoly over testing for the specific disease.

Therefore, many geneticists support the view that the establishment of an association between a monogenic disease and a specific (defect in a) gene should not be patentable (see below 4.3). This would be naturally achieved if everyone would accept that this is a discovery, not an invention: discoveries are not patentable. In addition, individual mutations in known disease genes should also not be patented. With the current technology, there is arguably no inventive step and a lack of novelty, which would exclude them from patenting under current patent law.

Clearly this reasoning would become more ambiguous in the case of associations between risk factor alleles and multifactorial disease. In this case it can be argued that with the current state of the art their discovery, as well as their validation still require significant inventiveness. Indeed, one might argue here that in view of the many unreplicated findings, the replication of such an identification is as essential as the first finding, so only the two together would constitute an invention. This is against current practice, but it would place the providers of replication cohorts in a better and fairer position.

In theory, only 'product claims' can assert rights over the DNA sequences themselves, whereas 'use claims' covers the use of the sequence. The Nuffield Council suggested in their report 'The ethics of patenting DNA' (2002) that narrow use patents on specific diagnostic tests might provide an effective means of rewarding the inventor while providing an incentive to others to develop alternative tests.[8] However,

[8] Nuffield Council on Bioethics, *The Ethics of Patenting DNA, A Discussion Paper,* 2002 (www.nuffieldbioethics.org).

from a molecular genetic viewpoint, this is misleading: alternative tests might involve different or novel technologies – which can indeed be inventive and become a proprietary tool – but all these methods still 'interrogate' the same genetic sequence, i.e. they are only alternative methods to obtaining genetic data.

This is easily illustrated on the basis of Myriad Genetics' BRCA1 patents. Patent EP 705902 essentially contained product claims, i.e. it covered, among other things, the BRCA1 DNA and polypeptide sequence, whereas patent EP 705903 originally claimed thirty-five individual (and mostly private) BRCA1 mutations. Patent EP 699754 contained a use claim on the diagnostic methods, i.e. it claimed 'a method for diagnosing a predisposition for breast and ovarian cancer in human subject which comprises determining in a tissue sample of said subject whether there is a germline alteration in the sequence of the BRCA1 gene coding for a BRCA1 polypeptide … said alteration being indicative of a predisposition to said cancer'.

In practice, the use claims in the latter patent are just as difficult to work around as the product claims in the former. Actually, EP 699754 was even more critical for diagnostics than EP 705902. Luckily, these patents have undergone modifications after the opposition and appeal procedures at the European Patent Office (EPO). We use them here as examples, to question the distinction that is often proposed in favour of 'purpose-bound' patent protection. Also note that all the methods that are described in the patent for the diagnostic use of the BRCA1 sequences, were established methods at the time of filing: the patent does not describe a new or specific diagnostic kit, nor instructions to built one; the patent describes the diagnostic method, i.e. the detection of a link between a genetic defect, in this case, mutations in the BRCA1 gene and a disease, in this case, breast and/or ovarian cancer. The easiest way to avoid blocking patents in genetic testing would be to reorient patenting policy and only allow patents on diagnostic methodology, limiting gene patents to the context of therapeutic development. This will not disfavour investments in the diagnostic field: companies and investors would still step into the diagnostic kit market, because the kits would be competitive on a technological and economical basis.

Licensing

The reality is, however, that many diagnostic gene patents have been granted, and that differences in the licensing policies dichotomise the field. Two examples illustrate how the attitude of the patent holders

greatly affects the availability of genetic testing for the patients, and influences the development of comprehensive and affordable tests.

CFTR

The situation is not too bad in the case of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene, which is mutated in patients with cystic fibrosis and which was discovered back in 1989.[9] The gene was patented by the Hospital for Sick Children of Toronto and the University of Michigan. However, the patent holders have granted free access to the gene sequence for diagnostic testing. The diagnostic laboratories have taken advantage of this and were rapidly able to offer testing for cystic fibrosis, using commonly available technologies for mutation analysis. In addition, the patent holders have also offered licences to several companies that have developed kits for the simplified identification of the most frequent mutations. This combination has greatly promoted the availability of the CFTR tests, at a reasonable cost. The difference between those kits solely resides in the technology which lies at the basis of the kit and in their ease of use, price etc. Several kits are available on the market, and as a result of the competition, they have become ever more performing and ever more accessible. Thus, while the patent holders collect royalties because most of the laboratories are now using the commercial kits anyway, the kit manufactures try to constantly improve the test. It is open for debate if the CFTR patent itself has 'promoted progress' (which is the essential and original aim of patenting) but at least it did not hamper the developments in the field of diagnostics. It seems that the genetic or medical community has no major objections to this model.

What is not publicly known is how much of the cost of the kits actually represents royalty fees. It would be nice to find out, to get an idea of the 'value' of a gene or mutation in IP terms.

BRCA

Almost all the drawbacks of gene patenting and licensing for patients and practitioners, and even for kit manufacturers, are exemplified by the breast cancer (BRCA) gene patents or *Myriad* case. Two major genes in which germ line mutations cause a strong breast and/or ovarian cancer susceptibility were identified in the early 1990s. The BRCA1 gene, which was localised by linkage analysis to chromosome 17 in 1990

[9] Kerem B., Rommens J.M., Buchanan J.A., Markiewicz D., et al., 'Identification of the Cystic Fibrosis Gene: Genetic Analysis', **245** *Science,* 1989, 1073–80.

by Mary-Claire King and co-workers,[10] was cloned and sequenced four years later by Myriad Genetics.[11] The BRCA2 gene was first localised to chromosome 13 in 1994[12] and partly sequenced shortly thereafter at the Institute of Cancer Research in the UK.[13] It was then further characterised by Myriad Genetics.[14]

Several patents on BRCA1 and BRCA2 have been granted by the US Patent and Trademark Office (USPTO) between 1997 and 2000. In Europe, three patents on the BRCA1 gene were granted to Myriad Genetics and co-inventors by the EPO in 2001. The first BRCA2 patent was granted to Myriad Genetics and co-inventors early in 2003, the other BRCA2 patent, which had been filed earlier by the Cancer Research Campaign (later renamed Cancer Research UK or CRUK), was granted early in 2004.[15]

Soon after the genes were identified, laboratories worldwide started to offer diagnostic testing for BRCA1 and BRCA2, using different methods for mutation detection. Thus, the diagnostic test for BRCA1 and BRCA2 was already widely available in European laboratories when the European patents were eventually granted in 2001. It was Myriad's policy not to license the test or at least not at conditions that were acceptable to the laboratories.[16] This meant that all the tests would have to be performed in its own laboratories in Utah. The reaction has been strong: several groups of European geneticists made use of the possibility, under the European Patent Convention (EPC), for opposition and appeal against a patent, at the EPO. European health care systems are largely publicly funded, and geneticists and cancer specialists in Europe were not willing to accept a monopoly on breast and

[10] Hall J.M, Lee M.K., Newman B., Morrow J.E., et al., 'Linkage of Early-Onset Familial Breast Cancer to Chromosome 17q21', **250** *Science,* 1990, 1684–9.

[11] Miki Y., Swensen J., Shattuck-Eidens D., Futreal P.A., et al., 'A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene BRCA1', **266** *Science,*1994, 66–71; Futreal P.A., Liu Q., Shattuck-Eidens D., Cochran C., et al., 'BRCA1 Mutations in Primary Breast and Ovarian Carcinomas', **266** *Science*, 1994, 120–2.

[12] Wooster R., Neuhausen S.L., Mangion J., Quirk Y. et al., 'Localization of a Breast Cancer Susceptibility Gene, BRCA2, to Chromosome 13q12–13', **265** *Science*, 1994, 2088–90.

[13] Wooster R., Bignell G., Lancaster J., Swift S. et al., 'Identification of the breast cancer susceptibility gene BRCA2', **378** *Nature*, 1995, 789–92.

[14] Tavtigian S.V., Simard J., Rommens J., Couch F., et al., 'The Complete BRCA2 Gene and Mutations in Chromosome 13q-Linked Kindreds', **12** *Nat Genet.*, 1996, 333–7.

[15] Matthijs G., 'The European Opposition against the BRCA Gene Patents', **5** *Familial Cancer,* 2006, 95–102; Verbeure B., Matthijs G. & Van Overwalle G., 'Analysing DNA Patents in Relation With Diagnostic Genetic Testing', **14** *Eur J Hum Genet.*, 2006, 26–33.

[16] Munktell P., 'Compulsory Patent Licensing. Master thesis', University of Lund, Sweden, 2004.

ovarian cancer testing. In the US, where the first patent was granted in 1997, the patent holders succeeded in stopping all laboratories from further testing. The reason is simple: the risk of a court case in the US is enough to frighten infringers, and unlike under EPC, an administrative opposition procedure does not exist under US patent law. The European laboratories chose to continue performing BRCA tests for their patients, risking to be sued for infringement, based on the principle that, yet aside from the high cost and limited scope of the test in the US, having to defer genetic testing of their local population to a commercial party in another country was seen as unacceptable.

Furthermore, manufacturers refrained from developing novel tests for BRCA1 and BRCA2 mutations. It is difficult to put or get the information on paper, but we know of several companies which develop technologies for mutation analysis but stay away from BRCA1 and BRCA2 because of these patents. They may change their mind now that the patents on these genes do not cause a problem anymore, at least not in Europe and for the time being. However, on a global scale the US patents and the exclusive licensing policy of the patentees may still present an impediment. So, regrettably, more than ten years were lost for the development of novel technologies applied to BRCA.

In general, the mechanisms of the market that normally set a fair price on products and promote the availability of these products, do not work properly in the case of genetic testing, simply because either there is no way to 'invent around' and put similar products on the market, or because the diagnostic laboratories lack the power (i.e. a patent portfolio or a suitable substitute for the diagnostic test) to negotiate reasonable conditions. In 2006, the Organisation for Economic Co-operation and Development (OECD) has issued guidelines that prescribe that licences should be non-exclusive and easily obtainable, both in practical and in financial terms.[17] Because there is a lack of legislation on licensing, one hopes that the OECD members states will at least adopt these guidelines.

It is highly undesirable from a clinical standpoint that a monopoly on a gene also risks to lead to a level of testing which is below state-of-the-art. Because Myriad Genetics capitalised on (the monopoly on) the BRCA1 and BRCA2 gene patents, it has quickly set up testing: the company offers sequencing of both genes with a turn-around-time that beats all the public laboratories. However, in DNA diagnostics, it is good practice to also look for deletions and duplications in disease

[17] OECD, *Guidelines for the licensing of genetic inventions*, OECD Council, 2006. (www.oecd.org/document/56/0,2340,en_2649_34537_34317658_1_1_1_1,00.html).

genes. It is now known that the latter account for a significant proportion of mutations in BRCA1 and BRCA2.[18] Interestingly, these types of mutations were only detected because different genetic laboratories continued to test breast cancer patients for mutations, using a plethora of different approaches.

The Nuffield Council has also raised the question whether it is in the public interest that there is only one diagnostic test available for a particular disease.[19] The monopoly not only inhibits further test development, it may even jeopardise the quality and the continuity of testing;[20] just imagine that the only laboratory in the world that offers the diagnostic test, decides to discontinue its service, it would take a while before another laboratory could take over – if anyone would still want or be capable to take over at that stage. Along the same line, the exclusive practice of clinical diagnostics also worried the National Academy of Sciences (NAS) which stated that

> the performance of a gene-based clinical test in an academic setting often generates rich databases of newly detected genetic variations that can be correlated with phenotypes of large and heterogeneous patient populations. Such admixed medical practice and research provides important new information about the mutational repertory of specific disease-linked genes, as well as the phenotypic correlations that provide new insights into disease mechanisms and identify potential new targets for therapeutic intervention.[21]

Another aspect that ruffled the scientists' feathers is the fact that the identification of the familial BRCA1 and BRCA2 genes was preceded, in the early 1990s, by a large international collaborative effort. The Breast Cancer Linkage Consortium (BCLC), founded in 1989, was so successful that the location of the BRCA1 gene, once disclosed in 1990, was very quickly narrowed down to a small region on chromosome 17.[22] Eventually, the BCLC database held genetic data on over 700 breast

[18] Reviewed in Walsh T., Casadei S., Coats K.H., Swisher E., Stray S.M., Higgins J., Roach K.C., Mandell J., Lee M.K., Ciernikova S., Foretova L., Soucek P., King M.C., 'Spectrum of Mutations in BRCA1, BRCA2, CHEK2 and TP53 in Families at High Risk of Breast Cancer', **295** *JAMA*, 2006, 1379–88.

[19] Nuffield Council on Bioethics, *The Ethics of Patenting DNA, A Discussion Paper,* 2002.

[20] Cho M., Illangasekare S., Weaver M., Leonard D., Merz J., 'Effects of patents and licenses on the provision of clinical genetic testing services', **5** *J Mol Diagn*, 2003, 3–8.

[21] NATIONAL ACADEMY OF SCIENCES (NAS), *Reaping the Benefits of Genomic and Proteomic Research: IP Rights, Innovation and Public Health*, National Academies Press, Washington DC, 2005 (www.nap.edu/catalog/11487.html).

[22] For an overview of the progress, see Easton D.F., Bishop D.T., Ford D. & Crockford G.P., 'Genetic Linkage Analysis in Familial Breast and Ovarian Cancer: Results From 214 Families. The Breast Cancer Linkage Consortium', **52** *Am J Hum Genet.*, 1993, 678–701.

cancer families from Europe, Canada, and USA, while the number of centres involved in the BCLC was nearly 100. Allowing patent protection to only one organisation tends to ignore and disregard in terms of IP rights the contribution of all the other collaborators.[23]

All these factors have contributed to the widespread reaction in Europe against the patents granted to Myriad.[24]

EPC allows a democratic control on patenting via an opposition procedure. Art. 100 EPC defines the 'Grounds for opposition'. In practice, anyone who disagrees with the granting of a patent by the EPO is allowed to call for such a procedure, within nine months after the granting date. It is handled by the Opposition Division of the EPO in Munich. Hence, in October 2001, a French association of research institutes and hospitals, and a coalition of the Belgian, Dutch, British, Danish and German genetic societies filed oppositions against the first BRCA1 patent (EP 699754). For the opposition against the second patent (EP 705903) in February 2002, the Belgian government joined the latter group, while the Dutch government filed a separate opposition, as did Greenpeace and the Social Democrats of Switzerland. For the opposition against the third patent (EP 705902) in August 2002, the original 'Belgian–Dutch' initiative was further extended, and included molecular and clinical geneticists, oncologists and cancer researchers from Austria, Belgium, the Czech Republic, Denmark, Finland, Germany, Greece, Italy, the Netherlands, Switzerland and the United Kingdom. Two Dutch and Belgian patient organisations have also joined the opposition. A comparable coalition filed an opposition to Myriad Genetics' BRCA2 patent (EP 785216). The coalition did not file an opposition against the other BRCA2 patent from CRUK (EP 858467), mainly because the patent holder had expressed the intention to grant free licences to the publicly funded laboratories in Europe.[25]

In brief, after oral hearings at the EPO in 2004, the first patent EP 699754 was revoked due to errors contained in the initially filed sequence. The correct sequence of the BRCA1 gene was only sent to the patent office in March 1995, whereas it had been made available through Genbank in October 2004, concomitantly with the publication

[23] Cf. Baldwin, T., 'Ethics and Patents for Genetic Diagnostic Tests', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 45–59.

[24] Matthijs G. and Halley D., 'European-Wide Opposition Against The Breast Cancer Gene Patents', **10** *Eur. J. Hum. Gen.*, 2002, 783–4; Matthijs, 2006.

[25] See Matthijs, 2006 for more details. Also see the minutes of the opposition proceedings are available for consultation in the Online Public File Inspection at http://ofi.epoline.org/view/GetDossier.

by Miki et al. in *Science*.[26] Hence, this led to a later priority date for the patent, which effectively 'killed' the inventive step.[27] In 2005, the other two BRCA1 patents were severely limited in their scope, largely on the same basis.[28] Myriad's BRCA2 patent suffered from the fact that part of the gene sequence had already been identified by the UK group before. It was strongly amended, to a single use claim on the 6174delT mutation in BRCA2, which is a frequent mutation in Ashkenazi Jewish patients.[29] The term 'Ashkenazi Jewish women' had to be included in the claim, because the mutation had already been described before, and the patent holders' only 'invention' had been to show that the mutation is frequent in that population. The patent owners have filed an appeal against the decisions of the EPO, so the story is not over yet. The patent holders lost the appeal against the decision of the opposition division on EP 705902, the other hearings are scheduled to take place in November 2008.

It is of note that none of the arguments listed above (the opinion that a disclosure of a link between a gene and a disease is little more than a discovery, the fact that the test was improved by others, the observation that the granting of the patent rewarded only one of the participants in the race for the BRCA genes etc.) were not admitted during the procedure at EPO. Also, the EPO has not questioned the patentability of the BRCA1 or BRCA2 genes per se.

Beyond BRCA: the recommendations of the European Society of Human Genetics

Some critical observers have emphasised that the Myriad case has been an exception. Unfortunately this seems not to be true: many more genes

[26] Miki et al, 1994.

[27] Abbott, A., 'Clinicians Win Fight to Overturn Patent for Breast-Cancer Gene', **429** *Nature,* 2004, (6990):329. Also see EUROPEAN PATENT OFFICE, 'Myriad/Breast Cancer Patent Revoked After Public Hearing'. Press release, 18 May 2004 (www.epo.org/about-us/press/releases/archive/2004/18052004.html).

[28] Abbott, A., 'Europe Pares Down Double Patents on Breast-Cancer Gene', **433** *Nature*, 2005, (7024):344. Also see EUROPEAN PATENT OFFICE, 'Patent on Breast and Ovarian Cancer Susceptibility Gene Amended After Public Hearing'. Press Release, 21 January 2005 (www.epo.org/about-us/press/releases/archive/2005/21012005.html); EUROPEAN PATENT OFFICE, 'European patent on mutations in breast and ovarian cancer susceptibility gene amended after public hearing'. Press release, 25 January 2005 (www.epo.org/about-us/press/releases/archive/2005/25012005.html).

[29] Abbott, A., 'Genetic patent singles out Jewish women', **436** *Nature,* 2005, 12. Also see EUROPEAN PATENT OFFICE, 'Patent on "Breast Cancer Gene 2" Patent Maintained in Amended Form After Public Hearing'. Press release, 29 June 2005 (www.epo.org/about-us/press/releases/archive/2005/29062005.html); Marshall E., 'European Patents. BRCA2 Claim Faces New Challenge', **308**, *Science*, 2005, 1851.

are covered by patents[30] and several articles have suggested that patents block research and development, as well as hinder patients' access to recently available diagnostic tests. A survey by Cho et al. found that patents and licences have had a significant negative effect on the ability of clinical laboratories to develop and provide genetic tests.[31] An increasing number of gene patents have been exclusively licensed to one or a few diagnostic companies, mainly in the US. These claims have also reached Europe: recently, several laboratories have received requests for paying licence fees on e.g. the familial Mediterranean fever (FMF) gene; given the frequency of the disease in the Mediterranean countries, this is an important diagnostic gene.

In 2005, the President and Board of the European Society of Human Genetics (ESHG) have asked the Public and Professional Policy Committee (PPPC) and Patenting and Licensing Committee (PLC) of the ESHG to create a working party and discuss the different problems with experts and stakeholders. The group explicitly aimed to 'go beyond the Myriad case', but with a specific focus on diagnostics. It is important to achieve a situation where useful tests are available at affordable costs. The working group has recently presented a background document to the Board and Membership of the ESHG.[32] This background document reviews the current status on patenting and licensing in genetic testing. It deals with different issues of patenting: it points to problems and remedies within the patenting system. It also deals with licensing: it explores novel models that could ease access to patented genetic inventions, like patent pools and clearinghouses, and supports the OECD guidelines. The group has drafted 'Recommendations on Patenting and Licensing in Genetic Testing' which were accepted by the ESHG board after a period of membership consultation and were published in April 2008.[33]

The ESHG's considerations and recommendations can be summarised as follows.

There are some problems with regard to patentability:

- The major problems seem to be in the breadth of the claims in genetic patents, in the criteria for patentability and in the number of (overlapping) patents.

[30] See e.g. Verbeure et al., 2006. [31] Cho et al., 2003.

[32] ESHG, 'Patenting and Licensing in Genetic Testing. Recommendations of the European Society of Human Genetics', Part 2. Background document. S. Aymé, G. Matthijs and S. Soini, **16** *Eur J Hum Genet*, 2008, S10 – S50.

[33] ESHG, 'Patenting and Licensing in Genetic Testing. Recommendations of the European Society of Human Genetics', 16 *Eur J Hum Genet*, 2008, 405–411.

- There is a need to improve the quality of the patents that will eventually be granted.
- The research exemption (permission for unlicensed research use) is unclear: it is differently phrased in different countries and not universal throughout Europe.

The problems reported with regard to licensing are:

- Licences are problematic when they are exclusive.
- In general, licensing seems to be prohibitive, both in practical and in financial terms, partly due to the complexity of the system, and to the lack of effective guidelines. It is clear that the mechanisms of the market do not – or cannot – work properly in the case of genetic testing.
- Most importantly, the licence agreements should not provide the licensor with exclusive control over human genetic information.

Proposed solutions with regard to patentability are:

- The patenting of individual mutations in known disease genes should be disallowed on the basis of an absence of novelty.
- The establishment of a link between a disease and a genetic sequence or defect should be considered merely a discovery and therefore not patentable, unless the identification of this link includes a real conceptual innovation.
- The EPO should consider establishing an ethics committee or advisory body to review issues of major interest, such as patents applied to genes.

As to licensing, it is recommended that:

- Policy makers should work on the development of licensing guidelines, and effectively support those that have already been issued by international organisations such as the OECD.
- Licences should be non-exclusive and easily obtainable, and the licensing terms should be public, which would allow the costs of licensing in the price of the final product to be known.

20.5 Novel models

Clearly the field is in flux, and further debate will be ongoing. It is quite possible that the limited profitability of the patents in the diagnostic field of (relatively) rare, monogenic diseases eventually leads to a lack of interest of industry and academia to establish and/or maintain diagnostic gene patents. The current development of high-throughput genomics technology will further reduce the inventiveness of finding

sequence variants causally connected to disease. On the other hand, the development of multi-component so-called 'biomarker'-diagnostics for common complex disease, rather based on association than causality, is on the rise. Sometimes these consist of several hundreds of elements compiled on a gene-chip or as a proteomics or metabolite profile. This presents a risk – if not a certainty – of many overlapping and/or complementary patents, or patent thickets.[34] One could envisage solving this with a clearinghouse exploitation model as in the music business, or a patent pool as in the airline manufacturing and ICT field.

The models have been discussed in the background document of the ESHG recommendations.[35] It was suggested that patent pools may not be easily adoptable to genetic disease testing, because, for instance, a patent owner cannot be forced to participate, which would be detrimental if (a) major patent(s) would be missing from the pool. Such a scenario is quite predictable.

In a clearinghouse, all the important patents are collected by a specific organisation that gives access to them against a fee. Some say that it would be almost impossible to know what is in there. Others argue that for gene patents a real clearinghouse model should be developed. It should not just be copied from the IT field but adopted to best suit the purpose. For instance, it could be split into several diagnostic topics, such as cancer, cardio-vascular diseases etc.

Several variants of the clearinghouse model have been presented in the present volume:[36] (1) the information clearinghouse, providing a mechanism for exchanging technical information and/or information related to IP status of said information, such as patent search sites or platforms;(2) the technology exchange clearinghouse model, providing a list for available technologies for further negotiations, and assisting in mediating and managing services; (3) the royalty collection clearinghouse model, settling payments of licence fees and (4) the open source clearinghouse model, fostering the free exchange of technology.

The genetic clearinghouse could be a derivative of those variants. For addressing current licensing issues, information and technology clearinghouses would be particularly useful when it is not a priori

[34] A patent thicket is 'an overlapping set of patent rights, which requires those who seek to commercialise new technology to obtain licences from multiple patentees', see Van Overwalle, G., van Zimmeren, E., Verbeure, B. & Matthijs, G., 'Models for Facilitating Access to Patents on Genetic Inventions', 7 *Nature Review Genetics*, 2006, 143–148. Also see Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume.

[35] ESHG, 2008.

[36] See van Zimmeren, E., 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume.

clear which IPs will be used. A fee structure used in royalty collecting clearinghouses, as in ASCAP (American Society of Composers and Performers) could be considered. Regional clearinghouses could be coordinated globally. The practical hurdle is, again, the limited foreseeable profit and the complexity of setting up the clearinghouse. Hence, we believe that, like with the other successful examples of technology exchange clearinghouses, the installation of the genetic clearinghouse will have to be publicly funded.

Notably, the Nuffield Council[37] and HUGO[38] also supported the further exploration of the clearinghouse model proposed by OECD[39] to ease the obtaining of licences for genetic inventions by commercial laboratories and to expedite the rapid and low-cost licensing of patented DNA sequences which have potential applications in clinical diagnosis.

REFERENCES

Abbott, A., 'Clinicians Win Fight to Overturn Patent For Breast-Cancer Gene', **429** *Nature*, 2004, 329.

'Europe Pares Down Double Patents on Breast-Cancer Gene', **433** *Nature*, 2005, 344.

'Genetic patent singles out Jewish women', **436** *Nature*, 2005, 12.

Baldwin, T., 'Ethics and Patents for Genetic Diagnostic Tests', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 45–59.

Cho M., Illangasekare S., Weaver M., Leonard D. and Merz J., 'Effects of patents and licenses on the provision of clinical genetic testing services', **5** *J Mol Diagn*, 2003, 3–8.

Easton D. F., Bishop D. T., Ford D. and Crockford G. P., 'Genetic Linkage Analysis in Familial Breast and Ovarian Cancer: Results From 214 Families. The Breast Cancer Linkage Consortium', **52** *Am J Hum Genet.*, 1993, 678–701.

European Patent Office, 'Myriad/Breast Cancer Patent Revoked After Public Hearing'. Press release, 18 May 2004 (www.epo.org/about-us/press/releases/archive/2004/18052004.html).

European Patent Office, 'Patent on Breast and Ovarian Cancer Susceptibility Gene Amended After Public Hearing'. Press Release, 21 January 2005 (www.epo.org/about-us/press/releases/archive/2005/21012005.html).

European Patent Office, 'European Patent on Mutations in Breast and Ovarian Cancer Susceptibility Gene Amended After Public Hearing'.

[37] Nuffield Council on Bioethics, *The Ethics of Patenting DNA, A Discussion Paper*, 2002.

[38] HUGO statement on the scope of gene patents, research exemption and licensing of gene patents for diagnostics (2003) (see www.hugo-international.org/PDFs/Statement on the Scope of Gene Patents, Research Exemption.pdf).

[39] OECD, 2002.

Press release, 25 January 2005 (www.epo.org/about-us/press/releases/archive/2005/25012005.html)
European Patent Office, 'Patent on "Breast Cancer Gene 2" Patent Maintained in Amended Form After Public Hearing'. Press release, 29 June 2005 (www.epo.org/about-us/press/releases/archive/2005/29062005.html).
European Society of Human Genetics, 'Patenting and Licensing in Genetic Testing. Recommendations of the European Society of Human Genetics', **16** *Eur J Hum Genet*, 2008, 405–11.
European Society of Human Genetics, 'Patenting and Licensing in Genetic Testing. Recommendations of the European Society of Human Genetics', Part 2. Background document. S. Aymé, G. Matthijs and S. Soini, **16** *Eur J Hum Genet*, 2008, S10–S50.
Futreal P.A., Liu Q., Shattuck-Eidens D., Cochran C., et al., 'BRCA1 Mutations in Primary Breast and Ovarian Carcinomas', **266** *Science*, 1994, 120–2
Hall J.M, Lee M.K., Newman B., Morrow J.E., et al., 'Linkage of Early-Onset Familial Breast Cancer to Chromosome 17q21', **250** *Science*,1990, 1684–9.
Hunter D.J., Khoury M.J. and Drazen J.M., 'Letting the Genome Out of the Bottle – Will We Get Our Wish?', **358** *N Engl J Med;*. 2008, 105–7
Hugo Position Statement on cDNA patents' (1992) (see www.hugo-international.org/PDFs/Position Statement on cDNAs Patents 1992.pdf)
Hugo Statement on Patenting of DNA sequences (1995) (see www.hugo-international.org/PDFs/Statement on Patenting of DNA Sequences 1997.pdf)
Hugo Statement on Patenting of DNA Sequences, in Particular in Response to the European Biotechnology Directive (2000) (see www.hugo-international.org/PDFs/Statement on Patenting of DNA Sequences 2000.pdf)
Hugo statement on the scope of gene patents, research exemption and licensing of gene patents for diagnostics (2003) (see www.hugo-international.org/PDFs/Statement on the Scope of Gene Patents, Research Exemption.pdf).
Kerem B., Rommens J.M., Buchanan J.A., Markiewicz D., et al., 'Identification of the Cystic Fibrosis Gene: Genetic Analysis', **245** *Science*, 1989, 1073–80
Marshall E., 'European patents. BRCA2 claim faces new challenge', **308**, *Science*, 2005, 1851.
Miki Y., Swensen J., Shattuck-Eidens D., Futreal P.A., et al., 'A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene BRCA1', **266** *Science*,1994, 66–71
Matthijs G. and Halley D., 'European-Wide Opposition Against The Breast Cancer Gene Patents', **10** *Eur. J. Hum. Gen.*, 2002, 783–4
Matthijs G., 'The European Opposition against the BRCA Gene Patents', **5** *Familial Cancer*, 2006, 95–102

Munktell P., 'Compulsory Patent Licensing. Master thesis', University of Lund, Sweden, 2004.

National Academy OF SCIENCES (NAS), *Reaping the Benefits of Genomic and Proteomic Research: IP Rights, Innovation and Public Health*, National Academies Press, Washington DC, 2005 (www.nap.edu/catalog/11487.html).

Nuffield Council on Bioethics, *The Ethics of Patenting DNA, A Discussion Paper*, 2002. (www.nuffieldbioethics.org).

OECD, *Guidelines for the licensing of genetic inventions*, OECD Council, 2006. (www.oecd.org/document/56/0,2340,en_2649_34537_34317658_1_1_1_1,00.html)

Tavtigian S.V., Simard J., Rommens J., Couch F., et al., 'The Complete BRCA2 Gene and Mutations in Chromosome 13q-Linked Kindreds', **12** *Nat Genet*., 1996, 333–7

Van Ommen G.J.B., 'Popper Revisited: GWAS Here, Last Year', **16** *Eur J Hum Genet*., 2008, 1–2

van Ommen G.J.B and Cornel M.C., 'Recreational Genomics? Dreams and Fears on Genetic Susceptibility Screening', **16** *Eur J Hum Genet*., 2008, 403–4.

Van Overwalle, G., van Zimmeren, E., Verbeure, B. & Matthijs, G., 'Models for Facilitating Access to Patents on Genetic Inventions', **7** *Nature Review Genetics*, 2006, 143–8.

van Zimmeren, E., 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume

Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume

Verbeure B., Matthijs G. and Van Overwalle G., 'Analysing DNA Patents in Relation With Diagnostic Genetic Testing', **14** *Eur J Hum Genet*., 2006, 26–33.

Walsh T., Casadei S., Coats K.H., Swisher E., Stray S.M., Higgins J., Roach K.C., Mandell J., Lee M.K., Ciernikova S., Foretova L., Soucek P., King M.C., 'Spectrum of Mutations in BRCA1, BRCA2, CHEK2 and TP53 in Families at High Risk of Breast Cancer', **295** *JAMA*, 2006, 1379–88.

Wooster R., Neuhausen S.L., Mangion J., Quirk Y. et al., 'Localization of a Breast Cancer Susceptibility Gene, BRCA2, to Chromosome 13q12–13', **265** *Science*, 1994, 2088–90

Wooster R., Bignell G., Lancaster J., Swift S. et al., 'Identification of the breast cancer susceptibility gene BRCA2', **378** *Nature*, 1995, SS–92.

21 'Patent tsunami' in the field of genetic diagnostics

A patent practitioner's view

Jacques Warcoin

21.1 Introduction

Patentability of human genes has always been a problematic issue in terms of ethics, but in fact the real problem is a practical one, especially in the field of genetic diagnostics. The key problem is a problem of 'freedom to operate'.

21.2 Projects including genes or proteins

A recent article in *Science* provides interesting information on the phenomenon of 'patent tsunami' in the field of genetic research.[1] From this analysis it appears for example that Bone Morphogenetic Protein 7, a particular protein, has been the subject of a patent application twenty times. The same is true for genes on protein CDKN2A. Furthermore, the survey demonstrates that 150 genes/proteins have been the subject of more than five patent applications.

So, if one intends to use such a protein or gene in a project, it is necessary to make a 'freedom to operate analysis' (FTO). Such a FTO involves identifying all corresponding patents and determining which ones are valid and pertinent for the project, as well as to determine the corresponding strategy, that is, negotiating, ignoring or challenging (depending on the strength of the patents), and negotiating if necessary.

The situation may be more complicated especially in the field of diagnostics. In this field, genes or proteins are used as biomarkers to characterize a certain pathology. Generally there is a need for several genes or proteins for only one diagnostic test.

As an example, for the pathological diagnosis of some sarcomas (Ewing tumor, alveolar rhabdomyosarcoma, desmoplastic tumor,

[1] K. Jensen, F. Murray, 'Intellectual property landscape of the human genome', **310** *Science*, 2005, 239 (2005)

synovialosarcoma) using PCR as a technology, eleven fusion transcripts have to be searched altogether, which involve fourteen different genes, namely EWS/FLI-1, ERG, ETV1, EIAF, FEV, PAX3, PAX7/FKHR, SYT/SSX1, SSX2, and SSX4.

When carrying out an FTO analysis, it appeared that only EWS, FLI-1, ERG, PAX3, PAX7 were patented. The patentees asked royalties of amounting to 12% of the sale price of the diagnostic kit (7% for EWS, FLI-1, ERG; 5% for PAX3 and PAX7). The royalties for the use of PCR were 21% of the sale price! Which means that royalties represent virtually one-third of the price of the diagnostic kit.

This analysis was done for Institut Curie (Paris) and the whole process (research analysis and negotiations) took one year with corresponding costs and impact of the royalties on the price of the test.

A new generation of tests is becoming increasingly significant, namely microarrays (biochips technology). With this technology it is possible to analyze up to 100,000 genes in one test; this is a wonderful tool but not devoid of problems! In the case of biochips design for diagnosis of central nervous system diseases (more than 100 diseases) there is a need of around 800 DNA sequences on the microarray for said diagnostic test. So apart from basic technology of microarrays (ten to twenty patents) most of DNA fragments are patented (several times each!). A complete analysis of the freedom to operate situation would involve several hundred hours of analysis with corresponding costs and would imply hundreds of negotiations, with corresponding costs!

But, said technology is vital for diagnostics in the future. So, what are the possible remedies taking into account the fact that the issue is taking an increasingly large place in other fields of research and development as well?

21.3 Possible remedies to handle the patent tsunami

The main issue is what IP policy or strategies can be considered to balance the interest of the public and the interest of the companies in the field of biotech and especially in the area of diagnostics.

The issue can be approached from two different points of view. A first point of view can be situated *upstream*. More particularly, how to limit the patent tsunami in the field? To limit the number and the scope of patents, a set of initiatives may be examined, such as limitation in term of patentability, limitation through formal requirements (US and EPO), limitation of the scope of the claims (product claims concerning genes are limited to the use described in the patent, cf. German and French law), compulsory licenses (Belgian and French law), exemption

from infringement for particular acts (research, registration (US situation)), and exemption from infringement for particular people (physicians, academic searchers).

A second strategy focuses *downstream*: how to organize patents in particular sub-fields of biotech to give a reasonable access to the corresponding DNA patents? To organize the patents in certain fields, concerted right organizations, such as patent pools and clearinghouses, may be set up.

An important point to keep in mind when analyzing the problem is the possible impact of the proposed solution on the patent field in general. It is well known in legal matters that when you create an exception to solve one problem in one field you may create lots of collateral damages in the surrounding areas (for examples in pharmaceutical area or in chemistry).

Limitations in terms of patentability

For a long time the proposed solution in Europe has been a rather drastic one: no patentability for genes. This solution has been discussed ad nauseam during negotiation of Directive EP 98/44 on the legal protection of biotechnological inventions.[2] The result of almost ten years of negotiations has been laid down in article 5 of the Directive which is a compromise but nevertheless acknowledges the principle of patentability of human genes "if obtained by a technical process" (to be fair, it seems very unrealistic to imagine a gene obtained by a non-technical process!).

Specific requirements for patentability have been introduced in article 5.3, which stipulates that "The industrial application of … gene must be disclosed." Equally relevant is recital 23, which states that "DNA without indication of a function" is not patentable. Furthermore, recital 24 is important, which requires "To specify which protein … is produced or what function it performs."

Said provisions and recitals are not limitations on the principle of patentability of human genes but merely provide the possibility to adapt the criteria of patentability (industrial application as laid down in art. 57 EPC and enabling disclosure as stipulated in art. 83 EPC) to this specific type of invention.

[2] Directive 98/44/EC of 6 July 1998 of the European Parliament and of the Council on the legal protection of biotechnological inventions (OJ L 213, 30/07/1998 p. 0013) (see http://europa.eu.int).

A similar position has been held by the USPTO, for which, in order to fulfill the criteria of utility and enabling disclosure (35 USC 101 and 112) a patent must describe a utility which is credible, substantial and specific. Said interpretation developed for biotechnology is now used for all inventions in US.

The above US terminology has recently been used by a Board of Opposition in the European Patent Office (EPO) in order to reject a patent in an opposition (namely EP 630405, *Icos* case claiming a particular human gene for V28 receptor). However, the terminology has been criticized and new wording has now been developed by the EPO. In the most recent decisions of the Board of Appeal of the EPO dealing with patentability of genes, it has been stated that industrial application of said genes must be "profitable" and must not be "vague, indefinite or obscure" and must also be "practical".[3]

Although said notions are not yet well defined, they give the impression that the 'golden age' of patentability of any gene for putative uses or theoretical use is definitely over. This is all the more so because it becomes more and more difficult to use 'post published data' to support the description of such putative use. The industrial application must be identified and described in the patent application as filed.

Once again, one should not think that these are new criteria for patentability of genes. These notions are only specific notions for applying the usual criteria in this specific field but can be implemented for interpretation in other fields as well.

Limitations in terms of scope of a product claim

Some countries in Europe have decided to go one step further. This is the case for France and Germany.

In France

In August 2004 France decided to implement Directive 98/44 in a special way by using the preamble of said directive and introducing a new article, which reads as follows:

> The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.
>
> Only an invention constituting the technical application of the function of a human body element can be protected by a patent. This protection only covers the element of the human body to the extent necessary for carrying out and

[3] See the EPO Board of appeal decisions T 0604/04 and T 0870/04.

making use of this specific application. This application must be specifically disclosed *in concrete terms* in the patent application.

Are not patentable:

…

d) Total or partial sequences of a gene taken as such.

New Article L.611–18 (2nd §) of the French Intellectual Property Code (FIPC)

From the above text it is clear that the French implementation goes one step further to reject the patentability of human genes. This is not really a problem because most of the patents in force in France are European patents designating France and so are not subjected as far as patentability is concerned to French patent law but remain governed by EPC articles and in theory by the corresponding jurisprudence. But no one knows what may be the final impact of the above article on decisions of French Courts.

Additionally, another provision was introduced, which stipulates:

The scope of a claim covering a gene sequence is limited to the part of this sequence directly linked to the specific function disclosed in concrete terms in the specification.

The rights generated by the grant of a patent including a gene sequence cannot be opposed to a subsequent claim covering the same sequence if this sequence complies as such with the requirements of Article L.611–18 and if it presents ["expose" in French] another specific application of this sequence. (New article L.613–2–1 of the FIPC)

Even if the wording of this provision is a little naive, the French version clearly intends to limit the scope of a gene product claim: to the extent necessary for carrying out and making use of this specific application; to the application specifically disclosed in concrete terms in the patent application; to the part of this sequence directly linked to the specific function disclosed in concrete terms in the specification.

One will appreciate "the specific application specifically described"; it is difficult to be more specific!

In Germany

On 28 February 2005, most of the provisions of the Directive had been implemented in Germany. However, the German legislator also added a major change to the German Patent Act (GPA).[4] Consequently, the German Patent Act differs from the Directive.

[4] German Patent Acts 1968–2004.

(3) The industrial application of a sequence or a partial sequence of a gene must be concretely disclosed in the application by indicating the function fulfilled by the sequence or partial sequence.

(4) If the subject matter of the invention is a sequence or a partial sequence of a gene the structure of which is concordant to the structure of a natural sequence or partial sequence of a human gene, then its use, for which the industrial application is concretely described in accordance with subsection 3, has to be included into the patent claim. (Art. § 1 a, *Patentgesetz,* (introduced by *Gesetz zur Umsetzung der Richtlinie* ü*ber den rechtlichen Schutz biotechnologischer Erfindungen,* Bundesgesetzblatt 2005, Teil 1, Nr. 6, 28 January 2005, p. 146–149))

This article clearly recommends limiting the scope of claim on human genes as in France, but the specific use must be included in the claim, which is not the usual rule especially in Europe for product protection. From a legal point of view it is not a limitation.

So from a practical point of view the German approach would solve the problem raised by the French draft (clear identification of the specific use), but would not as such introduce any limitation in the scope of the claim.

Anyway, both approaches constitute a clear signal from the legislator for an erosion of the scope of a product claim. In most European countries the Directive has been implemented as such, creating a lot of disharmony in Europe which is in contradiction with the purpose of the Directive.

Limitation through formal requirements

In order to limit the number of patents and especially of continuation applications, divisional applications, specific requirements are under development in the United States and in Europe. But the main drawback is that if it becomes more difficult to obtain several patents on closely related inventions, the rules of the game will become so complex that it will create uncertainty for the future.

Compulsory license

The principle of compulsory licensing is in theory the perfect solution when only one patent is concerned. Such a specific article exists for pharmaceutical products in French law. The provision on compulsory licensing existed for pharmaceutical products as such in French law since 1968, but has recently been adapted for diagnostics. Indeed, in France several types of compulsory licenses exist, but the interesting

one for the purpose of the present article is compulsory licensing for public health, which reads as follows:

In the public health's interest and in case of no amicable agreement with the owner of the patent, the Minister responsible for industrial property, at the request of the Minister responsible for health may subject to ex officio licenses in accordance with Article L613–17 any patents granted for:

a) medicines, medical device, medical device for in vitro diagnostic, side (annex) therapeutic product,
b) processes for obtaining said products, products necessary in obtaining such medicines or for processes for manufacturing such products
c) ex vivo diagnostic method (article L.613–17 of FCIP)

Patents for said products, processes or diagnostic methods may be submitted to ex officio licensing in public health's interest only in the event of such products, or the products obtained by said process or said methods are being made available to the public in insufficient quantity and quality or at abnormally high prices, or when the patent is enforced in conditions which are in contradiction with public health's interest or which are declared to constitute an anticompetitive practice further to a final judicial decision…[5]

My answer to the question as to whether such a provision on compulsory licensing is efficient in the pharmaceutical field, is yes because it has never been used! It is the purpose of said article: to remain a pure theoretical threat, no one in the pharmaceutical field would take the risk of having an important licensing done by a court! So, in case of a diagnostic (ex vivo), it is possible to request compulsory licenses for patented genes.

But in the case where hundreds of patents are involved, it would be virtually impossible to solve the problem even with compulsory licenses. So, in the case of biochips, a compulsory license mechanism would be unfeasible or would have a limited impact in the sense that it would only be helpful to convince one of the patentees found to be reluctant.

[5] For an in-depth analysis of the French compulsory licensing regime for public health, see van Zimmeren, E. and Requena, G., 'Ex-officio Licensing in the Medical Sector: The French Model', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 123–147. For an analysis of the compulsory licensing regime for public health in some other European countries, see for Belgium, Van Overwalle, G., 'The Implementation of the Biotechnology Directive in Belgium and its Aftereffects. The Introduction of a New Research Exemption and a Compulsory License for Public Health', **37** *International Review of Intellectual Property and Competition Law (IIC),* 2006, 889–920; for Switzerland, see Germann, C., 'The Swiss Approach to Compulsory Licensing for Diagnostic Products and Processes', in Van Overwalle, G. (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 149–156.

Specific organization in the field of genetics

The possibility to use patent pools or clearinghouses to solve the above problem has been studied, especially in the industrial property committee of the Human Genome Organization.[6]

A patent pool would request that all the patentees in a specific area put their patents together for example in a specific diagnostic area by signing a patent pool agreement (as it exists in the MPEG LA pool in the electronic field). In this case only one agreement would authorize a third party to have access to all necessary genes.[7] But in fact, this solution, which works in the electronic field because the patentees are big companies with a perfect understanding of their interest, is not possible with small start-ups in biotechnology, because all of them are convinced that "their genes" are essential and they are are therefore unwilling to pool them.

21.4 Conclusion

So for the time being, the only solution is to take the risk of infringing. No efficient solution exists to solve the problem of biochips even for large projects in biotechnology if said projects imply an unreasonable royalty stacking because of the number of patents which are needed.

REFERENCES

Jensen, K. and Murray, F., 'Intellectual property landscape of the human genome', **310** *Science*, 2005, 239

Germann, C., 'The Swiss Approach to Compulsory Licensing for Diagnostic Products and Processes', in Van Overwalle, G. (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 149–56.

van Zimmeren, E. and Requena, G., 'Ex-officio Licensing in the Medical Sector: The French Model', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 123–47

Van Overwalle, G., 'The Implementation of the Biotechnology Directive in Belgium and its Aftereffects. The Introduction of a New Research Exemption and a Compulsory License for Public Health', **37** *International Review of Intellectual Property and Competition Law (IIC)*, 2006, 889–920

Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume

[6] Personal communication.

[7] See the contribution of Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume.

22 Gene patents and clearing models

Some comments from a competition law perspective

Hanns Ullrich

22.1 Introduction

Competition law is not at the centre of the present book. It comes in as an additional concern, influencing the search for proper models for solving a problem of patent abundance, whose contours, however, are not yet well realized and recognized in biotechnology. Like in other areas of advanced technologies, the basic assumption is that the field is crowded by a large number of patents, with ownership being dispersed among many patentees, so that it becomes impossible for anyone to work naturally coherent pieces of the technology without first obtaining consent by many other patentees. Seeking such consent may delay innovation, and raise its costs as royalties may have to be paid. It also entails transactions costs relating to the search of relevant patents and patentees, to determining the patents' value, and to negotiating license agreements, provided always that an agreement may be found.

In the present volume, a large variety of models has been presented, which either seek to avoid or to overcome the problem resulting from the fragmentation of technologies into pieces of proprietary knowledge. In a competition law perspective, this by itself represents quite a remarkable merit of this volume, since it opens the view for a number of options among which to choose when looking for a "pro-competitive" or, at least, for a non anticompetitive solution of the problem. However, for the commentator, it creates an *embarras de richesse*. It is simply not possible to bring all of these rather heterogeneous models – pools, clearinghouses, open source licensing – into closer focus without losing oversight. Suffice it, therefore, to illustrate the application of competition law to such models by briefly setting forth its analytical framework, its problems and its limitations as they apply to patent pools (*infra* 22.2). They not only have a long history of exposure to antitrust investigation, and, as of recent,

a surprising come-back.[1] Rather, they may also be used to put other models in contrast (*infra* 22.3 'From pools to clearing houses'), and, as imperfectly as they work, they also point to the source of the problems, which is to be found in the design and the operation of the traditional systems of patent protection (*infra* 22.3 'Back to patent law').

22.2 Pooling

Competition law at the rescue of patent law

The comeback of patent pools is a result of both the – by now well known – expansion of the scope and use of the patent system, and of a reorientation, in fact a constriction of the understanding and the application of the laws against restraints of competition. Pools have been formed and recognized in the information and telecommunications industry as a matter of the joint establishment and exploitation of compatibility standards for patented information interfaces,[2] and they have been recommended as a way "to ensure reasonable access to patented genomic inventions".[3] They are expected to help both clearing the ominous "patent thicket" and breaking up blocking and facilitating the use of complementary patents, but also to help containing the overall sum of royalties due for using large numbers of patents, and to reduce the transactions costs of seeking so many licences.[4] Traditionally, however, pools are suspected to involve collusion as regards pricing of patented products and – almost necessarily – as regards royalty setting. In

[1] See in both regards R.Merges, 'Institutions for Intellectual Property Transactions: The Case of Patent Pools', in R.Dreyfuss, D. Zimmerman, H. First (eds.), *Expanding the Boundaries of Intellectual Property*, Oxford 2001, 123 *et seq*.

[2] See R. Bekkers, E. Iversen, K. Blind, 'Patent Pools and Standardization: coordination mechanisms for multi-party IPR holders', Paper for the EASST 2006 Conference, Lausanne, August 23–26th (available at http://www2.unil.ch/easst2006/); R. Bekkers, K. Blind et al., 'Case studies on the interface between research and standardisation, and case studies on patent pools as coordination mechanisms', (also: INTEREST – Integrating Research and Standardisation), Contract No. 503594, 6th Framework Program (available at www.interest-fp6.org/.); R. Merges, loc. cit. supra n. 1; H. Ullrich, Patent Pools- Policy and Problems, in J. Drexl (ed.), *Research Handbook on Competition Law and Intellectual Property*, Cheltenham, Edward Elgar, 2008 (139, *et seq*.) with references

[3] USTPO, 'Patent Pools: A solution to the Problem of Access in Biotechnology Patents?', Washington D.C., December 5, 2000 (authored by J. Clark, J. Piccolo, B. Stanton, K. Tyson)

[4] See Commission, Guidelines on the application of Article 81 EC-Treaty to Technology Transfer Agreements, OJEU 2004 C 101, 2 at no 214; US Dpt. Justice. FTC, Guidelines for Licensing of Intellectual Property, Washington, D.C. April 5, 1995 (4 Trade Reg. Rep. (CCH) 13.132) sub 5.5.; Ibid., Antitrust Enforcement and Intellectual Property Rights: Promoting Innovation and Competition, Washington D.C. 2007, 64 *et seq*.

addition, they may amount to tying arrangements in that they result in bundling patents, thus foreclosing market access for alternative technologies, and they tend to affect competition for alternative innovations as it may exist between both the pool partners and these and third parties.[5]

Both the US antitrust law authorities and the European Commission, which, as a competition policy maker and enforcer, tend to follow the welfare economics teachings of its US counterparts when proning a "more economics-based approach" to the application of the EC-competition rules,[6] seek to promote the exploitation of the benefits of patent pooling, and thus, its pro-innovation and pro-competition potential. To this effect, they rely on a set of narrow criteria which, within a complex analytical framework, are intended to exclude or at least to contain the risks of an (overly) anticompetitive operation or of too far-reaching anticompetitive effects of pools.[7] While this analytical framework and its criteria cannot be set forth here in any detail, its basic ambiguity and ambivalence results from the following features. On the one hand, the framework rests on an artificial separation of the different layers of pool building, which are: first, the internal cross-licensing agreement between the partners of the pool; second, the pooling arrangement as such with its agreement on third-party licensing and its terms;[8] and, third, the actual licensing agreement with third parties. Notwithstanding their interdependency, the Commission analyzes and assesses the first and the last mentioned agreements in isolation and separately from the pooling agreement as if all of them were not building blocks of an overall arrangement for the private regulation of the

[5] See Commission, Transfer of Technology Guidelines, loc. cit. sub no. 213 and US Dpt. Justice, FTC, *see* n. 4.

[6] See Commission, Guidelines on the application of Article 81(3) of the Treaty, OJEU 2004, C 101, 97 sub no. 5, et passim. The reasons for such follower conduct are manifold, both theoretical and practical, but also political in that regulatory competition of competition law and policy is driven by globalization and the objectives of maintaining international competitiveness (the Lisbon Agenda), See Commission, A pro-active Competition Policy for a Competitive Europe, COM (2004) 293 final, Brussels, 20 April 2004.

[7] See references *see* n. 4, and for a critical analysis Ullrich, *see* n. 2; ibid., 'Patents Pools: Approaching a Patent Law Problem via Competition Policy', in Cl.-D. Ehlermann, I. Atanasiu (eds.), *The Interaction between Competition Law and Intellectual Property Law*, **10** *European Competition Law Annual 2005*, Oxford 2007, 305 *et seq.*

[8] While pooling arrangements may take the form of a – legally separate – joint licensing agency of pool partners, the systematic and full acquisition on the market of bundles of patents for licensing of a technology by an independent enterprise, which makes itself a business out of acquiring and selling technologies does not raise pooling problems under the competition rules (but may raise concerns of controlling market power).

market.[9] On the other hand, the basic distinction between horizontal and vertical agreements in restraint of trade, which is all the more relevant in the context of pooling as technology and product markets need to be (and are) distinguished, and as pool partners may well be present on both or – following new business models which are now common in both informatics and biotechnology – only on the technology market, this distinction is made not with a view to existing relationships of rivalry on the market, but with respect only to the patents in question. The test is whether these relate to substitutive or to complementary technologies, the idea being that only the former indicate an actual horizontal relationship with its increased risks of anticompetitive collusion, whereas the latter would point to a need to their combined use, this being the way to fully and immediately bring the potential of the specific technology to bearing (*nota bene* of a technology, whose development, whether done jointly or independently, results, of course, from a business rivalry).[10]

While such a reductionist analysis may facilitate pooling, rather strict criteria of legality are intended to contain it within limits. Thus, it is only in case the pool relates to complementary patents that are "essential" to work a technology in accordance with some pre-defined (more or less mandatory) specifications that the pooling agreement as such will be considered to be pro-competitive by nature, and, therefore, admissible per se.[11] This is a formal test, which has been developed with respect to pools supporting technological compatibility standards in the informatics and telecommunication industries. While it may be used in other standardization contexts as well, such as standardized testing or measurement, in the absence of such a pre-set framework, it tends to become a rather loose test, unless it is construed strictly in accordance with its purpose. This, indeed, is to allow only pools supporting access to some crucial (technological) input or material, or

[9] For details see Ullrich, *see* n. 7.

[10] See Commission, Transfer of Technology Guidelines, loc. cit. at nos. 26 *et seq.*, 215 *et seq.*; the relationship between the determination of the competitive position of pool partners and the determination of the competitive nature of the pooled patents is not made entirely clear by the Guidelines.

[11] Under the competition rules of the EC Treaty, the distinction between pro-competitive arrangements, which, for this reason, remain outside Art. 81(1) of the Treaty, and agreements, which, due to their presenting anticompetitive features, need to be assessed under Art. 81(3) of the Treaty, mainly relates to the distribution of the burden of proof according to Art. 2 Reg 1/2003 of December 16, 2002 on the implementation of the competition rules laid down in Art. 81 and 82 EC Treaty (OJ EC 2003 L 1,1); for the relationship between Art. 81(1) and (3) and their different tests see CFI of 2 May 2006, case T- 328/03, O2/Commission (Rep. 2006 II 1231).

to some unavoidable gateway or "facility",[12] that cannot be obtained otherwise, in particular not by way of technological circumvention. Biotechnology may offer some examples, in particular in the field of gene research for medical purposes.

Likewise, the fact that outside pooling of essential patents, competition authorities – at least the European ones[13] – tend to be rather reluctant to admit pools in that they are critical of pooling of substitute patents, and vague as regards the balancing terms for weighing the pro- and the anticompetitive effects of broader pools, suggests that such pooling arrangements cannot be expected to become generally recognized.[14]

Competition law dilemmas

In fact, when evaluating patent pools, competition authorities face a dilemma. The need for pooling arises only in cases of abundance and dispersed ownership of patents, and it increases as the number of patents (and patentees) increases. To a certain extent, the efficiency justification becomes the more plausible the bigger the pool is. However, as the pool grows it is likely to acquire and expand market power, with, as a result, restrictive effects becoming ever more worrying.[15] While, under the economics-based approach of modern competition policy, competition authorities will not become concerned unless a restrictive arrangement passes the threshold of some market power, the criteria of art. 81(3) become ever more difficult to comply with as market power increases. Moreover, when "pools…hold a strong position on the market …",[16] the terms of assessment change in that art. 82 considerations are introduced: the pool now "should be open and non-discriminatory".[17] Whether this means only open and non-discriminatory access by third parties to the acquisition of licenses, or also their admission to the pool as members is not quite clear. Nor is it clear where the threshold of a

[12] The test is more related to the "indispensability" – criterion under Art. 81(3) EC-Treaty than to the "essential facility"– doctrine under Art. 82 of the Treaty, the latter, however controversial (see recently A. Castaldo, A. Nicita, 'Essential Facility Access in Europe: Building a test for Antitrust Policy', **3**(1) Rev. L. Econ 83 (2007); A. Stratakis, 'Comparative Analysis of the US and EU Approach and Enforcement of the Essential Facilities Doctrine', E.C.L R 2006, 434, both with references), having its own, independent scope of application in accordance with Art. 82 of the Treaty.

[13] US DoJ/FTC, Antitrust Enforcement, *see* n. 4 at 74 *et seq.* (77/78) take a more generous view.

[14] But see the references in n. 2 regarding empirical evidence.

[15] Commission, Transfer of Technology Guideline, 224. [16] Ibid.

[17] Ibid., 224, 226 ("open" meaning at least non exclusive licenses).

"strong market position" is to be set. At any rate, it is a critical one. On the one hand, it means that the pool is allowed to determine the general conditions of the market as long as it does so in a non-discriminatory way and without anti-competitive effects on downstream markets.[18] On the other, it necessarily imposes a system change, which generally tends to affect patents that can usefully be exploited only by way of pooling.[19] Indeed, facilitating third-party licensing via pooling is one thing. Requiring, as a matter of competition law, an open licensing policy, i.e. non-discriminatory licensing to everyone, tends to convert the exclusivity principle of patent protection into a mere liability system, i.e. into a reward-by-compensation rule.

22.3 Avoiding competition law

From pools to clearinghouses

Containing the power of pools by outlawing excessively restrictive arrangements will not always work[20] nor will it be enough. Even perfectly legitimate, because limited pools are subject to additional control as regards their licensing activities when they actually dominate the market.[21] Whether this is nevertheless a comfortable or, to the contrary, an uneasy position is a matter of the business strategy of the pool and of the enforcement policy of competition authorities. In any case, patent exploitation by pooling thus tends to come under a kind of a regulatory regime. One way to avoid this is to take competition law seriously by asking not only whether a specific, restrictive feature of the

[18] Ibid., 226 requiring also, apparently with a view to competition on down streams markets, "fair" royalties, whatever this means (see Ullrich, n. 2, sub. II. 2. b).

[19] See Merges, n. 1, and note that it is the patentee who, via the pool, determines the reward due to him, with the weapon of enjoining non-abiding 'infringers' from using the potential invention still being available to him as a matter of legal principle, unless additional competition law considerations come in.

[20] Commission, Transfer of Technology Guidelines, 227 insists that pool partners must remain free to individually license their pooled patents. However, given the transaction cost rationale of pooling, this is largely a hypothetical freedom. It may exceptionally become a reality in cases of big deals with important licensees, but it does little to reduce the overall problem of pooling.

[21] Thus, it is precisely pools of "essential" patents which will be most exposed to control of whether they really adhere to an open and non-discriminatory licensing practice under the case law of ECJ of 5 October 1988, case 238/87, Volvo/Veng, Rep. 1988 I 6211; of 6 April 1995, cases C-241/91P and C-242/91 P, RTE, ITP/Commission, Rep 1995 I 743; CFI of 17 September 2007, case T-201/04, Microsoft/Commission, not yet officially reported; BGH of 13 July 2004, WuW DE-R 1329 (Standard Spundfass II) = 36 *IIC* 741(245) annot. Leistner.

pool agreement is "indispensable" within the meaning of art. 81(3) of the EC Treaty. Rather the test should be whether, as such, pooling is indispensable or whether less restrictive institutional arrangements are available. The enormous merit of the present book is that it purposively pointed to just such alternatives, and that they were presented in all their diversity.

Again, these models cannot be commented upon here. Open source models have engendered a rich literature, including some on their antitrust implications.[22] How far these models may carry as regards expansive patent protection, and whether they always follow a free access rationale rather than a business strategy, needs to be examined more closely.[23] Clearinghouses as well may raise problems under competition law in case they allow too much information exchanges on competition related data, or in case they otherwise facilitate collusion.[24] However, such risks can easily be avoided by a proper design of the arrangement without affecting its efficient functioning. This essentially would be to identify, to classify, and to group relevant patents by reference to specific technological purposes, possibly also to translate the patented technical teachings into user friendly information, to help to interpret and to technically evaluate them, and possibly even to provide a platform for individual licensing transactions. Indeed, frequently enough the patent thicket is more a matter of the number and of the strategic positioning of patents than of the number of patentees. Once the boundaries and a roadmap[25] of the thicket have been established, individual negotiations with the limited number of patentees may become a feasible alternative to or an additional option of pooling arrangements.[26]

[22] See Chr. Heath, 'Kartellrecht', in G. Spindler (ed.), *Rechtsfragen bei open source*, Cologne 2004, 267; L. Böcker, 'Mit freier Software gegen den Wettbewerb? Die General Public License (GPL) als horizontale Wettbewerbsschränkung', in *Festschrift F. Säcker*, Berlin 2006, 69, all with references, but see for the *US Wallace* v. *IBM*, 38 *IIC* 252 (available at www.ca7.uscourts.gov/tmp/7P1FG159.pdf).

[23] See as regards a standardization context T. Simcoe, 'Open Standards and Intellectual Property Rights', in H. Chesborough et. al., *Open Innovation – Researching a New Paradigm*, Oxford 2006, 161; J.West, 'Does Appropriability Enhance or Retard Innovation', in Chesborough, *Open Innovation*, 109.

[24] See ECJ of 23 November 2006, case C-238/05, Asnef-Equifax, Ausbane, Rep. 2006 I 11145, and generally Wagner-von Pa ' "Who is it that can inform me"- The Exchange of Identifying and non-Identifying Information', *Eur. Comp.L.Rev.*, 2007, 264

[25] Its value depending on how precisely it presents the "intersection", i.e. the scope and limits of neighbouring and overlapping patents.

[26] E.g. so as to make individual licensing by pool partners a realistic option (*see* n. 20).

Back to patent law

Relying on clearinghouses rather than on pooling arrangements also corresponds better to the causes underlying the proliferation of patent thickets in certain fields of technology, a matter which need not be taken for unavoidable. True, increased patenting has to do with the way business models change in the information society, patented technology becoming itself a product for sale rather than being only a teaching for production. But both the expansion of patent protection as regards subject-matter and scope and the trend to strategic patenting by at least some segments of industry,[27] contribute to such overcrowding of some fields of technology by claims to exclusive use. The problem of patent thickets thus is, at least in part, a self-created one, which does not necessarily justify power building through pooling, on the contrary. On the one hand, a liberal attitude on pooling invites even more patenting,[28] thus aggravating the problem. On the other hand, competition law is only concerned with the containment of anticompetitive agreements and of abusive conduct in asymmetrically structured markets. It can neither induce private institution-building that adequately fits its purpose[29] nor provide the means for an optimization of the design and the operation of the patent system.[30]

Clearinghouses directly attack a deficit of the patent system, which is its insufficient transparency (notwithstanding its requirements of disclosure, examination – at least in major jurisdictions – and

[27] See O. Granstrand, *The Economics and Management of Intellectual Property*, Cheltenham 1999 (paperback 2000), 176 *et seq.*, 209 *et seq.*; K. Blind, *The Economics of Standards*, Cheltenham 2004, 125 *et seq.*; id. The influence of Strategic Patenting on Companies Patent Portfolios, Zentrum für Europäische Wirtschaftsforschung (ZEW), Discussion Paper 07–013 (available at ftp:/ftp.zew.de/put/zew-does/dp/dp07013.pdf); T. Simcoe, Explaining the Increase in Intellectual Property Disclosure (available at www.rotman.utoronto.ca/timothy.simcoe.papers/SU-IPR-Disclosure); more generally European Patent Office (ed.), *Scenarios for the Future*, Munich 2007, 15 *et seq.*; 34 *et seq.*

[28] But see Melamed and Lerch, 'Uncertain Patents, Antitrust, and Patent Pools', in Ehlermann, Atanasiu (eds), **10** *Eur. Comp. L. Ann.* 273 (2007).

[29] For a critique of the Commission's recommendation of "democratic pooling" (Technology Transfer Guidelines, 230 *et seq.*) see Ullrich, 'Patent Pools – Policy and Problems', in J. Drexl (ed.), *Handbook on Competition Law and Intellectual Property*, sub II 3f); Ullrich, 'Patent Pools', in Ehlermann, Atanasiu, **10** *Eur. Comp.L. Ann* at 320 *et seq* (2007).

[30] The need for such optimization and the reasons for current reform efforts, in particular in the USA (and unfortunately not in the EU), reach far beyond competition law and policy, see only S.Scotchmer, *Innovation and Incentives*, Cambridge (Mass.) 2004, 97 *et seq.*; 127 *et seq;* National Research Council, *A Patent System for the 21st Century*, Washington D.C. 2004, passim; for the limits of competition law, H.Ullrich, 'Le droit de la concurrence, proprieté intellectuelle et accès à l'information technologique', in M.Buydens,S.Dusollier (eds.). *L'intérêt général et l'accès à l'information en propriété intellectuelle*, Brussels 2007, 249.

registration).[31] Clearing may be left to private organizations or considered to be part of a patent office's service function,[32] and possibly it is a task to be taken in charge by both. In either case, it would facilitate access to "essential" technology while alleviating regulatory control by competition law.

Moreover, to the difference of open source models, and also to the difference of the practical operation of at least the larger pools, clearinghouses maintain the property rationale of the patent system, i.e. its principle of exclusivity-based individual exploitation.

22.4 Conclusion

Obviously, collaborative clearing models are not the answer to all problems. Frequently, pools are not a reaction to the patent thicket, but a result of joint research and development by the pool partners. Thus, pools cannot easily be transformed *ex post* in mere clearing arrangements. Also, clearing will do little, if anything, to solve the problem of cumulative royalties, a matter which is of particular concern in biotechnology.[33] The more general point then is to find out which exactly is the problem that needs to be solved, and which institutional arrangement is best suited to bring about the solution. Competition law has no answer to this question, except that it favors the least restrictive approach, if restriction needs to be tolerated at all. The concepts thus are a matter for other disciplines. Competition law is only concerned with their effects. It is not interested in the form of institutions or of organizational arrangements, but in the distortion of competition, which choosing and adopting such an arrangement actually produces.

REFERENCES

LITERATURE

Bekkers, R., Iversen, E. and Blind, K., 'Patent Pools and Standardization: coordination mechanisms for multi-party IPR holders', Paper for the

[31] Think only of the effects which the length of the granting procedure (almost 4 years at the European Patent Office, see EPO, Annual Report 2006,18,22) or the ratio of application to grants (less than 50%) must have on business decisions to innovate; the problem has been recognized by the EPO, see A. Brimelow, Press statement of 17 October 2007 (available at www.epo.org/topics/news/2007/20071017_de.html).

[32] These tend to be extended not only as a result of a division of labour between the European Patent Office and national offices, but as a matter of promoting innovation, see *Gowers Review of Intellectual Property*, London (HMSO) 2006, sub. 5.40, 6.

[33] But not dealt with by Commission, Transfer of Technology Guidelines, 45.

EASST 2006 Conference, Lausanne, August 23–26th (available at http://www2.unil.ch/easst2006/Papers/B/Bekkers%20Iversen%20Blind.pdf)

Bekkers, R., Blind, K. et al., Case studies on the interface between research and standardisation, and case studies on patent pools as coordination mechanisms, (also: INTEREST – Integrating Research and Standardisation), Contract No. 503594, 6th Framework Program (available at www.interest-fp6.org/).

Blind, K., *The Economics of Standards*, Cheltenham, 2004

Blind, K. et al. *The influence of Strategic Patenting on Companies Patent Portfolios*, Zentrum für Europäische Wirtschaftsforschung (ZEW), Discussion Paper 07–013 (available at http://opus.zbw-kiel.de/volltexte/2007/5501/pdf/dp07013.pdf).

Böcker, L., ‚Mit freier Software gegen den Wettbewerb? Die General Public License (GPL) als horizontale Wettbewerbsschränkung', in *Festschrift F. Säcker*, Berlin, 2006

Brimelow, A., Press statement of 17 October 2007 (available at www.epo.org/topics/news/2007/20071017_de.html)

Castaldo, A. and Nicita, A., 'Essential Facility Access in Europe: Building a test for Antitrust Policy', **3**(1) *Rev. L. Econ*, 2007, 83

Clark, J., Piccolo, J., Stanton, B. and Tyson, K., *Patent Pools: A solution to the Problem of Access in Biotechnology Patents?*, USPTO, Washington D.C., December 5 2000

European Commission, *A pro-active Competition Policy for a Competitive Europe*, COM (2004) 293 final, Brussels, 20 April 2004

European Patent Office (ed.), *Scenarios for the Future*, Munich, 2007

Granstrand, O., *The Economics and Management of Intellectual Property*, Cheltenham 1999 (paperback 2000)

Heath, C., ‚Kartellrecht', in G. Spindler (ed.), *Rechtsfragen bei open source*, Cologne, 2004, 267

Gowers Review of Intellectual Property, London, 2006 (available at www.hm-treasury.gov.uk/independent_reviews/gowers_review_intellectual_property/gowersreview_index.cfm)

Melamed, D. and Lerch, D., 'Uncertain Patents, Antitrust, and Patent Pools', in *European Competition Law Annual 2005: The Interaction between Competition Law and Intellectual Property Law*, Claus Dieter Ehlermann and Isabela Atanasiu (eds.), 2007, 273

Merges, R., 'Institutions for Intellectual Property Transactions: The Case of Patent Pools', in R. Dreyfuss D. Zimmerman and H. First (eds.), *Expanding the Boundaries of Intellectual Property*, Oxford, 2001, 123

National Research Council, *A Patent System for the 21st Century*, Washington D.C., 2004, passim

Simcoe, T., 'Open Standards and Intellectual Property Rights', in H. Chesborough et. al., *Open Innovation – Researching a New Paradigm*, Oxford, 2006

Scotchmer, S. *Innovation and Incentives*, Cambridge (Mass.), 2004

Simcoe, T., *Explaining the Increase in Intellectual Property Disclosure* (www.rotman.utoronto.ca/timothy.simcoe/papers/SSO_IPR_Disclosures.pdf)

Stratakis, A., 'Comparative Analysis of the US and EU Approach and Enforcement of the Essential Facilities Doctrine', *E.C.L.R.*, 2006
Ullrich, H. 'Patents Pools: Approaching a Patent Law Problem via Competition Policy', in Cl.-D. Ehlermann and I. Atanasiu (eds.), *The Interaction between Competition Law and Intellectual Property Law*, **10** *European Competition Law Annual 2005*, Oxford, 2007
'Patent Pools- Policy and Problems', in J. Drexl (ed.), *Research Handbook on Competition Law and Intellectual Property*, Cheltenham, Elgar, 2008, 139
'Le droit de la concurrence, proprieté intellectuelle et accès à l'information technologique', in M. Buydens and S. Dusollier (eds.), *L'intérêt général et l'accès à l'information en propriété intellectuelle*, Brussels, 2008, 249
Wagner-von Papp, 'Who is it that can inform me' – The Exchange of Identifying and non-Identifying Information', *Eur. Comp.L.Rev.*, 2007
West, J., 'Does Appropriability Enhance or Retard Innovation', in H. Chesborough, et. al., *Open Innovation – Researching a New Paradigm*, Oxford, 2006

LEGISLATION

European Commission, Guidelines on the application of Article 81 EC-Treaty to Technology Transfer Agreements, *OJEU-C*, 2004, 101/214
US Department of Justice (DOJ), Guidelines for Licensing of Intellectual Property, Washington, D.C. April 5 19954 Trade Reg. Rep. (CCH) 13.132
US Department of Justice (DOJ), *Antitrust Enforcement and Intellectual Property Rights: Promoting Innovation and Competition*, Washington D.C. 2007

23 Access to genetic patents and clearing models

An economic perspective

Reiko Aoki

23.1 Introduction

Several institutions have been identified as mechanisms that can be used to facilitate access to genetic patents:[1] research exemptions, compulsory licensing, patent pools,[2] various clearinghouses[3] and open source collectives.[4] Following van Zimmeren, a major distinction between mechanisms "for access" and mechanisms "for access and use" can be made.[5] Applying an economic logic, however, leads to a subcategorization which differs from van Zimmeren's classification, and leads to subdividing the second category into collective rights organizations (CRO) and incomplete contract structures (ICS). Incomplete contract structures is expansion of open source and includes contractually structured liability.

Each category has a different purpose: "for access" clearing mechanisms are characterized by network and transaction cost reduction, CROs set prices to IP so that they will be used optimally for production, and ICSs address incontractable, uncertain and dynamic nature of innovation. While there are working examples of the aforementioned

[1] Van Overwalle, G., van Zimmeren, E., Verbeure, B. and Matthijs, G., 2005. 'Models for Facilitating Access to Patents on Genetic Inventions', 7 *Nature Review Genetics,* February 2006, 143–8.

[2] Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume.

[3] van Zimmeren, E., 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume.

[4] Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume.

[5] van Zimmeren, see Chapter 5 of this volume. Also see van Zimmeren, E., Verbeure, B., Matthijs, G. and Van Overwalle, G., 'A Clearinghouse for Diagnostic Testing: the Solution to Ensure Access to and Use of Patented Genetic Inventions?', *Bulletin of the World Health Organization*, 2006, 352–9.

systems, we will also discuss the contractually constructed liability regime[6] which is a new concept.

We categorize the clearing mechanisms by function.[7] Mechanisms such as "information clearinghouses" (information CH) and "technology exchange clearinghouses" (technology exchange CH) are "for access" and purely for *exchange*. The purpose of information CH is for IP or technology owners to disseminate and the potential users to find the information about the technology. Technology exchange CH go one step further in that technology is sold or licensed in addition. The property owners and users interact directly and property owners retain ownership.

There are institutions that promote both "access and use" such as copyright collection societies (CCS) and patent pools.[8] We will refer to this subgroup as "collective rights organizations" (CRO).[9] In addition, we expand open source models to include another "access and use" institution, contractually constructed liability (CCL). Both open source and CCL take into account the uncertain and dynamic nature of innovation. I will refer to this subgroup as "incomplete contract structures" (ICS) because they define relationships and contingent transfers (fees) when there are non-contractable elements such as risk.

23.2 Exchanges

The benefits of information CH and technology exchange CH come from reduction of transaction costs, primarily search costs. Typical examples of this category are PIPRA[10] and GBIF.[11] There is additional reduction of contracting costs if the exchange offers some sort of standard licensing agreements that provider and user can adhere

[6] Rai, A.K., Reichman, J.H., Uhlir, P.F. and Crossman, C., 'Pathways across the valley of death: novel intellectual property strategies for accelerated drug discovery', Chapter 17 of this volume.

[7] Aoki, R. and A.Schiff, 'Promoting Access to Intellectual Property: Patent Pools, Copyright Collectives and Clearinghouses', **38** *R&D Management*, 2008, 118–204 at 186 also uses *ownership* to classify clearinghouses.

[8] May also include patent royalty collection clearinghouse (van Zimmeren, see Chapter 5 of this volume.

[9] Merges, R.,'Contracting into liability rules: intellectual property rights and collective rights organizations', **84** *California Law Review*, 1996, 1293–1393. The aforementioned "copyright collection societies" are equivalent to what Merges refers to as "royalty collection organizations".

[10] Bennett, B. and Boettiger, S., 'Case 5. The Public Intellectual Property Resource for Agriculture. A standard license public sector clearinghouse for agricultural IP', Chapter 8 of this volume.

[11] Edwards, J.L., 'Case 3. The Global Biodiversity Information Facility. An example of an information clearinghouse', Chapter 6 of this volume.

to. Standard licenses promote exchange and are provided as a service. The design of a license itself is not the objective as in "access and use" mechanisms. We therefore include standard licensing CH[12] in this group. We believe the Creative Commons[13] is another example. Creative Commons not only reduces search cost by providing information about available materials, but it also reduces contracting cost by providing licensing formats. That is, Creative Commons undertakes a "task of devising and encouraging the use, not of standard licences, but of standard clauses for licences, standard mechanisms for resolving common licensing problems" proposed by Spence.[14]

Exchanges are based on the "network effect" that arises from the exchanges' ability to reduce search costs. The particulars of the network effect must be taken into account for a successful formation of an exchange.

Network effects

An institution has a network effect when benefit to the members depends on the number of members. The following is a very simple model that captures this effect. There is a continuum of agents, represented by interval [0,1]. Agents are indexed by $x \in [0,1]$

An agent x gets benefit of $1 - x$ per interaction with another agent. In case of an exchange, benefit comes from learning about the others' technology. All agents benefit but the magnitude of the benefit depends on the agent and we index the agents by their magnitude of benefit. That is, if $x > y$, then agent y gets higher benefit per interaction than agent x. Suppose n is the number (in this case proportion of agents to be precise) that are members in the exchange. We can formulate the surplus of an agent $x \in [0,1]$ as,

$$U(x) = \begin{cases} n(1-x) - p & \text{if } x \text{ is a member} \\ 0 & \text{otherwise} \end{cases}$$

where p is the price of joining the exchange. Greater the number of members and lower the price, greater the surplus. The marginal agent, $\hat{x}$, is indifferent between joining and not joining the exchange,

$$U(\hat{x}) = n(1 - \hat{x}) - p = 0$$

[12] van Zimmeren, see Chapter 5 of this volume.
[13] Nguyen, T., 'Case 6. The Science Commons Material Transfer Agreement Project. A standard license clearinghouse?', Chapter 9 of this volume.
[14] Spence, M., 'Comment on the conceptual framework for a clearinghouse mechanism', Chapter 11 of this volume.

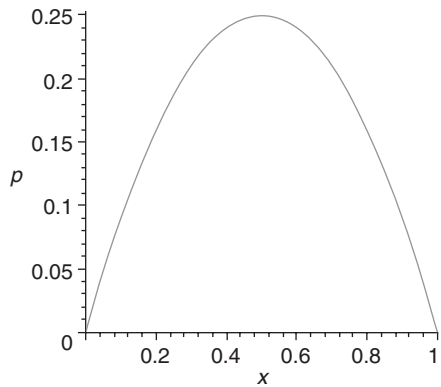

Figure 23.1 Network effect

This also means all the agents in interval $[0, \hat{x}]$ are in the exchange since all agents $y < \hat{x}$ have higher surplus. Noting that $n = \hat{x}$,[15] we have,

$$\hat{x}(1 - \hat{x}) = p.$$

This is the relationship between price and those that decide to be members, i.e., demand function of membership. However the relationship between demand (to be member) and price is not monotonic (Figure 23.1). Higher price can increase demand for some region. Furthermore, at any price, p, there are two levels of membership that are equilibria, one with low membership, $x_L(p)$ and the other high, $x_H(p)$.

It is possible for an exchange to be in equilibrium with very few members. However this is not a stable equilibrium. Any deviation of membership above $x_L(p)$ will move the market to the other equilibrium, $x_H(p)$. Since non-members have no surplus, it is better to be in equilibrium with larger membership.

Model of an exchange

The interesting question with exchanges is how they can be successfully formed. To answer this question we differentiate between providers of information or technology and the users. Only the number of providers matter for a user while only the number of users matter for a provider.

[15] Since all consumers with index $x \in [0, \hat{x}]$ join the exchange, $\hat{x}$ is also the proportion of consumers that join the exchange. If there are total of N consumers, then number of consumers that join the exchange is $n = N\hat{x}$. Rather than using this number in which case N cancels out, we use $\hat{x}$.

Except for the indirect effect of making the exchange attractive to the users, there is no gain to provider from having more providers. It would just increase competition.

Suppose both providers and users are separately distributed over interval [0,1]. The surplus of a provider (x_p) and a user (x_s) are given below. The variables n_P and n_U are the number of exchange members and cost (price) of participating are denoted by c_P and c_U.

$$U(x_P) = \begin{cases} n_U(1 - x_P) - c_P & \text{if member of exchange} \\ 0 & \text{otherwise} \end{cases}$$

$$U(x_U) = \begin{cases} n_P(1 - x_U) - c_U & \text{if member of exchange} \\ 0 & \text{otherwise} \end{cases}$$

Again, as in the case of simple network example, if the marginal agent is x_P, then $n_P = x_P$. From the indifference conditions we obtain the following two demands for memberships, one for users and the other for providers,

$$x_U(1 - x_P) = c_P, \qquad x_P(1 - x_U) = c_U.$$

We can rewrite the first equation as,

$$x_P = 1 - \frac{c_P}{x_U}.$$

This is a provider's demand function for membership: how many providers join the exchange given cost is c_P, and there are x_U users in the exchange. There will be more providers joining when cost is low and there are more users.

Equilibrium memberships, $x_P(c_P, c_U)$ and $x_U(c_P, c_U)$, satisfy the two demand functions at once. Curves D_P and D_U in Figure 23.2 are the graphs of the two functions. There are two intersections, meaning there are two levels of equilibrium membership: one when membership from both sides is high and one when membership is low. Because of the network effect, exchange can be in equilibrium at a very small scale.

If the costs are too high, there may be no intersection between the two curves, such as D_P and D'_U, i.e., no one will join the exchange. In a case like this, one can subsidize the users to make them join. This will also induce providers to join.

It is not necessary to lower the cost (price) for both sides. In the graph D'_U is user demand when $c_U = 0.3$. One only needs to lower c_U from 0.3 to 0.1 (curve D_U) in order to have an equilibrium. It is also possible to reduce providers' cost and shift D_P instead. A typical example of this

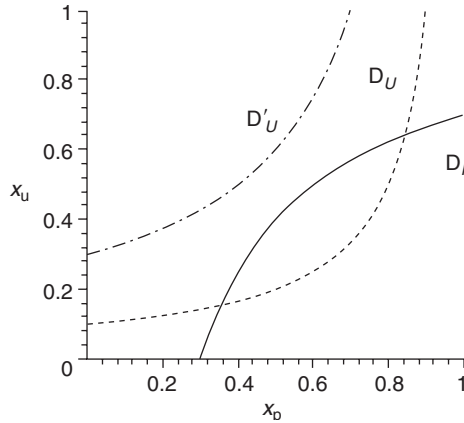

Figure 23.2 Exchange membership demand

is how community newspapers are financed. Some allow free classified advertisement so people will buy the newspaper while some charge for advertisement and distribute the paper for free.

Formation and stability

Because of the network effect, some form of coordination is necessary to form an exchange. It is necessary to get a critical mass, at least as large as $x_L(p)$. If price is lowered slightly to $p' < p$, the exchange will converge to a higher equilibrium, $x_H(p')$. This demonstrates the importance of coordinated subsidy to guarantee an equilibrium. The role of financial resource at early stage of formation may be essential for a successful launch of an exchange. It is not surprising that SNPs had financial backing from the Welcome Trust and GBIF had NSF support.

This equilibrium is stable, meaning the economy will not move away even if there is a small perturbation of prices. In this sense, once attained, institutions with network effects are very stable.

We observed with the simple model that in order to accumulate critical mass, one does not have to lower price (or cost) to everyone. It is sufficient to make it attractive to one side, providers or users. Call to join can concentrate on one side of the exchange. If institutions such as governments and international organizations are to subsidize formation, it may be more cost effective to concentrate on one side. Of course, information about the exchange's existence must be disseminated to both sides.

23.3 Collective rights organizations

Collective rights organizations (CROs) provide a bundle of goods, usually IP rights and prices are set as a bundle. We focus on copyright collection societies (CCS) and patent pools. We may also include open source CH as special case of CRO. Open source is "priced" so that the price is not a payment to the organization prior to use but is the forgone future earnings. This can also be interpreted as an extreme example of "low payment"[16] required for blanket licenses to be pro-competitive.

CCS and patent pools differ in the access patterns of the users. Each CCS licensee (IP user) accesses a different combination of goods from the bundle. Open source is similar to CCS in this regard. For instance, in case of American Society of Composers, Authors, and Publishers (ASCAP), each radio station has a different play list made up of ASCAP music catalogue. On the other hand, every patent pool licensee uses the same combination of patents. For example, if a patent pool is for implementing a standard, a particular combination of patents must be used to implement the standard. That is, all MPEG LA licensees basically use same bundle of patents.[17]

When a bundle of goods such as set of IPs must be used together, i.e., goods are complements, there is economic benefit other than reduction of transaction costs through elimination of double-marginalization, originally pointed out by Cournot.[18] For this reason patent pools offer a completely different advantage from CCS. Even if there is no benefit from elimination of double-marginalization, the fact that licensees choose subset of IPs means the marginal constraint does not bind[19] and a pool is welfare enhancing. On the other hand, there is no similar economic efficiency justification for CCS pricing the whole bundle of IPs as a "blanket license".

Patent pools

Notable patent pools were already established in the nineteenth century, such as the sewing machine pool formed in 1856. Today, the most prominent patent pools are formed to implement technological standards.

[16] van Zimmeren, see Chapter 5 of this volume.
[17] Horn, A.L., 'Case 1. The MPEG LA® Licensing Model. What problem does it solve in biopharma and genetics?, Chapter 2 of this volume.
[18] Also discussed by Verbeure, Chapter 1 of this volume.
[19] Lerner, J. and J. Tirole, 'Efficiency of Patent Pools', **94**(3), *American Economic Review*, 2004, 691–711.

The Motion Pictures Experts Group Licensing Administration (MPEG LA)[20] and Digital Versatile Disc (DVD) are such examples.[21]

Example

There are three firms, A, B and C, that each have a patent to implement a standard. The total number of licenses demanded when total royalty is r is,

$$Q = 1 - r. \tag{1}$$

If there is only one licensor that charges r_0, then $r = r_0$. If there are two licensors charging r_1 and r_2 respectively, then $r = r_1 + r_2$.

There are three possible licensor configurations:

- Patent pool – all three firms form a single pool, there is only one licensor.
- Independent licensing – all three firms license independently, three licensors.
- Firm C is an outsider – firms A and B form a pool but firm C is independent, two licensors.

Each licensor sets its royalty r_i to maximize own revenue, $Qr_i = (1 - r) \times r_i$. If there is only one licensor, $r = r_i$, otherwise $r > r_i$. Revenue maximizing royalty and revenue according to number of licensors is shown in table 23.1.

Note that total royalty increases with number of licensors. This is due to double marginalization. When choosing royalty rates separately, each licensor does not take into account the decline in profit of other firms from reduction in license demand when it raises its own royalty. When they choose a royalty rate together as a pool, loss of profit for all members from raising royalty is taken into account. This phenomenon occurs because the patents must be used together (complements). This observation is the principle behind competition authorities' positive views of standard implementation patent pools. A patent pool of all firms reduces number of licensors to one, achieving lowest possible total royalty, which is 30 in the example. Total royalty is 45 if the three firms license independently.

Another important observation is that because of low total royalty, firms are better off organizing into a single pool. Pool revenue is 900

[20] Horn, see Chapter 2 of this volume.

[21] Aoki, R. and S.Nagaoka, 'Coalition Formation for a Consortium Standard through a Standard Body and a Patent Pool: Theory and Evidence from MPEG2, DVD and 3G'. Institute of Innovation Research Working Paper 2005, WP\#05–01, Institute of Innovation Research, Hitotsubashi University.

Table 23.1 *Royalties and revenues with different number of licensors*

Regime	Patent pool	Firm C outsider	Independent licensing
No. of licensors	1	2	3
Each licensor royalty	30	20	15
Total royalty	30	40	45
Total licenses demanded	60	20	15
Each licensor revenue	900	400	225

which is greater than the total of all three licensees were they to license independently which will be 675 in the example.

Formation and stability

Standard implementation patent pools consist of complementary patents, that is, patents that must be used together. In the example, this is reflected in equation (1): for a given level of total royalty, r, demand for all patents are the same. There is no trade-off between patents when royalty rates differ (which would be case if patents were substitutes). For such a bundle of patents, price of a bundle will be cheaper than the total price if patents were priced independently, as seen in the example. This is something that patent owners are keen to take advantage of which makes forming a pool of complementary patents attractive. In addition when the patents are for implementing a new standard, reduction of total royalty rate will help promote adoption of the new standard.

However many pools suffer from instability, that is, some members leave. This occurs because reduction of licensors (by bundling) means an independent licensor can charge more. Unless appropriate compensation is given to the patentee by the pool to make it attractive enough to stay in the pool, a member may leave and license independently.

In the example, focus on firm C's profit in the three different regimes. If all three firms are independent, firm C's profit is 225. If firms A and B form a pool so that there are only two licensors, then firm C's profit is 400. This is more than one third of 900 – what it would get if it joined the pool and revenue was divided equally. This explains why some firms leave the pool or refuse to join when others have formed into one licensing organization. Firm C refusing to join is very unfortunate for the other two firms which only get 200 each.

In this case, firms A and B should guarantee a bit more than 400, say 410, to induce firm C to join the pool. Even after giving firm C's 410, firm A and B can split 900–410 = 490, which is more than 200 each!

The incentive to leave and free rider on the patent pool which leads to *ex post* instability also contributes to *ex ante* instability and impedes formation of a pool.

Instability of patent pools is well documented. The DVD standard established by the DVD Consortium made up of ten patent owner firms in 1995. They agreed that a patent pool should be formed to maintain the cost of licensing low in order to promote the new standard. In 1996, Thompson left the consortium and started to license independently. The nine firms continued efforts to license but Phillips, SONY and Pioneer expressed dissatisfaction with how the revenue of the pool would be distributed. In 1997 the three firms left to license their patents together but separate from the Consortium. The two groups started licensing separately the following year. As result, it is necessary to have three separate licenses in order to implement the DVD technology. However in many cases, by adjusting the payment it is possible to induce firms to join.[22] Distribution of patent pool revenue (licensing fees) must be designed to prevent members from leaving and licensing independently. This means distribution according to number of patent ownership may be inappropriate.

It is also known that heterogeneity contributes to instability.[23] That is, a non-manufacturing firm such as Rambus has a very different incentive from that of Toshiba whose profit is primarily from manufacturing. Distribution of pool revenue should also take this heterogeneity into account.

Copyright collection societies

There are many successful examples of CCS, including ASCAP (US), and BELGRAMEX (Belgium), GVL (Germany), Associatione Nazionale dei Fonografica Italiani (Italy) and Phonographic Performance Limited (UK). There are also many copyright collectives that collect royalties from photocopy of books and articles, such as Copyright Clearance Center (US) and Copyright Licensing Agency (UK), and many others in Europe.[24]

A CCS issues "blanket licenses" to licensees that charges a fixed fee, independent of which music is played or which photograph is used or

[22] Aoki,R. and S.Nagaoka, 'The Consortium Standard and Patent Pools', **55**(4), *The Economic Review*, 2004, 345–56

[23] Aoki and Nagaoka, 'The Consortium Standard'.

[24] Corbet, J., 'Case 7. The collective management of copyright and neighbouring rights. An example of a royalty collection clearinghouse', see Chapter 10 of this volume.

intensity of use. The fixed fee is usually a proportion of licensee's revenue which is set to reflect licensee's value of music or photographs. For instance, music would be more valuable to a radio station than a restaurant whose main business is serving food. Thus the rates for radio stations are higher than for restaurants. This pricing policy is rational because it is very difficult for CCS to know which particular music or photograph is most valuable to the licensee. Under such circumstance, it is better not to price the individual IPs separately for it may distort the choice. Blanket license is designed so that each licensee will choose whatever combination of IPs will maximize its profit. CCS will take a fixed proportion that maximized profit. CCS charges the same price (actually zero) for each IP so it will not distort licensee's profit maximizing choice.

CCS distributes license revenue to members according to how much the member's music or photograph was used. Intensity of use is obtained by combination of reporting by major licensees such as major television and monitoring of other licensees.[25]

Simple model

The following model is due to Bensen, Kirby and Salop.[26] When the size of intellectual property (IP) rights is N, the value to society of the catalogue is $V(N)$. We assume $V(N)$ is increasing concave function of N. Each licensee would be paying their individual value of the catalogue and the sum of all the fees should be equal to $V(N)$. Thus, this is CCS's licensing revenue. The CCS's administration cost is $C(N) = F + cN$, where F is the fixed cost of administration and c is the cost per IP. Typically c would be the monitoring cost. The surplus is $\pi(N) = V(N) - cN - F$.

For simplicity we assume one member has one IP right and CCS surplus is divided equally among its N members. Then in order to maximize per member profit, membership size should be chosen to maximize

$$\frac{\pi(N)}{N} = \frac{V(N) - cN - F}{N}$$

The per member maximizing size, N^m satisfies,

$$\frac{d}{dN}\frac{\pi(N^m)}{N^m} = 0 \quad \Leftrightarrow \quad V'(N^m) - c = \frac{V(N^m) - cN^m - F}{N^m} \tag{2}$$

[25] Corbet, see Chapter 10 of this volume.

[26] Bensen, Stanley M., Sheila N. Kirby and Steven C. Salop, 'An Economic Analysis of Copyright Collectives', **78** *Virginia Law Review*, 1992. 383–411.

The membership size N^m to maximize per member surplus is set so that marginal surplus equals surplus per member.

$$\pi'(N) = 0 \quad \Leftrightarrow \quad V'(N^*) = c.$$

The socially optimal membership size is to maximize total surplus, $\pi(N)$.

The socially optimal membership size, N^*, is set to equate marginal surplus to marginal cost. Comparing equations (1) and (2), we observe that membership is kept too small if CCS tries to maximize surplus per member, $N^m < N^*$.

Formation and stability

One advantage of CCSs is the reduction of transaction cost for enforcing property rights. CCS saves monitoring cost by monitoring all music or photograph use on behalf of the members, making individual monitoring by each IP owner unnecessary. However, the economies of scale effect of monitoring cost is not the only reason why CCSs do not suffer from instability. First of all, there is no externality that non-members can free ride on as in the case of patent pools. Instead the blanket license practiced by CCS contributes to stability. Because licensees pay a fixed fee, there is no marginal cost of using more from the CCS IP catalogue. On the other hand, licensee must pay a separate royalty to use a non-member's IP, making it costly not to be a CCS member. Thus not only is there incentive to stay, there is an incentive to join CCS. It is not surprising that CCSs have been stable over time and memberships have grown.

23.4 Incomplete contract structures

Arrow in his seminal work[27] argued that risk was *not* the essence of innovation since this can be contracted away in a perfect capital market. The reality is that the capital market is not perfect. Both open source and CCL address the issue of uncertainty in innovation.

An outcome of innovation is uncertain and not always successful. Which idea (which may be protected by IP)[28] or molecule is most likely to succeed is often unknown a priori. Which researcher will be most

[27] Arrow, K. 'Economic Welfare and the Allocation of Resources for Inventions' in Nelson, R.(ed), *The Rate and Directions of Inventive Activity*, Princeton, Princeton University Press, 1962, 635 p.

[28] An idea may be the subject of an IP right. (Access and) use of an idea differs according to the fact whether there is IP on the idea or not. The author is grateful to Geertrui Van Overwalle for pointing to this very important distinction.

effective may also be unknown. In addition to these uncertainties, there are informational problems. That is, the IP owner may be more informed than a researcher about quality and likely success of IP or a molecule. Similarly, a researcher may be better informed about his or her ability than the IP owner. Furthermore, the IP owner may only not be able to observe how much talent a researcher has (hidden information) but also may not be able to observe how hard she is working (hidden action).

While some uncertainties are possible to contract away, it is difficult to write contracts when there are informational asymmetries (hidden information).[29] It is also not easy to induce optimal effort with contracts when effort is not observable (hidden action) and it is usually not possible to have an efficient outcome. That is, the IP owner will have difficulty having others conduct or invest in innovation to improve or develop its IP.

Open source and CCL are functioning as a form of incomplete contracts when there are these uncertainty and informational problems. The problem is made worse by the dynamic nature of innovation. In case of software improvements, improvements are cumulative. This means rents from innovation need to be distributed between generations and these distribution rules in turn affect incentive to innovate. As Hope[30] argues, it is possible to obtain private returns from open source material through complementary goods, return from market positioning etc., meaning there are rents appropriated by each generation of cumulative innovation with open source.

An important function of ICS is to provide an environment to innovate and to realize value of IP. In this sense, The Alliance Centers of the Consultative Group on International Agricultural Research, the CGIAR,[31] has aspects that should be included in this group. It maintains germplasm from around the world that can be distributed to crop breeders upon request, a function similar to the Molecular Libraries Initiative – CCL regime. It provides opportunity to realize value.

23.5 Concluding remarks

We have categorized various clearing mechanisms and contractually constructed liability according to economic functions. **Exchanges**

[29] Bolton, P. and M. Dewatripont, *Contract Theory*, Boston, MIT Press, 2005, 724.
[30] Hope, see Chapter 12 of this volume.
[31] Henson-Apollonio, V., 'Case 10. The International Treaty on Plant Genetic Resources for Food and Agriculture: the Standard Material Transfer Agreement as implementation of a limited compensatory liability regime', Chapter 18 of this volume.

reduce transaction costs (search and contracting costs). Any resulting contracts are bilateral and IP owners retain ownership. **Collective rights organizations** include well-established clearing mechanisms: copyright collection societies and patent pools. Their main function is to provide access to a large catalogue of IPs and collect royalties. IPs are complements in case of patent pools while existing copyright collection societies offer blanket licenses because relationships among IPs are not clear a priori.

The last group of clearing mechanisms, the **incomplete contract structures** exist to facilitate access to IP and innovation using them. By definition structures are for IP used for further research, either because they are very basic as in molecules (contractually constructed liability) or because knowledge is part of an ongoing cumulative innovation process (open source). Open source is already in existence although not very well understood. Contractually constructed liability is a new concept yet to be put into practice. Both systems are promising and surely will attract future research interest.

Last but not least, all clearing mechanisms are based on the network effect. There is danger of an equilibrium with very few participants. Coordination, by public or private or by national or international entities, is essential for successful formation. The network effect by itself is very stable, meaning it becomes self-enforcing once an organization has been established.

REFERENCES

Aoki, R. and S. Nagaoka, 'The Consortium Standard and Patent Pools', **55**(4) *The Economic Review*, 2004, 345–56

'Coalition Formation for a Consortium Standard through a Standard Body and a Patent Pool: Theory and Evidence from MPEG2, DVD and 3G'. Institute of Innovation Research Working Paper, 2005, WP\#05–01, Institute of Innovation Research, Hitotsubashi University.

Aoki, R. and A. Schiff, 'Promoting Access to Intellectual Property: Patent Pools, Copyright Collectives and Clearinghouses', **38** *R&D Management*, 2008, 118–204.

Arrow, K. 'Economic Welfare and the Allocation of Resources for Inventions' in Nelson, R.(ed), *The Rate and Directions of Inventive Activity*, Princeton, Princeton University Press, 1962, 635.

Bennett, B. and Boettiger, S., 'Case 5. The Public Intellectual Property Resource for Agriculture. A standard license public sector clearinghouse for agricultural IP', Chapter 8 of this volume

Bensen, S.M., Sheila N. Kirby and S.C. Salop, 'An Economic Analysis of Copyright Collectives', **78**(3) *Virginia Law Review*, 1992, 83–411.

Bolton, P. and M. Dewatripont, *Contract Theory*, Boston, MIT Press, 2005, 724.
Corbet, J., 'Case 7. The collective management of copyright and neighbouring rights. An example of a royalty collection clearinghouse', Chapter 10 of this volume
Edwards, J.L., 'Case 3. The Global Biodiversity Information Facility. An example of an information clearinghouse', Chapter 6 of this volume
Henson-Apollonio, V., 'Case 10. The International Treaty on Plant Genetic Resources for Food and Agriculture: the Standard Material Transfer Agreement as implementation of a limited compensatory liability regime', Chapter 18 of this volume
Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume
Horn, A.L., 'Case 1. The MPEG LA® Licensing Model. What problem does it solve in biopharma and genetics?', Chapter 2 of this volume
Lerner, J. and J. Tirole, 'Efficiency of Patent Pools', **94**(3), *American Economic Review*, 2004, 691–711.
Merges, R., 'Contracting Into Liability Rules: Intellectual Property Rights and Collective Rights Organizations', **84** *California Law .Review*, 1996, 1293–393.
Nguyen, T., 'Case 6. The Science Commons Material Transfer Agreement Project. A standard license clearinghouse?', Chapter 9 of this volume
Rai, A.K., Reichman, J.H., Uhlir, P.F. and Crossman, C., 'Pathways across the valley of death: novel intellectual property strategies for accelerated drug discovery', Chapter 17 of this volume
Spence, M., 'Comment on the conceptual framework for a clearinghouse mechanism', Chapter 11 of this volume
Van Overwalle, G., van Zimmeren, E., Verbeure, B. and Matthijs, G., 'Models for Facilitating Access to Patents on Genetic Inventions,' **7** *Nature Review Genetics*, 2006, 143–8.
van Zimmeren, E., Verbeure, B., Matthijs, G. and Van Overwalle, G., 'A Clearinghouse for Diagnostic Testing: the Solution to Ensure Access to and Use of Patented Genetic Inventions?', *Bulletin of the World Health Organization*, 2006, 352–9
van Zimmeren, E., 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume
Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume

24 The role of law, institutions and governance in facilitating access to the scientific research commons

A philosopher's perspective

Tom Dedeurwaerdere[*]

24.1 Introduction

Innovation in the life sciences depends on how much information is produced as well as how widely and easily it is shared. As shown by the contributions in this volume, policies governing the science commons – or alternative, more restricted information spaces – determine how widely and quickly information and research tools are distributed. The purpose of this chapter is to highlight why the science commons matters, and to analyse its organization. The concern for the governance of the science commons has caught the attention of a wide range of scholars in the mid 1990s, especially in legal scholarship.[1] The interest of these scholars is in the cooperative use of scientific data, information, materials and research tools that actually are not in the public domain, and whose licensed use is legally protected by an intellectual property (IP) regime.[2] In its more general meaning however, the "commons"

* The author wishes to express his gratitude to Geertrui Van Overwalle for her constructive comments on an earlier draft of this chapter and to the participants of the June 2006 workshop on "Gene Patents and Clearing Models" in Leuven, Belgium, and the October 2007 meeting of the World Federation of Culture Collections in Goslar, Germany.

[1] Benkler, Y., 'Overcoming Agoraphobia: Building the Commons of the Digitally Networked Environment', **11**(2) *Harvard Journal of Law and Technolgy*, 287–400; Reese, R. A., 'Reflections on the Intellectual Commons: Two perspectives on Copyright Duration and Reversion', **47**(4) *Stanford Law Review*, 1995, 707–47; Lessig, L., *Code and Commons*, Keynote Address at the Conference on Media Convergence, Fordham University Law School (9 February, 1999). Online at www.lessig.org/content/articles/works/Fordham.pdf (accessed February 2008).

[2] Reichman, J. and Uhlir, P.F., 'A contractually reconstructed research commons for scientific data in a highly protectionist intellectual property environment', **66** *Law and Contemporary Problems*, 315–440, 2003; David, P.A. and Spence, M., 'Towards institutional infrastructures for e-science: the scope of the challenge', Oxford Internet Institute, *Research Report* No. 2, September 2003, 98

designates any resource shared by a group of people that is subject to problems of underprovision or overconsumption of the shared resource, independently of its legal nature.[3] From this general perspective, the scientific research commons, which we will call hereafter shortly the science commons, designates the scientific data, information and materials which are shared under conditions of non-exclusive use (though perhaps limited in its extent or use, depending on the collective agreements) within limited or global research communities.[4]

The main hypothesis of this chapter is that both the formal legal models and the institutional and governance characteristics of the various research and users communities – think of the Bermuda principles in the human genome case[5] or the National Institutes of Health (NIH) guidelines on the licensing of genomic inventions[6] – matter in organizing the translation of research results into usable knowledge, products and procedures.

Our analysis will proceed in two steps. First we will focus on one of the main lessons of this book from the point of view of institutional analysis: the involvement of the scientific and the user communities in innovative contractual agreements has proven to be successful in alleviating some of the collective-action problems that are raised in genomics research. Second, we will show the necessity of going beyond a formal legal analysis of the agreements and models. Indeed, the legal rules interact with the formal and informal institutions which regulate

[3] Hess Ch. and Ostrom E., *Understanding Knowledge as a commons. From Theory to Practice*, Cambridge (MA), MIT Press, 2007, 3–10.

[4] There is some wobble in the term "science commons". The term the "commons" has been used extensively in legal scholarship to designate goods in open access (cf. references in footnote 1). In the same time, "Science Commons" is a specific organization that has spun out of the Creative Commons movement. Science Commons has moved from concept to action in the year 2005, with an office and executive director to carry out its mission of "making it easier for scientists, universities, and industries to use literature, data, and other scientific intellectual property and to share their knowledge with others. Science Commons works within current copyright and patent law to promote legal and technical mechanisms that remove barriers to sharing". While we endorse their mission, they may not endorse our analysis, and we have no direct connection to the organization, and do not speak for it. As explained above, we adopt the more general definition that has been adopted at major international conferences on these issues (the "Conference on the Public Domain", organized at Duke University in November 2001 and the "Workshop on Scholarly Communication as a Commons", organized at Indiana University in Bloomington, spring 2004) the results of which have been published in a collective volume at MIT Press (Hess and Ostrom, *Understanding Knowledge as a commons*).

[5] See www.ornl.gov/sci/techresources/Human_Genome/research/bermuda.shtml for an overview of the Bermuda principles (last visited 15 October 2007).

[6] National Institutes of Health, *Best Practices for the Licensing of Genomic Inventions: Final Notice*, Federal Register, Vol. **70** (68), Monday, April 11, 2005.

individual behaviour in communities and organizations. This interaction can be mutually reinforcing, neutral or antagonistic. Based on the insights of the literature on institutional analysis, we will analyze the role of formal and informal institutions in the organization of research in genomics, and indicate how the interaction between different types of rules can be addressed.

24.2 The contractually reconstructed public domain in diagnostic genetic testing

The problem of access to genes as research tools for diagnostic genetic testing suggests that the theory of the science commons, which focuses on the public good properties of resources that are essential for scientific research, may also have some use in the case of applied research, here in the case of genes as research tools which are used in a broad set of more specific applications. The discussion of the different legal models for reconstructing the commons in this volume shows that a variety of social goals can benefit from a robust scientific commons in genomics: these include advancing science, improving public health, improving food security, contributing to understanding and conserving biological diversity, and contributing to industrial R&D and commercialization.

When Robert Merton wrote about the sociology of science, the central task at hand was explaining how a set of social norms and practices yielded reliable knowledge.[7] Our concern here is about a related but distinct topic – how reliable knowledge can be turned to social benefit and used in practical applications. The point of connection is science that falls squarely into what has been called "Pasteur's Quadrant", where it both contributes to insights about how the world works and promises to make the world a better place through practical application.[8] This field of research in between pure basic research and pure applied research is especially important in the life sciences, because of the complexity of biological systems which are characterized by non-linear processes that are path dependent, can show abrupt change and have unpredictable dynamics. These features call for knowledge which is context specific and which can enhance human adaptability and cope with uncertainty when biological processes unfold in different specific environments, such as genes being expressed differently in different metabolisms or

[7] Merton, R. K., *The Sociology of Science*. Chicago, University of Chicago Press, 1973.
[8] Stokes, D.E., *Pasteur's Quadrant: Basic Science and Technological Innovation*. Washington DC, Brookings Institution Press, 1997.

organisms co-evolving with complex human managed ecosystems.[9] Producing knowledge in this intermediary field of research implies looking beyond the norms of the scientific communities.[10] Indeed, it necessitates institutions for organizing collective action which cross the borders between different scientific and user communities.

Collective-action institutions aim to alleviate collective-action problems. Collective-action problems occur whenever individuals in interdependent situations face choices in which the maximization of short-term self-interest yields outcomes which leave all participants worse off than feasible alternatives. These problems are often presented in the form of so-called "social dilemmas", where the optimal outcome is contrasted with the outcome resulting from the pursuit of individual self-interest. One subcategory of social dilemmas is a public-good dilemma. In a public-good dilemma, all those who benefit from the provision of a public good – such as open access to genetic-sequence information, access to crop-genetic resources, or better biosecurity regulation – find it costly to contribute and would prefer others to pay for the good instead. If everyone follows the equilibrium strategy, then the good is not provided or is underprovided. Yet, everyone would be better off if everyone contributed. In those situations of social dilemmas, collective-action institutions introduce a certain level of collective constraint, whether through formal or informal rules, with the aim to produce better outcomes. Because the creation of collective-action institutions is costly, however, it is important to assess the relative costs and benefits of the different types of formal and informal institutional arrangements

[9] Two important examples of these complex dynamics within the field of the life sciences are the management of antibiotics resistance in health care and the management of pest resistance in agriculture landscapes. In the case of antibiotics, it has been shown that increased use of antibiotics has an effect on increasing resistance of the viruses. In the case of agricultural innovation, pest resistance declines dramatically after a period of about 5 to 10 years (depending on the crops) due to adaptation of the ecosystem to the new breeds (Goeschl, T. and Swanson, T., 'On the economic limits of technological potential: will industry resolve the resistance problem?, in Swanson T. (ed.), *The Economics of Managing Biotechnologies*, Dordrecht: Kluwer Academic Publishing, 99–128).

[10] The key norms of the scientific communities as analyzed by Robert Merton are the norms of openness, community, mutual criticism, and fair allocation of credit (Merton, *The Sociology of Science*). The norms of the user communities (both public and private) can be supportive of these norms or antagonistic (such as in the case of privately funded research contracts that impose a certain time lag before publication). These problems have been analysed elsewhere (Rai, A. K., 'Regulating Scientific Research: Intellectual Property Rights and the Norms of Science', 77(1) *Northwestern University Law Review*, 1999, 77–152; Reichman and Uhlir, 'A Contractually Reconstructed Research Commons'). Here we do not focus on the sociological analysis of the exact content of these different norms and their changing dynamics, but on the governance questions of how to bridge different communities with different norms.

that can alleviate the collective action problems. In particular, the creation of a formal legal rule presents itself a new public good dilemma (a so-called "second-order dilemma"), because, even if all will benefit from the rule, not everybody has an incentive to contribute to its creation and maintenance.[11]

Social dilemmas are found in all aspects of life-sciences research. This can be illustrated through two major social dilemmas in the life sciences: the diffusion/innovation dilemma and the exploration/exploitation dilemma.[12] In the first dilemma, collective action is required to organize wide and early diffusion of research results, while recognizing the importance of private property rights for creating individual or organizational incentives for innovation. As discussed in this volume, this first dilemma is at the core of anticommons problems leading to patent thickets,[13] but diffusion problems are also present in cases where "holdouts"[14] maintain unreasonably restrictive licensing practices. In the second dilemma, collective action is required for exploring new lines of development and deepening general understanding, especially when the benefits for the organizations investing in this research are still uncertain. This problem is clearly at the core of the discussion on the liability regime by Rai et al. in this volume,[15] where the goal is to create incentives for investing in uncertain downstream product development.

The lesson to be learned from the models that are analysed in this volume is the following: granting non-exclusive use rights on intangible assets, in situations where IP is attached to these assets, allows to address some of the collective action problems related to diffusion of research results and the organization of exploratory research. A famous example in the field of life science research is the Cohen-Boyer license for the patent of Stanford University on DNA replication technology,

[11] Public goods can be of different natures: they can be materials or information, but they can also be institutions and regulations. Indeed, the benefit from well-functioning institutions and regulations are non-exclusive and non-rival. So there is a major incentive to free-ride on others' effort to create institutions, exposing institutional innovation to classic public-good problems of undersupply.

[12] For a more extensive discussion of these dilemmas, see Cook-Deegan, R. and Dedeurwaerdere, T., 'The Science Commons in Life Science Research: Structure, Function and Value of Access to Genetic Diversity', **188** *The International Social Science Journal*, 2006, 309–2.

[13] Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume.

[14] Goldstein, J.A., 'Critical analysis of patent pools', Chapter 4 of this volume.

[15] Rai, A.K., Reichman, J.H., Uhlir, P.F. and Crossman, C., 'Pathways across the valley of death: novel intellectual property strategies for accelerated drug discovery', Chapter 17 of this volume.

creating facilitated access to this technology for academic and non-commercial research.[16] This strategy has been described in the literature as the creation of a reconstructed commons.[17] In general, the reconstructed commons is established by a set of institutional agreements amongst the right holders and between the right holders and the users, in order to create a domain of non-exclusive use for intangible goods with IP rights attached, or on which IP can be claimed[18] (see Figure 24.1). These agreements can define standard contractual templates, establish general guidelines endorsed by a hierarchical authority for the use of the rights by the right holders or define a set of informal rules and practices. The first type, the contractual reconstructed commons, is established by a group of right holders who decide to use standard contracts to construct conditions of shared use that emulate the key features of the public domain.[19] However, the use of contract is only one of the strategies that are used in the institutional design of the reconstructed commons. As we will argue below, the contractual rules interact with other formal rules (hierarchies, organizations etc.) and informal rules (norms, ethical codes etc.), which play a role in prescribing, monitoring and enforcing non-exclusive use. For instance, as

[16] Rai A. K. and Eisenberg R. S., 'Bayh-Dole Reform and the Progress of Biomedicine', **66** *Law and contemporary problems*, 2003, 289–314.

[17] For the original concept of the reconstructed commons, see David, P.A. and Spence, M., 'Towards Institutional Infrastructures for E-Science…' and Reichman, J. and Uhlir, P.F., 'A Contractually Reconstructed Research Commons…'. For a discussion of the applications of this concept in genomics see Cook-Deegan, R. and Dedeurwaerdere, T., 'The Science Commons in Life Science Research'.

[18] Clear examples of a reconstructed commons discussed in this volume are the open-access licensing models for software (Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume) and the proposed liability rules for small molecule collections. As suggested in Figure 24.1, patent pools are more of a hybrid nature. They share some of the characteristics of the reconstructed commons (non-exclusive use within the pool) and some characteristics of the exclusive use domain (restricted to a limited group).

[19] In particular, the access to these shared resources by cooperating parties is rendered open (though perhaps limited in its extent or use) under minimal transactions cost conditions. For tangible goods, this is reflected for example in the concept of a "handling fee", which parties sometimes have to pay to access the resources, but which only includes the incremental and supplementary cost that the provider incurs by the access and distribution transaction, not the real cost the provider has for producing and maintaining the biological resource, which often is 10 to 20 times higher (for example, in the case of microbials, Baker, D., 'Microbial Diversity and Pharmaceutical Industry Culture Collections', in M. M. Watanabe, K. Suzuki and T. Seki (eds.), *Innovative Roles of Biological Resources Centres*, Tsukuba: World Federation for Culture Collections, 2004, 435–8). For intangibles, this can include for example a participation in the administrative costs incurred for making a website publicly available. However, there is no uniform use of handling or administrative fees in case of public goods and the issue when it is appropriate to ask a fee is an issue of debate.

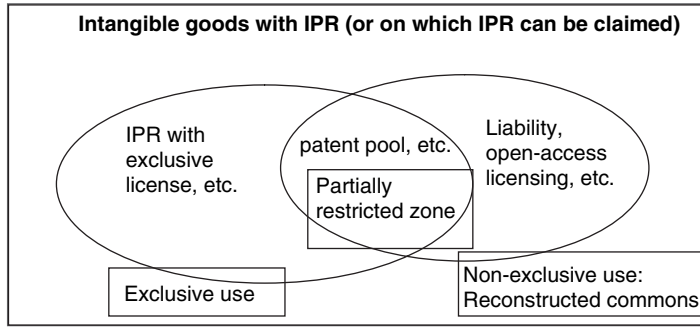

Figure 24.1 Domain of the reconstructed commons: domain of non-exclusive use for intangible goods with intellectual property rights. Patent pools share some of the characteristics of the reconstructed commons (non-exclusive use within the pool) and the exclusive use domain (restricted to a limited group).[20]

has been developed in the second part of this volume, even in markets well served by the profit motive, a formal organization such as an information clearinghouse can in some circumstances improve efficiency of the reconstructed commons, for example, when many disparate firms can draw on a common clearinghouse of technological and biological data, rather than having to construct the same information firm by firm (resulting in substantial duplication costs).[21]

24.3 The role of collective-action institutions in facilitating access

The building of the science commons is a social process where both formal and informal institutions constrain the options available to the individual scientist and health practitioner. In the context of facilitating

[20] The author wishes to thank Geertrui Van Overwalle who suggested this representation. This figure differentiates between different intangible goods, based on the effective use rights that are granted by the rights holders, and not so much on the difference between the legal entitlements.

[21] A clearinghouse is essentially an information sharing device. From an institutional analysis point of view, it contributes to the reduction of transaction costs and facilitates the enforcement of the formal and informal rules are adopted. As such it is not linked to any one specific ownership regime: it can be part of the reconstructed commons (as in the case of the SNP consortium), the exclusive ownership regime (as in the case of patent clearinghouses), or be a hybrid of both (as in the model of the Public Intellectual Property Resource for Agriculture (PIPRA) clearinghouse). For a discussion of these examples, see van Zimmeren, E., 'Clearinghouse Mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume.

access to genetic diagnostic testing, understanding this process is important for different reasons. First, it is important to know if the formal legal rules of patent legislation *per se* or restrictive ownership rights *per se* are the main factors impeding access, or if we are just speaking of bad patents, for instance due to organizational problems in the implementation. Second, it might be that other formal non-legal constraints within organizations, such as the pressure to publish, competition for research grants and secrecy of research results in public–private partnerships, play a more important role in the explanation of the adoption of exclusive or non-exclusive use strategies. Third, in the cases where patents could become a problem for access to research tools, it remains to be seen if the solution is to rely on formal standard contractual agreements, such as the recourse to dual-licensing policies in standardized contracts, or formal rules in organizational hierarchies such as in the clearinghouse models. Moreover, in some cases it might also be interesting to consider the contribution of informal institutions, which are enforced through social norms such as reputation and social recognition, such as informal guidelines or ethical codes, which define common principles for the use of the formal rights in matters of general interest.

Analyzing the complex relationships between law and institutions is of course beyond the scope of this chapter. For that reason, I will limit myself here to some examples of cases where non-legal constraints in organizations and informal norms have played a complementary role to the use of contractual agreements in facilitating access to information and research tools in the life sciences. In doing this I will adopt the definition now generally used, both in economics and in political science, of institutions as the "rules of the game", which constrain the behaviour of the actors.[22] The interaction between law and institutions as rules of the game has been studied mainly by two bodies of research:[23] the first within "Law and Norms", initiated by the seminal work of Ellickson,[24] and the second within institutional economics, especially related to Elinor Ostrom's work on self-organized institutional arrangements in

[22] Ostrom E., *Understanding Institutional Diversity*, Princeton, Princeton University Press, 2005, 151; 166.

[23] Both the research tradition from institutional economics and law and norms theory draw mainly on an economic vocabulary, based on notions from game theory and transaction cost economics. Because our interest here lies in one of the key problems that is addressed in this literature, which is the alleviation of social dilemmas and the understanding of the effect of different types of rules on cooperative behaviour, we have also adopted here this vocabulary.

[24] Ellickson, R. C., *Order Without Law: How Neighbours Settle Disputes*, Cambridge (MA), Harvard University Press, 1991[a].

the governance of the commons[25] and Oliver Williamson's work on the role of organizational hierarchies as being complementary both to the market and the state.[26] Because of the different origin of these research traditions, the first from within legal theory and the second from within economics, the definition of the different types of institutions tends to be very different from one author to another. For the sake of clarity, we will adopt here a simple set of categories.[27] We distinguish between formal rules (legal rules, institutional policies in organizations and contracts), and informal rules (community norms, customs and intrinsic values). Formal rules are prescriptions that are imposed and enforced in a formal, organized manner, by some members of society, such as the state, the president of a university or parties in a contract.[28] Informal rules are prescriptions that are followed because of the existence of certain norms, without any formal agreement on the sanctions to be applied, such as moral preferences or social identity. Within formal rules, we make a distinction between institutions where the sanction for violating the rule is determined by national or transnational state actors (formal legal rules) and institutions where the sanctions are determined by other recognized authorities (formal institutional policies and contracts). This gives us a set of four basic categories for the discussion of different types of collective-action institutions:

1. Formal rules: prescriptions that are imposed and enforced in a formal, organized manner, by some members of society (the recognized authorities)
   a. Formal legal rules: the recognized authority = the state / the government / the federation / formal multilateral agreement

[25] Ostrom, E., *Governing the Commons. The Evolution of Institutions for Collective Action*, Cambridge, Cambridge University Press, 1990.

[26] Willamson, O., *The Mechanisms of Governance,* Oxford, Oxford University Press, 1996.

[27] Our discussion is based in particular on Aoki M., 'Endogenizing Institutions and Institutional Changes', **3**(1) *Journal of Institutional Economics*, 2007, 1–31. The advantage of Aoki's approach is to go beyond the tendency to build a hierarchy of different types of rules, and instead focus on the complementary or antagonistic interaction between different domains of formal or informal rule-like behavior. This approach is also adopted for example in Rai A., 'Regulating Scientific Research …'.

[28] The category of formal rules overlaps with the standard definition of the notion of a rule in institutional economics (Ostrom, *Understanding Institutional Diversity*, 150–151). In this context, Crawford and Ostrom develop a more detailed definition of the difference between formal rules, compared to informal rules (the latter being designated as norms by Crawford and Ostrom). Formal rules are defined by an institutional statement that assigns an explicit sanction to detected noncompliance with the rule and which must meet three qualifications: (1) a collective decision must have been made in a relevant collective-choice arena to determine the sanction; (2) the collective decision identifies and/or establishes a sanctioning authority; (3) and prescribes monitoring responsibilities (150–1).

b. Formal institutional policies in organizations: the recognized authority = authorized person or persons of a collective entity other than the state (which can be a private organization or a governmental bureaucracy)
c. Formal rules of contracts: the recognized authority = the contracting parties (in bilateral contracting) or an independent third party (contracting amongst a large number of (mutually unknown) players)

2. Informal rules: interaction with norms of communities and individuals.

In the "Law and Norms" literature, informal rules are often designated as social norms or informal norms,[29] while formal institutional policies are often designated as formal norms[30] or private rule making.[31] Hence, in what follows, we will use these different notions as synonyms.[32]

What is common to these different research traditions is the recognition of the complementarities between legal and non-legal sanctions. Indeed, as stressed for instance by Cooter,[33] the complexity of modern economies is so great that centralized law creation cannot effectively cope with the need to achieve normative regulation among communities of individuals who repeatedly face collective-action problems. From the point of view of institutional analysis, it is the combination of formal legal rules, formal institutional policies, contracts and informal rules that produces effective common-access regimes. In the remaining text, we will focus on some examples, where institutional policies and informal rules played an important complementary role in facilitating access to biological resources on which IP has been claimed or can be claimed.

A clear case where common norms and institutional policies play a role in creating a *de facto* open-access regime in genetic and biological resources are the common guidelines adopted in 2003 by the organizations that are member of the Consultative Group for International

[29] Posner, E. (ed.), *Social Norms, Nonlegal Sanctions, and the Law*, Edward Elgard, 2007.
[30] Rai, A., *Regulating Scientific Research*.
[31] Bernstein, L., 'Private Commercial Law in the Cotton Industry: Creating cooperation through rules, norms and institutions', **99** *Michigan Law Review*, 2001, 1724–1790.
[32] Similar notions to the one's developed here have also been developed in other literatures that analyze the role of different forms of non-legal regulation, such as in the literature on self-regulation or on soft *versus* hard law. For an overview of the latter in the context of the debate on patents in the life sciences, see for example Van Overwalle, G., *Study on the Patenting of Inventions Related to Human Stem Cell Research*, European Communities, Luxembourg, 2002, 218.
[33] Cooter, R. D., 'Structural adjudication and the New Law Merchant: A Model of Decentralized Law', **14** *International Review of Law and Economics*, 1994, 215–31.

Agricultural Research (CGIAR). This case is also relevant because these guidelines (and *a fortiori* earlier versions of them) were adopted before the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPRGFA) came into existence.[34] There is some overlap between these two examples, as the objectives of the Treaty are to create a facilitated access regime for plant genetic resources. However, the application of the Treaty is limited to the resources that are essential to preserving world food security, and which are listed in annex 1 to the Treaty.

Historically, the CGIAR has played a leading role in promoting open access to biological resources through the organization of a network of specialised *ex-situ* conservation facilities throughout the world. As the 2003 CGIAR policy guidelines state:

> The germplasm[35] designated by the Centers is held in trust for the world community in accordance with the agreements signed with the FAO … Based on the conviction that their research will continue to be supported by public funds, the Centers regard the results of their work as international public goods. Hence full disclosure of research results and products in the public domain is the preferred strategy for preventing misappropriation by others.[36]

The CGIAR IP policy clearly reflects this open-access strategy.[37] The implementation of these formal policies is facilitated by the existence of a set of common norms which prescribe the sharing of resources and information amongst the CGIAR centers. These commons norms depend on the existence of relations of reciprocity that enforce the normative behaviour of the researchers in the Centers and other public and private partners worldwide. For instance, a quantitative analysis of fifteen years of exchange of maize germplasm between the International

[34] Henson-Apollonio, V., 'Case 10. The International Treaty on Plant Genetic Resources for Food and Agriculture: the Standard Material Transfer Agreement as implementation of a limited compensatory liability regime', Chapter 18 of this volume.

[35] Technically "germplasm" refers to seeds, plants or plant parts that are useful in crop breeding, research or conservation because of their genetic attributes.

[36] CGIAR, *Booklet of CGIAR Centre Policy Instruments, Guidelines and Statements on Genetic Resources, Biotechnology and Intellectual Property Rights, Version II*, produced by the System-wide Genetic Resources Programme (SGRP) with the CGIAR Genetic Resources Policy Committee, Rome, July 2003, 37

[37] It states that "the Centres will not assert intellectual property control over derivatives except in those rare cases when this is needed to facilitate technology transfer or otherwise protect the interests of developing nations" and "In the event that a Centre secures financial returns as a result of the commercialisation by others of its protected property, appropriate means will be used to ensure that such funds are used for furthering the mandate of the Centre and the objectives of the CGIAR" (CGIAR, *Booklet of CGIAR Centre Policy Instruments*, 31–2).

Maize and Wheat Improvement Center (CIMMYT) in Mexico and fifteen other developing countries shows that the recipient countries received four times as many specimens as they contributed to the international CGIAR repository.[38] Hence, being part of the open access network for germplasm produces a network externality: researchers provide access to their own limited resources and information and in turn they gain access to resources and information from all other member organizations. Moreover, this reciprocity also plays a role in the relations between the *ex-situ* centers and their direct and indirect commercial partners. Indeed, it has been shown that an estimated 75% of all seeds sold by private companies in Latin America in 1996 contained CIMMYT-derived germplasm.[39]

The implementation of the International ITPRGFA in the CGIAR centers could bring less openness to the system. Indeed, the ITPRGFA specifies that IPR will not be asserted on the unmodified material as received from other parties in the system, but allows IPR to be asserted on the modified material, if applicable. This would extend the use of IPR in the CGIAR centers beyond the policy specified in the guidelines, which prescribed an open-access strategy also for the modified materials as the general rule.[40]

A second example illustrates the role of institutional policies and common norms in facilitating open access to genomics information. The International Nucleotide Sequence Database Collaboration (INSDC), more commonly known as "GenBank" (which is the name of the US access point), provides open on-line access to the major sequence information that is referred to in the published literature, both for patented and non-patented material.[41] The DNA sequence data in

[38] Fowler C., Smale M., and Gaiji S., 'Unequal exchange? Recent transfers of agricultural resources and their implications for developing countries', **19** *Development Policy Review*, 2001, 181–204.

[39] *Ibid.*, 194.

[40] The liability provisions of the treaty are part of the formal legal rules codified in international law. Because the CGIAR centres have officially joined the treaty, these provisions override the provisions of the policy guidelines, as far as they have the same subject matter (that means, in any case for annex 1 material that is held in CGIAR centres). This situation is different from the one described in Rai, Reichman, Uhlir and Crossman, where the liability rules are not part of codified or formal legal regime, but are part of the proposed institutional policy and contractual agreements within the multiple-firm partnership (the so-called framework agreement, Rai, Reichman, Uhlir and Crossman, 'Pathways Across the Valley of Death', 80).

[41] GenBank is publicly accessible through the DNA DataBase of Japan (www.ddbj.nig.ac.jp/Welcome.html), European Molecular Biology Laboratory Nucleotide Sequence Database (www.ebi.ac.uk/embl/index.html) and US National Centre for Biotechnology Information GenBank (www.ncbi.nlm.nih.gov) portals. These are three mirror sites, situated in Japan, the EU and the USA, respectively, that exchange and update new

the INSDC databases were collected primarily by a trio of teams in the United States, Europe and Japan, which shared data among themselves. Creating and coordinating these databases was a major struggle. In 1996, the Wellcome Trust sponsored a Bermuda meeting of the major sequencing centers throughout the world. A set of "Bermuda Principles" emerged from the meeting, mandating public disclosure of DNA sequence data. The Bermuda principles confer prior right of publication on the scientist who first deposits the information on the gene sequence in the INSDC databases or any alternative recognized international e-repository. The provision of gene sequences to this international open-access infrastructure is thus assured through a set of institutional rules directly related to the organization of the scientific publication markets in the life sciences. As such the INSCD databases function *de facto* as an information clearinghouse for gene sequence information, both of non-patented and patented material.

In some cases, purely informal norms without institutional policies can also play a role in creating an open-access environment for biological material. Recourse to informal rules in facilitating access can be motivated by various factors. Well-studied cases are situations where communitarian mechanisms based on norms can easily be enforced through mechanisms of face-to-face communication,[42] or those where it is rewarding to invest time and money in building a good reputation and extended confidence.[43] This is true for the exchange of microbiological material between scientists working in the culture collections that are member of the World Federation of Culture Collections (WFCC). In principle, the scientists working in these culture collections use contracts, called material transfer agreements (MTAs), when exchanging biological material between themselves or with third parties. These contracts specify whether the material can be further distributed by the recipient and, in many countries, require negotiations on access and benefit sharing before they can be used for the development of commercial applications. In those cases, granting IPR to modified material is conditioned by a negotiation with the provider countries (so-called countries of legal provenance).

However, a recent survey amongst WFCC members showed that the scientists only explicitly used MTAs in 40% of the cases when they

information on the sequences every night. The information on DNA sequences on the three sites is thus the same, but each of them also offers specific services.

[42] Ostrom E., *Governing the Commons*.

[43] Rai, A. K., 'Regulating scientific research …'.

exchanged resources.[44] They usually shared the materials in an informal way. This practice is based upon a sense of reciprocity between the scientists, who do not want to impose any restrictive conditions upon each other.[45] However, this does not mean that the informal sharing practice is not based upon well-established rules. On the contrary, it depends on a common research ethic based on concern for quality in the management and curation of the material and a sense of fairness in the exchange.[46] The real challenge for this regime of facilitated access does not come from increasing commercial use of the material and the importance of patents, but from the erosion of the research ethic due to increasing competition amongst scientists for publication and access to project funding.[47]

24.4 Conclusion: adaptive governance for facilitated access

In this chapter, I have introduced some concepts from contemporary research into institutional analysis and showed their relevance to the analysis of the structure of the scientific research commons in the field of genomics. I have illustrated how the successful examples of facilitating access that are discussed in this volume can be understood as the result of a combination of formal legal rules, formal institutional policies, contracts and informal rules such as guidelines or ethical norms. Due to the diversity of the institutional rules that have been implemented for building the scientific research commons, it is clearly impossible for the analyst to make a complete analysis of all the possible combinations of rules. Therefore, efforts at institutional design have to be understood as policy experiments based on the partial analysis of specific problems in the context of an available set of rules. Theory and empirical evidence both play an important role in enhancing the probability of selecting rules that will lead to better outcomes. But every institutional creation will remain a situated experiment that has to be evaluated and adapted over time.

[44] Stromberg, P., Pascual, U., and Dedeurwaerdere, T., 'Information sharing among culture collections', unpublished survey report, 2 November 2006.

[45] This is confirmed by the analysis of MTAs in Nguyen, T., 'Case 6. The Science Commons Material Transfer Agreement Project. A standard license clearinghouse?', Chapter 9 of this volume.

[46] Dagmar Fritze, President of the European Culture Collections Organisation, personal communication, 11 October 2007.

[47] For example it is current practice for a researcher to ask that a deposited strain of biological material be kept secret until his or her publication on that strain is published. This delay in allowing open access to the strain is often informally agreed, and can mean a delay of months or even years.

REFERENCES

Aoki M., 'Endogenizing Institutions and Institutional Changes', **3**(1) *Journal of Institutional Economics*, 2007, 1–31.

Baker, D., 'Microbial Diversity and Pharmaceutical Industry Culture Collections', in M. M. Watanabe, K. Suzuki and T. Seki (eds.), *Innovative Roles of Biological Resources Centres*, Tsukuba: World Federation for Culture Collections, 2004, 435–8.

Benkler, Y., 'Overcoming Agoraphobia: Building the Commons of the Digitally Networked Environment', **11**(2) *Harvard Journal of Law and Technolgy*, 287–400.

Bernstein, L., 'Private Commercial Law in the Cotton Industry: Creating cooperation through rules, norms and institutions', **99** *Michigan Law Review*, 2001, 1724–90.

Cgiar, *Booklet of CGIAR Centre Policy Instruments, Guidelines and Statements on Genetic Resources, Biotechnology and Intellectual Property Rights, Version II*, produced by the System-wide Genetic Resources Programme (SGRP) with the CGIAR Genetic Resources Policy Committee, Rome, July 2003, 37

Cook-Deegan, R. and Dedeurwaerdere, T., 'The science commons in life science research: structure, function and value of access to genetic diversity', **188** *The International Social Science Journal*, 2006, 309–12.

Cooter, R. D., 'Structural adjudication and the New Law Merchant : A Model of Decentralized Law', **14** *International Review of Law and Economics*, 1994, 215–31.

Dagmar Fritze, President of the European Culture Collections Organization, personal communication, 11 October 2007.

David, P. A. and Spence, M., 'Towards institutional infrastructures for e-science: the scope of the challenge', Oxford Internet Institute, *Research Report* No. 2, September 2003, 98.

Ellickson, R. C., *Order Without Law: How Neighbours Settle Disputes*, Cambridge (MA), Harvard University Press, 1991.

Fowler C., Smale M., and Gaiji S., 'Unequal Exchange? Recent Transfers of Agricultural Resources and Their Implications for Developing Countries', **19** *Development Policy Review*, 2001, 181–204.

Goeschl, T. and Swanson, T., 'On the Economic Limits of Technological Potential: Will Industry Resolve the Resistance Problem ?, in Swanson T. (ed.), *The Economics of Managing Biotechnologies*, Dordrecht: Kluwer Academic Publishing, 99–128).

Goldstein, J. A., 'Critical analysis of patent pools', Chapter 4 of this volume

Henson-Apollonio, V., 'Case 10. The International Treaty on Plant Genetic Resources for Food and Agriculture: the Standard Material Transfer Agreement as implementation of a limited compensatory liability regime', Chapter 18 of this volume

Hess Ch. and Ostrom E., *Understanding Knowledge as a commons. From Theory to Practice*, Cambridge (MA), MIT Press, 2007, 3–10.

Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume

Lessig, L., *Code and Commons*, Keynote Address at the Conference on Media Convergence, Fordham University Law School (9 February, 1999). Online at www.lessig.org/content/articles/works/Fordham.pdf (accessed February 2008).

Merton, R.K., *The Sociology of Science*. Chicago, University of Chicago Press, 1973.

National Institutesof Health, '*Best Practices for the Licensing of Genomic Inventions: Final Notice'*, **70**(68) *Federal Register*, 11 April 2005.

Nguyen, T., 'Case 6. The Science Commons Material Transfer Agreement Project. A standard license clearinghouse?', Chapter 9 of this volume

Ostrom E., *Governing the Commons: The Evolution of Institutions for Collective Action*, Cambridge, Cambridge University Press, 1990.

Understanding Institutional Diversity, Princeton, Princeton University Press, 2005, 151; 166.

Governing the Commons. The Evolution of Institutions for Collective Action, Cambridge, Cambridge University Press, 1990.

Posner, E. (ed.), *Social Norms, Nonlegal Sanctions, and the Law*, Edward Elgard, 2007

Rai A.K. and Eisenberg R.S., 'Bayh-Dole Reform and the Progress of Biomedicine', **66** *Law and contemporary problems*, 2003, 289–314.

Rai, A.K., 'Proprietary Rights and Collective Action: the Case of Biotechnology Research With Low Commercial Value', in K. Maskus and J. Reichman (eds.), *International Public Goods and Transfer of Technology*, Cambridge: Cambridge University Press, 2005, 288–306.

Rai, A.K., 'Regulating Scientific Research: Intellectual Property Rights and the Norms of Science', **77** *Northwest University Law Review*, 1999, 77–152.

Rai, A.K., Reichman, J.H., Uhlir, P.F. and Crossman, C., 'Pathways across the valley of death: novel intellectual property strategies for accelerated drug discovery', Chapter 17 of this volume

Reese, R.A., 'Reflections on the Intellectual Commons: Two perspectives on Copyright Duration and Reversion', **47** *Stanford Law Review*, 707–47.

Reichman, J. and Uhlir, P.F., 'A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment', **66** *Law and Contemporary Problems*, 2003, 315–440.

Stokes, D.E., *Pasteur's Quadrant: Basic Science and Technological Innovation*, Washington DC, Brookings Institution Press, 1997.

Van Overwalle, G., *Study on the Patenting of Inventions Related to Human Stem Cell Research*, European Communities, Luxembourg, 2002, 218.

van Zimmeren, E., 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume

Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume

Willamson, O., *The Mechanisms of Governance*, Oxford, Oxford University Press, 1996.

Part VI

Summary and concluding analysis

25 Of thickets, blocks and gaps

Designing tools to resolve obstacles in the gene patents landscape

Geertrui Van Overwalle[*]

25.1 Introduction

Human genes have been the subject of patent protection for quite some time. It has become common practice to grant patents for genes isolated from the human body, meeting the conditions of novelty, inventive step and industrial applicability.[1] Even though the initial wave of criticism against human gene patents has quieted down, the controversy lingers on as the current patent landscape for human genomic science gives rise to new concerns.

Objections have especially been raised with regard to the exploitation and licensing of gene patents. Mixing metaphors, thoughtful observers are increasingly expressing concerns that the exponential growth of patents claiming human DNA sequences may lead to a 'patent thicket' [2] or even a 'patent tsunami'.[3] It is feared that an abundance of patents will lead to royalty stacking and ultimately frustrate the use of technology, leading to a 'tragedy of the anticommons'[4] in upstream research. An anticommons effect may not only arise from the emergence of patent

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[1] For the purpose of the present paper, the terms 'inventive step' and 'capable of industrial application' may be deemed to be synonymous with the terms 'non-obvious' and 'useful'.

[2] Shapiro, C., 'Navigating the Patent Thicket: Cross Licenses, Patent Pools and Standard Setting' in E. Jaffe et al. (eds.), **1** *Innovation Policy and the Economy,* MIT Press, 2001, 119–50 (also available at http://haas.berkeley.edu/wshapiro/thicket.pdf).

[3] Warcoin, J., '"Patent tsunami" in the field of genetic diagnostics. A patent practitioner's perspective', Chapter 21 of this volume.

[4] Heller, M.A. and Eisenberg, R.S., 'Can Patents Deter Innovation? The Anticommons in Biomedical Research', **280** *Science,* 1998, 698–701. Also see Depoorter, B. and Vanneste, S., 'Putting Humpty Dumpty Back Together: Experimental Evidence of Anticommons Tragedies', **3** *Journal of Law, Economics & Policy,* 1–25.

thickets, but also from 'blocking patents'. Concerns have equally been expressed with regard to downstream research in the genetic field. New inventions might not find their way into products and a 'translational gap' might widen to form a 'valley of death'.

The authors in the present collection have reflected on the impact of gene patents and have explored various measures to deal with possible hindering effects, each in their own way and from their own, theoretical or practical, experience. Their papers form the very basis of this book. The present contribution recapitulates their major findings, takes a fresh look at the alleged problems and adds a new dimension by testing the suggested solutions against a set of goals and pre-assumptions.

Section 25.2 revisits the *problems* observed in the current patent landscape. It adds depth, shade and nuance to the metaphors, collects empirical evidence to document their appearance, and describes their (alleged) impact. In an attempt to capture the deeper root of the problems, it then examines them against the rationale and the objectives of patent law theory. Section 25.3 articulates the central *question* resulting from this analysis. In light of the alleged negative impact of patents in genetics, what measures should be contemplated to facilitate access to and use of gene patents and – ultimately – safeguard access to health care? This central question is made more explicit and exacting by refining the goals to be achieved and by introducing a series of assumptions. It is argued that if the common goals are (a) to maintain the current patent system, meant to serve as a (positive) incentive for the production of drugs and therapies important in health care, and (b) to remedy some of its (hindering) effects in the field of genetics and in diagnostics in particular (c) within a reasonable period of time, designing tools which optimize access to and use of a multitude of (blocking) patents may well be considered the most adequate remedy. Expediting access and use of genetic inventions may well be best served by the design of (1) contractual, collaborative models (2) which are based on the pre-existence of IP rights, (3) which are economically viable and commercially sustainable without overriding social motives, (4) thus restoring trust in the patent system and offering an alternative for ignoring the patent norm. Section 25.4 then takes stock of the various collaborative models which have been suggested to *remedy* the hindering effects patents may have: patent pools, clearinghouses, open source models and liability regimes. It describes characteristics, benefits and disadvantages, points to working examples and explores the potential for translation to the genetic field. Section 25.5 finally tests the various measures against the starting goals, the various postulated assumptions and the findings of the authors. Section 25.6 concludes the analysis.

Let us now turn to the next section and see how the contributors to the present book have couched current impasses in the gene patents landscape. And let us explore how these obstacles can be explained through the lens of the limits-of-the-law theory and the institutional analysis' literature, both focusing on the objectives of patent law.

25.2 Framing the problem

Overlooking current trends in the patent landscape for human genomic science, obstacles and impasses can be witnessed ranging from patent thickets, over blocking patents to translational gaps. An examination of the commonly used metaphors in more depth suggests that the phenomena cannot be defined that easily and that some nuance needs to be added to the debate. However, testing the alleged concerns against empirical data indicates that the reported phenomena are real and may affect health care. Patent thickets and blocking patents may hinder the supply of diagnostic testing services or lead to the development of suboptimal diagnostic tools,[5] and translational gaps may diminish the development of new drugs and treatments, all to the detriment of patients.

Obstacles in the patent landscape

Patent thickets

Although the term 'patent thicket' has been widely used over the last years, its exact meaning and scope is still not clear. In his path-breaking article 'Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations', Merges defines an intellectual property thicket as "a tangled, twisted mass of intellectual property rights, which criss-cross the established walkways of commerce" and where progress requires "numerous contracts with multiple, independent right holders".[6] In turn Shapiro speaks of "a dense web of overlapping

[5] Cf. European Society of Human Genetics, 'Patenting and Licensing in Genetic Testing. Recommendations of the European Society of Human Genetics', **16** *Eur J Hum Genet*, 2008, 405–11.

[6] Merges, R.P., 'Contracting Into Liability Rules: Intellectual Property Rights and Collective Rights Organizations', 84 *Calif. Law Rev.*, 1996, 1293–393. Merges already introduced the 'thickets' metaphor in this article: "Intellectual property experts, especially scholars, have responded to this burgeoning *thicket* of rights…" (1386) and "This Article is aimed at providing conceptual guidance for those who need to traverse the new *thicket* of intellectual property rights. Each vine, each plant, standing in one's path represents a distinct IPR owned by an individual. To pass through, one needs a license from each owner. Where a single right blocks the path, this is easy: a

intellectual property rights that a company must hack its way through in order to actually commercialize new technology".[7] Carefully reading these definitions suggests that a patent thicket is likely to emerge when a *multitude* of patents is held by *multiple* patent owners. Verbeure applies this approach where she refers to "the existence of multiple patents held by multiple patent owners"[8] and argues that "a patent thicket occurs when multiple patents cover the same application or technology".[9] In the same sense, Horn states that "Where standards and other technology platforms consist of many patents owned by many patent owners, the number of licences required of users may be too costly and inefficient for users to negotiate. This is often referred to as a patent thicket."[10] Ullrich argues that when searching for proper models for solving a problem of patent abundance, the basic assumption is "that the field is crowded by a large number of patents, with ownership being dispersed among many patentees, so that it becomes impossible for anyone to work naturally coherent pieces of the technology without first obtaining consent by many other patentees".[11] Although most definitions suggest the presence of a large number of patents, it may very well be that in a certain field of technology a relatively small number of scattered patents (and the related transaction and royalty costs) leads second comers to decide not to engage in related research or to enter the market.

The definition of Merges and Shapiro does not clarify whether a patent thicket is present when the patents are numerous, or whether a thicket only appears when the many patents at stake are also *essential*. Horn suggests that a patent thicket is really present if there is a "critical mass of essential patent holders with a critical mass of essential patents".[12] Goldstein equally argues that "If multiple patent owners hold patents over different mutational correlations, and all of them are

single licensing contract does the trick. Today, however, business people more often than not encounter a tangled, twisted mass of IPRs, which criss-cross the established walkways of commerce. Progress along this path does not come cheaply: rather, it requires numerous contracts with multiple, independent right holders" (1295).

[7] Shapiro, 'Navigating the Patent Thicket', 2001.

[8] Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', see Chapter 1 of this volume.

[9] Verbeure, see Chapter 1 of this volume.

[10] Horn, A.L., 'Case 1. The MPEG LA® Licensing Model. What problem does it solve in biopharma and genetics', Chapter 2 of this volume.

[11] Ullrich, H., 'Gene patents and clearing models. Some comments from a competition law perspective', Chapter 22 of this volume. Ullrich subtly adds, however, that the patent thicket is more a matter of the number and of the strategic positioning of patents than of the number of patentees.

[12] Horn, see Chapter 2 of this volume.

necessary for a successful test, then a thicket may appear".[13] In the line of Horn and Goldstein, the present volume takes the view that a 'patent thicket' refers to a multitude of *essential*, 'blocking'[14] patents which are held by a multitude of patent owners. A patent thicket is likely to emerge when the patent ownership of a number of essential patents is highly fragmented.

Recent empirical data does not confirm the concern for the emergence of a wide patent thicket in *genetics* at present.[15] However, several of the surveys clearly point to possible problems in the field of *diagnostic testing*.[16] A genetic diagnostic test is a test aiming at detecting pathogenic mutations in genes responsible for inherited and acquired genetic disorders.[17] Conversely, a genetic diagnostic method encompasses any method or technology to detect a link or association between a disease (e.g. breast and/or ovarian cancer) and a specific (defect in a) gene (e.g. a mutation in the BRCA1 gene).[18] Genetic tests are an important

[13] Goldstein, J.A., 'Critical analysis of patent pools', Chapter 4 of this volume.

[14] Infra, p. 389.

[15] Most empirical studies focus on the *issuance* of human gene patents by patent authorities. See Hopkins, M.M., Mahdi, S., Patel, P. and Thomas, S., 'DNA Patenting: The End of an Era?', **25** *Nature Biotechnology,* 2007, 185–7; Hopkins, M.M., Mahdi, S., Patel, P. and Thomas, S., *The Patenting of Human DNA: Global Trends in Public and Private Sector Activity* (A Report for the European Commission – PATGEN Project – 6th FP-2003- LifeSciHealth-II), Brighton, Science and Technology Policy Research (SPRU) – University of Sussex, 2006, 14 (available at: www.sussex.ac.uk/spru/documents/patgen_finalreport.pdf); Jensen, K. and Murray, F., 'Intellectual Property Landscape of the Human Genome', **310** *Science,* 2005, 239–240; National Research Council of the National Academies (Committee on intellectual Property Rights in Genomic and Protein Research and Innovation), *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health*, Washington, National Academies Press, 2005, 161; Verbeure, B., Matthijs, G. and Van Overwalle, G., 'Analysing DNA patents in relation with diagnostic genetic testing', **14** *European Journal of Human Genetics (EJHG),* vol. 1, January 2006, 26–33; Walsh, J.P., Cho, C. and Cohen, W. M., *Patents, Material Transfers and Access to Research Inputs in Biomedical Research* (Final Report to the National Academy of Sciences Committee [on] Intellectual Property Rights in Genomic and Protein-Related Research Inventions), Washington, National Academies Press, 2005, 172. Few empirical studies focus on the set of gene patents that have been asserted in *court* to assess the actual restrictive effect of patents. See Holman, C.M., 'The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation', **76** *University of Missouri-Kansas City Law Review,* 2007, 295–362 (also available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1090562).

[16] See references in previous footnote. Also see Caulfield, T., Cook-Deegan, R.M., Kieff, F.S. and Walsh, J.P., 'Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies', **24** *Nature Biotechnology*, 2006, (1091), 1092.

[17] Matthijs, G. and Van Ommen, G.-J., 'Gene patents: from discovery to invention. A geneticist's view', see Chapter 20 of this volume.

[18] Matthijs and Van Ommen, see Chapter 20 of this volume.

component of health care services, as they provide a way to establish difficult diagnoses and to detect persons at risk, before expressing the disease. Testing is also useful in planning clinical interventions that may benefit the concerned individuals, by attenuating or even efficiently treating their disease.

The precarious assessment that the diagnostic sector is more prone to patent thickets, may be refined on the basis of a twofold distinction: a distinction between technology-specific and diagnosis-specific patents,[19] on the one hand, and a distinction between vertically and horizontally oriented thickets, on the other hand.[20] *Technology*-specific patents encompass general molecular biological technologies such as amplification, labelling or detection of nucleic acid fragments. The technology used can be the same for different diagnostic tests. Conversely, different technologies may be used for a particular diagnostic test.[21] *Diagnosis*-specific patents encompass elements which are specific for the diagnosis of a certain defect or disease, such as specific nucleic acid sequences, mutations or polymorphisms correlated with that certain defect or disease (disease gene patents). Those elements are not only different for each diagnosis performed, but are essential to the gene-based diagnosis of that particular disease. Contrary to technology specific patents, there is no alternative to possibly circumvent such an essential diagnosis patent when performing genetic testing for the particular disorder.[22] According to Verbeure, especially within the group of diagnosis specific patents, blocking positions may arise,[23] as many of the genes associated with the more than 1,000 genetic diseases which can be diagnosed today, are patented.[24]

Furthermore, due to the cumulative nature of research in this area, a *vertically* oriented thicket may develop: a first patent may be granted on the initially unravelled diagnostic gene-disease link, while at a later stage of the research additional patents may be filed on specific mutations within that gene.[25] These types of patents centre on a single gene and exhibit a high degree of interdependence urging patent owners to cooperate. A *horizontally* oriented thicket may pop up with multi-trait

[19] Vlassak, K. and Schüller, K., '*The Effect of Patents on Diagnostic Research and Kit Development*', in G. Van Overwalle (ed.), *Gene Patents and Public Health,* Brussel, Bruylant, 2007, 99–113, at 104.

[20] Verbeure, see Chapter 1 of this volume.

[21] Verbeure, see Chapter 1 of this volume with reference to Vlassak and Schüller, '*The Effect of Patents on Diagnostic Research and Kit Development*', 2007, 99–113.

[22] Verbeure, see Chapter 1 of this volume.

[23] On blocking patents, infra, p. 389.

[24] Verbeure, see Chapter 1 of this volume.

[25] Ibid.

or multi-gene based disorders, where one disease may be caused by defects caused by different genes, independently or cooperatively.

In conclusion, empirical data have not demonstrated an actual and acute problem yet, and recent literature sometimes appears, as Goldstein states, "to reflect more a premonition of problems to come than existing paralysis of commerce".[26] However, the problems of patent thickets in the field of genetics are "real",[27] especially in the field of diagnostics. Concerns on how these thickets may hinder access to health care and the supply of diagnostic testing services therefore merit further attention.

Blocking patents

An anticommons effect may not only arise from the existence of multiple patents covering the same application or technology and held by multiple patent owners. The phenomenon may also appear in case of a single, so-called 'blocking' patent. The term 'blocking patent' is not clear and can be used in different ways. In its widest sense, *any* patent is by definition a blocking patent, as a patent confers upon its proprietor the right to stop others from making, using, offering for sale, selling or importing the patented invention.[28] Used in this sense, the notion blocking patent is a tautology. In a more narrow sense, a blocking patent is a patent covering *essential* features of the invention which cannot be invented around. Verbeure uses the term in this way and suggests (albeit using the term 'blocking position') that a blocking patent position is "a patent covering all or part of the technology that is essential to a certain activity".[29] In its strictest sense, a blocking patent is a patent covering essential features which are *licensed* in a very restrictive manner. Correa interprets the term in this manner and argues that the risk of a blocking position arises with IP fragmentation "if one of the essential technologies is licensed on exclusive terms so third parties cannot have access to part of the technology deemed necessary to manufacture a product".[30]

It should be borne in mind that a blocking patent is a *relative* concept, bearing on the presence of two distinct components or layers: an essentiality component and an instrumentality component. Judging whether a patent is blocking or not, cannot take place in the abstract, but requires a case-by-case evaluation. Given that a certain activity or function is envisaged (instrumentality component), an assessment is

[26] Goldstein, see Chapter 4 of this volume. [27] Ibid.
[28] See art. 28 1 TRIPs Agreement.
[29] Verbeure, see Chapter 1 of this volume. My italics.
[30] Correa C.E.M., 'Case 2. The SARS case. IP fragmentation and patent pools', Chapter 3 of this volume.

required as to which elements are essential *to* perform that activity or function and whether these essential elements are claimed by the patent at stake (essentiality component). Only when the elements are indispensable or essential *to* achieve that specific result – in other words, when the essential elements are a necessary means *to* an end – and only when they are claimed in the patent, that patent is a blocking patent. In the area of genetic diagnostics, a patent encompassing claims on the entire (or relevant part of the) gene sequence, on a common pathogenic mutation or on the fundamental method to determine the association between a mutated gene and an inherited disease is blocking *for* carrying out the genetic test based on nucleotide analysis for that disease. A patent including the same claims is most likely not blocking *for* carrying out the test based on an analysis at the protein level (a so-called protein determination assay).[31]

In the present volume, the term 'blocking patent' will be used in the second, more narrow, albeit multi-layered sense. A blocking patent refers to a patent covering (some or more) features which are essential *for* a certain activity or function, irrespective of the way in which the patent is being licensed.

In the field of diagnostic testing blocking patents are likely to appear. For diagnostic testing based on DNA sequences, a prognosis is usually based on the disclosure of a link between a disease and a genetic defect (mutation). As Verbeure,[32] and also Matthijs and Van Ommen indicate, a major problem with diagnostic gene patents stems from the fact that it is impossible "to invent around, i.e. to invent an alternative test that would not require the gene sequence or gene product".[33] In that regard it is misleading to talk about alternative tests: "alternative tests might involve different or novel technologies – which can indeed be inventive and become a proprietary tool – but all these methods still interrogate the same genetic sequence".[34] Thus, the owner of a gene patent effectively has a 'blocking patent', as he holds a patent covering all or part of the features (namely a gene) that are essential *to* a certain activity (namely testing).

Several studies have pointed to blocking patents and have additionally documented restrictive licensing in the area of gene-based diagnostic genetic services.[35] Over the last years, some biotech companies

[31] In view of the definition of a genetic diagnostic test given above, a protein determination assay would not be qualified as a 'genetic diagnostic test'.

[32] Supra. [33] Matthijs & Van Ommen, see Chapter 20 of this volume. [34] Ibid.

[35] Cho M.K., Illangasekare, S., Weaver, M.A., Leonard, D.G. B. and Merz, J.F. 'Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services.',

have either refused to license some inventions or have licensed them exclusively at relatively high prices. Laboratories have been confronted with cease-and-desist letters from patent holders or exclusive licensees, which have induced some of them to cease performing specific tests and/or refrain from test development.[36] A case that received wide public attention was the breast cancer (BRCA) case where the gene patents and the restrictive licensing policy of the patent holder Myriad manifestly illustrated the foul reality of a blocking patent.[37] Blocking patents and unreasonable licensing practices may jeopardize the quality and continuity of testing, hinder the supply of diagnostic testing services and drive up costs.[38] Concerns about the impact of blocking patents and restrictive licensing on health care should therefore not be underestimated.

5(1) *Journal of Molecular Diagnostics*, 2003, 3–8; Matthijs, G., 'DNA Diagnostics in Practice', in G. Van Overwalle (ed.), *Gene Patents and Public Health,* Brussel, Bruylant, 2007, 27–44; Leonard, D., 'Gene Patents: A Physician's Perspective', Paper presented at a meeting of the US National Academies' Science, Technology and Economic Policy (STEP) Board (available at http://www7.nationalacademies.org/step/Leonard_presentation_October_proteomics.ppt); Walpole, I.R., Dawkins, H.J.S., Sinden, P.D. and O'Leary P.C. 'Human Gene Patents: The Possible Impacts on Genetic Services Healthcare', **179** *Medical Journal of Australia* 2003, 256–83.

[36] Merz, J. F., Kriss, A. G., Leonard, D. G. B. and Cho, M., 'Diagnostic testing fails the test', **415** *Nature,* 2002, 577–9; Walpole et al., 'Human Gene Patents: The Possible Impacts on Genetic Services Healthcare', 2003; Cho et al., 'Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services', 2003. Also see van Zimmeren, E., 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume.

[37] See Matthijs and Van Ommen, Chapter 20 of this volume. Also see, Baldwin, T., 'Ethics and Patents for Genetic Diagnostic Tests', in G. Van Overwalle (ed.), *Gene Patents and Public Health,* Brussel, Bruylant, 2007, 45–59; Caulfield, T., Bubela, T. and Murdoch C.J., 'Myriad and the Mass Media: the Covering of a Gene Patent Controversy', **9** *Genetics in Medicine,* 2007, 850–5; Caulfield et al., 'Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies', 2006; Matthijs, G. and Halley, D. 'European-wide opposition against the breast cancer gene patents', **10** *European Journal of Human Genetics*, 2002, 783–4.

[38] See Matthijs and Van Ommen, Chapter 20 of this volume, with a reference to Cho et al., 'Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services', 2003. Also see van Zimmeren, Chapter 5 of this volume: "[It] could impede further development of an existing test and research into complementary or alternative methods of diagnosis. Furthermore, testing will be quantitatively limited to the capacity of the patent owner, which will not necessarily meet the demands of the number of patients. Additionally, there would be no price competition which might lead to a substantial increase in genetic testing costs and thus a serious drain on funds of public health services. The medical practice could be dictated by the single provider without procedures for ensuring quality control and peer review. And the close link between testing, clinical and counselling services could be disrupted. Even in the case where the patent owner would be rather 'cooperative' and would issue exclusive licenses for a specific territory and/or a specific type of testing, further research and the provision of clinical testing services could be seriously hampered."

Translational gap

Next to patent thickets and blocking patents, attention has also been drawn to the cumbersome interaction between early-stage genetic research and particular clinical applications, in other words 'translation'. New genetic inventions may not find their way into products and a 'translational gap' might widen to form a 'valley of death' between the traditional finishing point of research (supported by academic grants) and clinical and therapeutic applications (funded by the private sector).[39]

The definition of translational research is in flux and can have both a specific and a general meaning. The narrowest definition is 'bench-to-bedside' research wherein a basic laboratory discovery becomes applicable to the diagnosis, treatment or prevention of a specific disease and is brought forth by either a physician-scientist who works at the interface between the research laboratory and patient care or by a team of basic and clinical science investigators.[40] Translational research may also refer to the wider spectrum of patient-oriented research that embraces innovations in technology and biomedical devices as well as the study of new therapies in clinical trials.[41] In translational research, traditional boundaries among basic research, clinical research and patient-oriented research are yielding to a single, continuous, bidirectional spectrum.[42,43]

Recent surveys indeed seem to confirm the emergence of major obstacles to translational research in genetics[44] and have identified the transaction costs associated with academic–industry negotiations over drug-related problems as a significant barrier.[45] The problems in the

[39] Moran, N., 'Public Sector Seeks to Bridge 'Valley of Death', **25** *Nature Biotechnology,* 2007, 266.

[40] Pizzo, P., 'Letter from the Dean', *Stanford Medicine Magazine,* Fall 2002.

[41] Ibid.

[42] Hörig, H., Marincola, E. and Marincola, F., 'Obstacles and Opportunities in Translational Research', **11** *Nature Medicine,* 2005, 705–8.

[43] Scientists are increasingly aware that translational research is really a two-way street, where the drive to cure should be complemented by the pursuit to understand human diseases and their complexities (Marincola, F., 'Translational Medicine: a Two Way Road', **1** *J Transl Med*, 2003, 1). Thus, one important aspect of translational medicine is going back from the bedside to the laboratory with observations made in human studies. Although the goals of translational research are essentially no different from those of traditional academic clinical research, translational research emphasizes strategies to expedite their successful implementation (Hörig et al., 'Obstacles and Opportunities in Translational Research', 2005).

[44] Hörig et al., 'Obstacles and Opportunities in Translational Research', 2005, 705–8.

[45] Walsh, J.P., Cho, C. and Cohen, W.M., 'Where Excludability Matters: Material Versus Intellectual Property in Academic Biomedical Research', **36** *Research Policy,* 2007, 1184–1203, see 1185–87; Lipinski, C.A., 'The Anti-Intellectual Effects of Intellectual Property', **10** *Current Opinion in Chemical Biology*, 2006, 380–383.

field of diagnostics seem to be less prominent here, however, as useful products may arise directly from basic genomic research.[46] Unsolved problems of translation diminish the development of new drugs and treatment, at the detriment of patients, and should therefore be taken to heart.

Comparison of obstacles

A first, tentative comparison[47] between the reported obstacles indicates that patent thickets and blocking patents mainly seem to occur in *upstream* research, whereas the valley of death mainly seems to be present in *downstream* research. Upstream refers to a position within the production stream closer to manufacturing processes, and downstream points toward the latter stages of a usually industrial process or the stages (as marketing) after manufacture.[48] Upstream research may include products (research tools or platform technologies) which are required by downstream researchers in the course of their further R&D.[49]

The distinction between upstream and downstream research has only been introduced recently. Traditionally, a major distinction was made between basic research, which is curiosity driven, and applied research, directed to a particular application (the development of a new drug or vaccine). This distinction has been blurred in the wake of genomics-based research, where useful products (e.g. diagnostic tests) may arise directly from basic genomic research.

[46] See World Health Organisation (WHO), *Public health, Innovation and Intellectual Property Rights*, Report of the Commission on Intellectual Property Rights, Innovation and Public Health, WHO, April 2006, 53 (available at www.who.int/intellectualproperty/documents/thereport/CIPIH23032006.pdf). Cf. Verbeure, Chapter 1 of this volume: "Unlike gene-based drug development, the development of a gene-based diagnostic test based on the fundamental finding of the link between a particular nucleic acid sequence and the aetiology of a disease does not involve the same enormous investment. A principal argument for patenting biomedical inventions is the fact that typically, post-invention development costs far exceed pre-invention research expenditures, and firms are unable to make this substantial investment without protection from competition. Patents therefore facilitate transfer of technology to and within the private sector by providing exclusive rights to preserve the profit incentives of innovating firms. Additionally, for drug development based on genomic knowledge one could envisage parallel but different routes to obtain a drug. In other words, in contrast to diagnostic testing, for drug development there is still some room for inventing around. The justification of a right to exclude others from exploitation of the technology seems therefore less obvious and acceptable with regard to gene-based diagnostic testing as for drug development."

[47] A more in-depth analysis is developed below, see p. 437.

[48] See *Merriam-Webster's Online Dictionary* available at www.merriam-webster.com.

[49] World Health Organisation, *Public Health, Innovation and Intellectual Property Rights*, 2006, 49 ff.

An additional observation is that the major problem caused by patent thickets and blocking patents relates to *access* to and *use* of patented inventions. In contrast, the major problem in the valley of death relates to *translation* of early-stage upstream inventions into applications.

Deeper root: limits to the functions of patent law

In an attempt to deepen our understanding of how patent thickets, blocking patents and translational gaps are caused, and grasp the deeper root of the current tensions, we briefly turn to patent law theory. Traditional patent law theory teaches that the major objective of patent law is to encourage the development of new goods and services and to disclose underlying technologies, by granting the patentee a temporary monopoly on the patented invention in return for the disclosure of the description of the invention. In doing so, patent law aims at serving both private and public interest. This consequentialist, utilitarian justification, focusing on both the incentive to invent/innovate and the incentive to disclose argument, is probably most accepted to date.

Applying a functions-and-limits approach[50] to traditional patent law theory might offer helpful insights on current impasses in the genetic patent landscape. This approach suggests that law fulfils various functions, amongst which are the regulatory function, the symbolic function and the function to provide legal guarantees. The major function, the regulatory function, aims at regulating relations between the authorities and the citizens and amongst citizens. Patent law develops a vertical regulatory function by establishing competent authorities assigning rights to patent applicants and prescribing patentability criteria, formal requirements and granting procedures. Patent law also warrants a horizontal regulatory function, by defining the contours of the right between the patent holder and the potential licensees and the public at large, in the post-grant phase.[51]

Cross-industry based research has suggested that the effectiveness of the patent system may vary across different industry sectors.[52]

[50] See Claes, E., Devroe, W. and Keirsbilck, B., 'Introductory Chapter – The Limits of the Law', in E. Claes, W. Devroe and B. Keirsbilck (eds.), *Limits of the Law,* Springer, 2009, pp. 1–24.

[51] See Van Overwalle, G. and Van Zimmeren, E., 'Functions and Limits of Patent Law', in E. Claes, W. Devroe and B. Keirsbilck (eds.), *Limits of the Law,* Springer, 2009, pp. 415–42. In doing so, we partly apply the analytical model set forth by Claes et al.

[52] Moser, 'How Do Patent Laws Influence Innovation? Evidence from Nineteenth-Century World's Fairs', **95** *The American Economic Review*, No. 4, September 2005.

This is not entirely unexpected since the impact of the patent system depends on its interaction with environmental conditions, which vary across sectors.[53] According to conventional wisdom, patent law fulfils its regulatory function quite well in the pharmaceutical sector where it is believed to stimulate the delivery of drugs and therapies important for health care. However, patent law seems to experience some limits in achieving its objectives (foster innovation, public health interests) and regulatory function in the area of genetics. The occurrence of patent thickets and blocking patents in genetics may indicate that the patent system has some adverse effects. As the explosion of gene patents arises to a great extent from current patent legislature and judiciary formally recognizing the patentability of genes, the current impasse might be interpreted as a failure of the vertical regulatory function within the patent system.[54] The restrictive licensing behaviour of some patent owners, equally suggests that patent law may have a blocking effect. As unfair licensing largely results from the patent (and competition) law legislature not setting clear limits and not providing enforceable guidelines with regard to the exploitation and licensing of patent rights, the current problems might well be interpreted as a failure of the horizontal regulatory function.

[53] Cowan, R., van der Eijk, W., Lissoni, F., Lotz, P., van Overwalle, G. and Schovsbo, J., *Policy options for the improvement of the European patent system*, Report commissioned by STOA (Scientific Technology Options Assessment) of the European Parliament, 2007, 13 (www.europarl.europa.eu/stoa/publications/studies/stoa16_en.pdf).

[54] For Europe, the patentability of human gene patents was formally recognized in art. 5 of the European Biotechnology Directive (Directive 98/44/EC of 6 July 1998 of the European Parliament and of the Council on the legal protection of biotechnological inventions, *Official Journal L* 213, 30 July 1998, 13, also available at http://europa.eu.int/eur-lex/en/lif/dat/1998/en_398L0044.html) which is now implemented in all 27 EU member states and in the EPC Implementing Regulations. For the US, the patentability of living material took a start with the Chakrabarty decision of the Supreme Court in 1980. Although the USPTO holds that a human gene as it occurs in nature cannot be patented, a DNA sequence which is purified and isolated in the form of a cDNA or is part of a recombinant molecule or vector, is patentable under the precedent of the so-called *andrenaline* case of 1912 in *Parke-Davis* v. *H. K.Mulford*. This case upheld a patent on adrenaline, a natural hormone that was found in animal glands. The patent applicant identified, isolated and purified the active ingredient namely adrenaline. This created a product that did not exist in nature in that precise form and that could be used for medical treatment. Also see 'Utility Examination Guidelines', **66** *Federal Register,* 4, 5 January 2001, Notices, (1092), 1093: "An isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent because (1) an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature, or (2) synthetic DNA preparations are eligible for patents because their purified state is different from the naturally occurring compound".

Contemplating on the discomfort within current IP from a critical angle, leads Taubman to specify that the root problem may spring from three levels: the inherent legitimacy of the foundational principles of IP law and policy (system design), the application in practice at the level of governance and administration (execution) or the impact of the individual exercise of rights granted under the system (perverse individual choices).[55] Translating his analysis into the functions-and-limits narrative, suggests that the current problems in the genetic patent landscape mainly result from shortcomings in the regulatory function, aggravated by individual choices made within the system which are at odds with the basic objectives of the system.

Reflecting on current problems through the institutional analysis' literature, as suggested by Dedeurwaerdere, leads to a similar uncomfortable conclusion. This literature equally focuses on the objectives of patent law and sets them forth in terms of a response to the 'diffusion/innovation dilemma' and the 'exploration/exploitation dilemma'.[56] Dedeurwaerdere suggests that the first dilemma is at the core of the anticommons problems leading to patent thickets, and that the diffusion problems are also present in cases where 'holdouts' maintain unreasonably restrictive licensing practices. The second dilemma is at the core of the discussion on translational measures where the goal is to create incentives for investing in uncertain downstream product development and where collective action[57] is suggested to organize wide and early diffusion of research results, while recognizing the importance of private property rights for creating individual or organizational incentives for innovation.[58]

25.3 Research question

A more conceptual analysis of the trends and concerns observed in the current genetic patent landscape reveals some limits in patent law. These

[55] Taubman, A., 'Several kinds of "should": the ethics of open source in life sciences innovation', Chapter 16 of this volume.

[56] For a more extensive discussion of these dilemmas, see Cook-Deegan, R. and Dedeurwaerdere, T., 'The Science Commons in Life Science Research: Structure, Function and Value of Access to Genetic Diversity', **188** *The International Social Science Journal*, 2006, 309–12.

[57] 'Collective action' is the pursuit of a goal or a set of goals (e.g. the provision of public goods) through the collaboration of two or more individuals. For more, see Olson, M., *The Logic of Collective Action: Public Goods and the Theory of Groups,* Harvard Economic Studies, 1965, 108. Also see footnote 62.

[58] Dedeurwaerdere, T., 'The role of law, institutions and governance in facilitating access to the scientific research commons. A philosopher's perspective', Chapter 24 of this volume.

limits relate to the objectives and the regulatory function of patent law. The limits encountered entice an in-depth reflection on *possible* measures to assist modern patent law in achieving its major objectives again and in coping with its regulatory function.

One way to deal with the current 'patent paradox' is to preclude the coming into existence of gene patents and twist patent law around again to exclude genes from its field of application, in other words act upon the vertical regulatory function. An alternative strategy might be to regulate and monitor the exercise of patent rights and licensing, in other words, affect the horizontal regulatory function.

Starting goals

But, how to determine the *best* measure? In order to single out the most adequate measure it is necessary to identify a (set of) well-defined goal(s) against which the measures can be calibrated.[59] However, different stakeholders may have different goals, or interpret similar goals in a different way. The public opinion, the research community, health care professionals and biotechnological companies may all have different opinions on what to achieve and what to avoid when it comes to patenting and licensing of human genes. The public opinion might aim at banning the patent system; the research community might favour a patent system with a maximum of freedom to operate in order to develop high-quality genetic tests; health care professionals might want a system promoting low prices for genetic tests; small and medium biotech enterprises might support a protection system with low transaction costs; and big biotech companies might aim at a patent system with maximum exclusivity to recoup investments and protect markets. Analysing the goals of all relevant stakeholders is beyond the scope of the present book. Furthermore, collecting information on the goals of the various stakeholders on an empirical basis, will not resolve the normative choice which will then have to be made, requiring considerable thought on underlying values.[60] Therefore, it is assumed in the present volume that the common goals are (a) to maintain the current function

[59] The author is grateful to Göran Hermerén for insisting on the need to articulate the goals explicitly, in order to enable a comparison between the various measures at hand and the *best* measure. The conceptual, multi-step scheme set forth in Hermerén's paper on 'Challenges in the Evaluation of Nanoscale Research: Ethical Aspects' (*Nanoethics,* 2007, 223) was also very helpful in this regard.

[60] Cf. Hermerén, G., in Part II. Philosophical Considerations, in Fleischhauer, K. and Hermerén, G., *Goals of Medicine in the Course of History and Today,* Stockholm, Kungl. Vitterhets Historie och Antikvitets Akademien, 2006, 354 ff.

of the patent system to serve as a (positive) incentive for the production of drugs and therapies important in health care and (b) to remedy some of its (hindering) effects in the field of genetics and in diagnostics in particular. If what we want to achieve is to look (a) within the boundaries of the patent system (b) for solutions that mitigate possible harmful effects of patents in genetics, then both strategies (exclude genes from patent law again and regulate licensing behaviour) might prove to be helpful in remedying current problems.

If we assume that an additional goal is to achieve some improvements (c) within a reasonable period of time, then facilitating licensing in genetics might turn out to be more adequate than carving out gene patents from patent law. However valuable the exclusion of gene patents may be,[61] the feasibility and pace to do so will greatly be hampered by processes of domestic and/or international patent law reform. As (centralized) decision making by state regulators tends not to be very pliable, swift and plastic responses to changing conditions may take quite some time. (Decentralized) decision making by stakeholders might be more flexible and conducive to change. Focusing on the contractual design of tools which optimize the use of a multitude of (blocking) patents may therefore be the *best* option.

Translating this solution into patent law theory language suggests that the best way to remedy current obstacles in the genetic patent landscape is to work on the horizontal regulatory function of patent law[62] by designing formal rules of contract.[63]

Research assumptions

The following assumptions will act as a point of departure in further designing adequate measures to improve access to and use of patents in the field of genetic diagnostics, an area in human genomic science

[61] The exclusion of gene patents might not only prevent some recently emerging problems, such as patent thickets and blocking patents, but might equally respond to old criticisms relating to unacceptable instrumentalisation of the human body through appropriation by patents. For more, see Van Overwalle, G. 'Legal and Ethical Aspects of Bio-Patenting. A Critical Analysis of the EU Biotechnology Directive', in C. Baumgartner and D. Mieth (eds.), *Patente am Leben? Ethische rechtliche und politische Aspekte der Biopatentierung*, Paderborn, Mentis, 2003, 145–58 and the references cited there.

[62] For the distinction between the *vertical* and the *horizontal* regulatory function of patent law, see p. 394.

[63] For the distinction between formal *legal* rules and formal rules of *contract,* see Dedeurwaerdere, Chapter 24 of this volume.

which seems to be most prone to suffer from patent bottlenecks in the near future.

Contractual and collaborative shape

The first hypothesis of this collection is that in the current state of affairs, the problems created by patent law in genetic diagnostics are best served by contractual, collaborative measures. Our first assumption is that access to and use of (patented) innovations may be achieved more adequately and rapidly through private, collaborative efforts. These efforts are in essence *contractual* in nature, as they are the result of a consensus between parties, rather than an initiative from the legislator. These efforts are *collaborative*, as they presuppose active cooperation between various parties.[64, 65]

Studying the role of contractual, collaborative rights organizations in mediating the use of IP rights is not new. In a path-breaking work, Rob Merges already explored collective rights organizations, "industry groups that collect IP rights from owners and license them as a package".[66] Merges found that these organizations ease some of the tensions created by strong IP rights and may play a valuable role in facilitating transactions in IP rights. His efforts (and also later writings from other scholars) have mainly focused on patent pools for *ICT* and *copyright* collecting societies for music. The present book aims at taking the debate further and theorizes on the role of contractual, collaborative rights organizations in mediating the use of patents in genetics, more in particular by examining *genetic* patent pools and *patent* collecting societies, next to open source genetics. Only over the last decade scholars have started to gain a deeper understanding on how these mechanisms should be conceptualized in a genetic context.

[64] A distinction can be made between 'collaborative' and 'collective' measures. To collaborate means "working jointly with others or together especially in an intellectual endeavor". Hence collaborative measures refer to measures where people *work together*. Collective means "involving all members of a group as distinct from its individuals" (cf. collective action). Hence collective measures refer to measures which *involve* all members (See *Merriam-Webster's Online Dictionary* – also for further etymological background – available at www.merriam-webster.com).

[65] The definition of 'collaborative' set forth in the present book is wider than the definition employed by Rai in her article 'Open and Collaborative Research: A New Model for Biomedicine' (in Robert W. Hahn (ed.), *Intellectual Property Rights in Frontier Industries: Software and Biotechnology*, 2005, (131), 136) where 'collaborative' refers to "scientists work[ing] closely with others outside their own lab or small firm".

[66] Merges, R.P., 'Of Property Rules, Coase, and Intellectual Property, **94** *Columbia Law Review*, 1994, 2655–73.

This first hypothesis calls for some nuance. Differing collaborative measures might be needed to take care of upstream and downstream problems. Various observers have argued that the impasse patents cause in upstream research on early-stage genetic inventions might best be remedied by patent pools or clearinghouses, or may be open source. Several suggestions have also been put forward to overcome the impasse IP protection may cause in downstream research, amongst which the establishment of translational research centres or liability regimes. However, it is difficult to imagine that collaborative models might be helpful to overcome the adverse effects of blocking patents. It is not to be expected that patent pools or clearinghouses will be adequate to mitigate the problems resulting from one or more patents belonging to a single, uncooperative or excessive patent holder. Rather, compulsory licence schemes and informal norms of fair licensing might come to the rescue here.[67]

IPR based

At the start of our explorative *tour d'horizon* a second assumption is that the contractual, collaborative measures can only function properly, if they are based on the pre-existence of IPRs in general, and patent rights in particular. A pivotal prerequisite for innovative and successful contractual and collaborative licensing to cut through the patent thicket or accomplish translation, is the power of the knowledge and/or technology owners involved to enforce users to behave in a certain way. Patent rights invest knowledge and/or technology owners with such authority.

The suggestion that collective rights organizations are based on IPRs is not totally new. When analysing collective rights organizations in the light of the literature on entitlements,[68] Merges already argued that this is the case.[69] The present book aims at investigating whether this assumption also holds when it comes to genetics, and especially in the context of open source models for genetics.

Economically viable

A third assumption is that models need to be designed which are commercially sustainable and prove to be economically viable. It is our aim to explore and perfect measures which are viable in a for-profit context. Although recent experiences in the genetic sector suggest

[67] Van Overwalle, G., 'Gene Patents and Public Health. Setting the Scene', in G. Van Overwalle (ed.), *Gene Patents and Public Health,* Brussel, Bruylant, 2007, 11–24.

[68] See p. 431 ff. [69] Merges, 'Contracting into Liability Rules', 1996, (1293), 1302.

that collaborative models are more easily established in genetics when serving social and humanitarian motives in a not-for-profit context,[70] the models should also prove to be efficient and adequate to deal with knowledge production, protection, exchange and translation in markets served by the profit motive, nonetheless, thereby vigilantly attempting that the profit motive does not totally override social motives and the economic model concurrently yields socially acceptable outcomes. Existing collaborative non-for-profit institutions may nevertheless act like laboratories where different conditions and approaches are tested and operationalized, and may inspire and catalyse successful examples in a for-profit context.[71]

Restoring trust and halting ignoring the norm

A fourth hypothesis when examining collaborative models is that they might help to restore trust of the research community and the general public in the patent system.[72] Recent events have convincingly shown that the genetic community[73] and public opinion at large are very sensitive to possible unfair use of the patent system in the field of genetic inventions, witness the strong reactions against the grant to Myriad Genetics of patents dealing with diagnostic testing for early onset breast and ovarian cancer based on the genes BRCA1 and BRCA2.[74] The impasses identified and the criticism voiced is not always directed to the *existence* of the patent *system* as such, but rather to some excesses in the *exercise* of patent *rights* and the unrestrained behaviour of individual patent owners, in an effort to maximize profit. Not responding to the public reserve with

[70] See Van Overwalle, G., van Zimmeren, E., Verbeure, B. and Matthijs, G. 'Models for facilitating access to patents on genetic inventions', **7** *Nature Reviews Genetics*, 2006, 143–54. Also see Verbeure B., Van Zimmeren E., Matthijs G., and Van Overwalle G., 'Patent Pools and Diagnostic Testing', **24**(3) *Trends in Biotechnology,* 2006, 115–120.

[71] Schwab, K. and Hartigan, P., 'Social Innovators with a Business Case. Facing 21st Century Challenges. One Market at a Time', **1** *EconPapers,* issue 4, 2006, 7–11 (available at http://econpapers.repec.org/article/tprinntgg/).

[72] See Van Overwalle, G., 'Reshaping Bio-Patents: Measures to Restore Trust in the Patent System', in H. Somsen (ed.), *The Regulatory Challenge of Biotechnology. Human Genetics, Food and Patents*, Cheltenham, UK – Northhampton, US, Edward Elgar Ltd., 2007, 238–56 (Proceedings of a Conference held at the University of Amsterdam 27–28 May 2004).

[73] See Matthijs and Halley, 'European-wide opposition against the breast cancer gene patents', 2002. Also see, Baldwin, T. 'Ethics and Patents for Genetic Diagnostic Tests', 2007; Bird, W., 'Using the EPO Opposition Procedure as a Strategy Against Patents on Diagnostic Methods', in G. Van Overwalle (ed.), *Gene Patents and Public Health,* Brussel, Bruylant, 2007, 73–83; Caulfield et al., 'Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies', 2006; European Society of Human Genetics, 'Patenting and Licensing in Genetic Testing', 2008.

[74] For more details, see Matthijs, 'DNA Diagnostics in Practice', 2007.

regard to the current use of patents by the bio-industry might turn out to be injudicious. One day the bio-industry might find itself being confronted with a public opinion taking the view that ethical concerns and moral principles are more important than greater competitiveness, economic growth and biotechnological development.[75] For the patent system to be widely accepted, it is vital that it is generally recognized as a tool fostering both private *and* public interest. Formally expanding the concept of public interest to encompass health care has been one attempt to do so.[76] Taking full account of human rights discourse in patent law and making a human rights approach in patent law more explicit and exacting would be another way to act.[77] Constructing adequate clearing mechanisms and conditions of exchange through innovative licensing schemes can be another alternative to restore trust in both the private *and* public interest objectives of the patent system in the wider society, pertaining to economic *and* social welfare.

A closely related assumption is that the set-up of collaborative models offering fair and reasonable licensing terms, might lead to a decrease of the tacit, wilful ignorance of patents amongst users. Empirical work in the biomedical sciences suggests that many scientists, both in universities and in industry, currently ignore the question of whether their activities are covered by a patent.[78] It has been suggested that this strategy is an inappropriate and unstable policy.[79] The introduction of

[75] See Van Overwalle, 'Legal and Ethical Aspects of Bio-Patenting. A Critical Analysis of the EU Biotechnology Directive', 2003.

[76] First suggested in legal doctrine (see e.g. Correa C., 'The GATT Agreement on Trade-related Aspects of Intellectual Property Rights: New Standards for Patent Protection', *European Intellectual Property*, 1994, 327–31; Van Overwalle, G., 'Klinische proeven en volksgezondheid. Naar een herijking van het algemeen belang in het octrooirecht', *Tijdschrift voor Privaatrecht*, 2000, 899–968), article 8 (1) TRIPs, supplemented with the various Declarations, now offers a firm legal basis for such an interpretation.

[77] See Van Overwalle, G., 'Human Rights' Limitations in Patent Law', in W. Grosheide (ed.), *The Human Rights Paradox in Intellectual Property Law*, Oxford, Edward Elgar Publishing Ltd, 2009 (in press). Also see Van Overwalle, 'Reshaping Bio-Patents: Measures to Restore Trust in the Patent System', 2007.

[78] Walsh, J. P., Arora, A. and Cohen, W.M., 'Effects of Research Tool Patents and Licensing on Biomedical Innovation' in W.M. Cohen and S.A. Merrill (eds.), *Patents in the Knowledge-Based Economy*, Washington, The National Academies Press, 2001, 285–340; National Research Council of the National Academies, *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health*, 2003, 119–27. Also see Strandburg, K., 'Sharing Research Tools and Materials: Homo Scientificus and User Innovator Community Norms', in Dreyfuss, R. and Zimmerman, D. (eds.), *Working Within the Boundaries of Intellectual Property*, Oxford University Press (forthcoming), and the references cited there. Article on file with the author.

[79] Caulfield et al., 'Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies', 2006, (1091), 1093. Also see National Research Council of the National Academy of Sciences (Committee on Intellectual Property Rights in the

one-stop licences, through the establishment of collaborative arrangements might promote a spontaneous registration by the users.[80]

Research hypothesis

Given the growing concern that gene patents might curb the use of genetic inventions, increase costs, frustrate the development of tests and treatments and – ultimately – lead to restricted access to healthcare, the present book focuses on the question how access to research and development can be achieved, and what measures should be taken to render patented genetic inventions accessible for further use. This central question is narrowed down to what measures should be contemplated to safeguard research and development in genetic diagnostics, as this area seems to be most prone to suffer from the impact patents may have in the near future. This question is also made more explicit and exacting by introducing well-identified goals and a series of assumptions. Based on the preset goals and assumptions, the research question can be rephrased as a research hypothesis.

The central research hypothesis and starting point of the present book is that access in genetic diagnostics is best served by the design of (1) contractual, collaborative models (2) based on the pre-existence of IP rights, (3) which are economically viable, without overriding social motives, (4) thus restoring trust in the patent system and offering an alternative for ignoring the patent norm.

25.4 Proposed solutions

Over the years, various models have been suggested and put to work to 'clear' patents and facilitate the use of patented inventions. Just think of bilateral licences, cross-licences or multiparty agreements (see Table 25.1, text in italic). Studies of these conventional collaborative models and other models have indicated, however, that they tend to have limited capacity in solving current problems in the genetic patent landscape in an efficient and secure manner.[83]

Knowledge-Based Economy), *A Patent System for the 21st Century*, Washington, National Academies Press, 2004, 172; Eisenberg, R., 'Science and the Law: Patent Swords and Shields', **299** *Science*, 2003, 1018–9.

[80] Cf. Verbeure et al., 'Patent Pools and Diagnostic Testing', 2006.

[81] A 'clearing *mechanism*' is any mechanism aiming to clear patent thickets. A clearing-*house* is a specific type of clearing mechanism.

[82] See previous footnote.

[83] See Van Overwalle, et al., 'Models for facilitating access to patents on genetic inventions', 2006.

Table 25.1 *Models facilitating access, use and translation of proprietary (genetic) inventions*

Clearing mechanisms[81]	*Working solutions*		*Ignoring the patent* *Inventing around*
	Non-collaborative models		*Research exemption*
	Collaborative models	*Conventional*	*Bilateral licensing* *Cross licensing* *Multiparty licensing*
		New	Patent pool Clearinghouse[82] Open source Liability regime

In the present collection we aim to deepen our understanding of *new* collaborative licensing models and to test their potential to solve impasses in upstream and downstream research in genetics. The collaborative models subjected to further analysis in the present book are patent pools, clearinghouses, open source and liability regimes (see Table 25.1, text in black). The distinction between upstream and downstream is important here, as different solutions have been proposed for different areas of application. Patent pools, clearinghouses and open source have been suggested to solve the patent thicket problem emerging in upstream research. Translational research centres and liability regimes have been put forward to remedy the translational problem faced in downstream research.

The various authors of the present volume have carefully explored those *new* licensing models. Their papers form the quintessential part of the present collection. The following sections recapitulate their major findings and put them in a wider (comparative) context.

Patent pools

A first model that has been suggested to deal with patent thickets and to make proprietary genetic inventions more easily accessible for further use is the patent pool model. Do patent pools indeed remedy the problems resulting from patent proliferation in the genetic diagnostic field? The authors in Part I and Part V have explored patent pools and their potential to solve said problems from a panoply of perspectives,

both theoretical and practical. In the next section we will take a closer look at their analyses.

General concept and framework

A patent pool has been commonly defined as an agreement between two or more patent owners to license one or more of their patents to one another or as a package to third parties who are willing to pay the royalties associated, either directly by patentees to licensees or, indirectly, through a new entity specifically set up for the pool administration.[84] This standard definition is also applied by Verbeure in her concept paper.[85] Verbeure and Horn further remind us that a patent pool thus allows interested parties to gain access to all patents to work an invention with one single licence, hence the term 'one-stop-licence' or 'all-in-one-licence' has been set forth to qualify this type of licence agreement.

Various types of patent pools can be distinguished.[86] Depending on the way the patent pool came into being, a distinction can be drawn between a patent pool set up amongst a group of licensors for a technology or standard, and between a patent pool established after an open call for a certain standard.[87] Depending on the way the agreements with third parties are accomplished, a distinction can be made between a pool which is managed by one licensor acting as an intermediate agent between patentees and licensees, and a pool which is governed by an

[84] Clark, J., 'Patent Pools: a Solution to the Problem of Access in Biotechnology Patents? White Paper commissioned by Q. Todd Dickinson, the Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office, 2000 (available at www.uspto.gov/web/offices/pac/dapp/opla/patentpool.pdf); Klein, J.I., Business Review Letter to Gerrard R. Beeney, 1997 (available at www.usDoJ.gov/atr/public/busreview/1170.htm); Merges, R.P., 'Institutions for Intellectual Property Transactions: the Case of Patent Pools' in R. Dreyfuss, D.L. Zimmerman and H. First (eds.), *Expanding the Boundaries of Intellectual Property,* Oxford University Press, 2001, 123–66.

[85] Verbeure, see Chapter 1 of this volume. Also see Verbeure et al., 'Patent Pools and Diagnostic Testing', 2006; Van Overwalle, et al., 'Models for facilitating access to patents on genetic inventions', 2006. A figure of a patent pool can be found at Verbeure, see Chapter 1 of this volume (Figure 1.1).

[86] See Clark, 'Patent Pools: a Solution to the Problem of Access in Biotechnology Patents?', 2000; Merges, 'Institutions for Intellectual Property Transactions: the Case of Patent Pools', 2001; Shapiro, 'Navigating the Patent Thicket', 2001; Van Overwalle, 'Models for Facilitating Access to Patents on Genetic Inventions', 2006.

[87] The first has been termed 'joint licensing scheme' in Bekkers, R., Iversen, E. and Blind, K. 'Patent Pools and Non-Assertion Agreements: Coordination Mechanisms for Multi-Party IPR Holders in Standardization', Paper for the EASST 2006 Conference, Lausanne, Switzerland, August 23–26, 2006 (available at http://www2.unil.ch/easst2006/Papers/B/Bekkers%20Iversen%20Blind.pdf). Also see Verbeure, Chapter 1 of this volume.

independent body. A typical example of a pool managed by one party is the DVD pool.[88] Prominent examples of pools managed by an independent authority are the MPEG-2 pool, illustrated by Horn,[89] and the SARS (Severe Acute Respiratory Syndrome) corona virus pool, described by Correa.[90, 91]

The reasons put forward for setting up a patent pool have varied considerably over time, but as Verbeure argues and as Ullrich confirms, many late-modern pools are set up in an endeavour "to deal with substantial patent thickets for technologies that were essential to one and the same technical standard".[92] A standard is a norm or measure that may be the result of a formal consensus-building procedure that is managed by a standardization body[93] (*de jure* standards) or arise spontaneously due to the degree of market penetration of a particular technical solution (*de facto* standards).[94]

Patent pools have been successfully employed in consumer electronics, telecommunications, computer and related industries. A prominent example is the MPEG LA licensing model.[95] As Horn highlights, in the 1990s, the MPEG LA model enabled multiple MPEG-2 users to acquire essential patent rights from multiple patent holders in a single transaction for the MPEG-2 standard, required for DVD, satellite, cable and other digital video applications. Over time, the MPEG-2 patent portfolio licence has grown from the original 8 patent owners and 100 essential patents to include more than 825 essential patents in 57 countries owned by 25 patent owners and approximately 1,200

[88] The DVD4C patent pool is managed by Philips and the DVD6C patent pool is managed by Toshiba (see www.dvd6cla.com).

[89] See Horn, Chapter 2 of this volume.

[90] See Correa, Chapter 3 of this volume: "an entity shall be appointed as the pool manager".

[91] In literature references can also be found to a 'patent platform', which has features in common with both a patent pool and a patent forum. An example of such an approach is the 3G platform (www.3g.co.uk/). For more, see Verbeure, Chapter 1 of this volume and the references cited there. Also see Goldstein, L.M. and Kearsey, B.N., *Technology Patent Licensing: an International Reference on 21st Century Patent Licensing, Patent Pools and Patent Platforms,* Aspatore, 2004, 576.

[92] Verbeure, Chapter 1 of this volume; Ullrich, Chapter 22 of this volume.

[93] Cf. European Commission Communication COM (92) 445 final of 27 October 1992 on Intellectual Property Rights and Standardisation: "Standards are technical specifications relating to a product or an operation, which are recognized by a large number of manufacturers and users."

[94] See Lemley, M.A., 'Antitrust, Intellectual Property and Standard Setting Organizations' (see http://econ.tau.ac.il/papers/applied/0109037.pdf); Hovenkamp, H., Janis, M. & Lemley, M.A., *IP and Antitrust: An Analysis of Antitrust Principles Applied to Intellectual Property Law*, Aspen Publishers Online, 2002. Also see Verbruggen, J. and Lorincz, A., 'Patents and Technical Standards', in **33** *IIC* 2002, 125–132.

[95] See www.mpegla.com.

licensees.[96] Over the years, the MPEG LA model became the template for the type of patent pools with a licensing administrator.

Patent pools may have significant benefits. The authors in the present volume join the tenor in current literature referring to reduction of transaction costs, elimination of stacking licences, decrease in patent litigation and exchange of technical information.[97] Aoki further suggests that when a bundle of goods such as patents, must be used together – i.e. goods are complements – there is economic benefit other than reduction of transaction costs through elimination of double marginalization.[98] It is also underlined that patent pools may offer an interesting instrument for government policy: it is better to encourage companies to establish a pool than to force them into a compulsory licence scheme.[99] However, non-voluntary patent pools have been established in the past as well.[100]

Pools may equally hide some risks. The various authors confirm reported dangers, such as the shielding of invalid patents[101] or entail the risk of inequitable remunerations. The major criticism, however, is the danger of covering for a cartel and the subsequent anticompetitive effects this would have.[102] The risk of improper collusion may already be present during the standard-setting process.[103]

In an attempt to deal with any potential anticompetitive effects of multiparty licensing agreements, such as patent pools, the US antitrust agencies and the European Commission have established guidelines. Close examination of foregoing guidelines, regulations and related decisions provides valuable information on the attitude of the US and

[96] Horn, Chapter 2 of this volume.

[97] Verbeure, Chapter 1 of this volume; Correa, Chapter 3 of this volume; Horn, Chapter 2 of this volume; Ullrich, Chapter 22 of this volume.

[98] Aoki, R., 'Access to genetic patents and clearinghouse models. An economic perspective', Chapter 23 of this volume. Also see Verbeure, Chapter 1 of this volume.

[99] Merges, 'Institutions for Intellectual Property Transactions: the Case of Patent Pools', 2001. Also see Verbeure, Chapter 1 of this volume.

[100] For example, in 1917 an aircraft pool was formed that encompassed almost all aircraft manufacturers and was crucial to the US entering World War I, see Dykman, H.T., 'Patent Licensing within the Manufacturer's Aircraft Association', **46** *Journal of the Patent Office Society*, 1964, 646. Also see Verbeure, Chapter 1 of this volume.

[101] Carlson, S.C., 'Patent Pools and the Antitrust Dilemma', **16** *Yale Journal on Regulation*, 1999, 359–399. See Correa, Chapter 3 of this volume; Verbeure, Chapter 1 of this volume.

[102] Carlson, 'Patent Pools and the Antitrust Dilemma', 1999; Merges, 'Institutions for Intellectual Property Transactions: the Case of Patent Pools', 2001; Shapiro, 'Navigating the Patent Thicket', 2001. Also see Ullrich, Chapter 22 of this volume and Verbeure, Chapter 1 of this volume.

[103] Verbeure, Chapter 1 of this volume and the references cited there.

European authorities towards patent pools. In short, Verbeure points out that patent pools should avoid creating anticompetitive restraints and will most probably be accepted if they meet the following conditions: the patents taken up by the pool are valid, the technologies covered are essential and complementary, the licensing terms are fair, reasonable and non-discriminatory, and the licences are non-exclusive.[104] According to Ullrich, however, the current criteria are most ambiguous and ambivalent. First, they are based on an artificial separation of the different layers of pool-building agreements, which are assessed in isolation.[105] Second, they are focused on a scrutinous examination of the patents at stake, rather than on the relationships of rivalry between patent owners involved. He concludes that the current framework exemplifies a rather 'reductionist' analysis and tends to become a formal, rather loose test, unless it is construed strictly in accordance with its purpose, which is "to allow only pools supporting access to some crucial (technological) input or material, or to some unavoidable gateway or facility, that cannot be obtained otherwise, in particular not by way of technological circumvention".[106] What obscures a rigid approach even more, according to Ullrich, is the basic dilemma authorities face between efficiency (the bigger the patent thicket, the bigger the need for a pool and – eventually – a big pool) and competition (the bigger the pool, the bigger the market power, the bigger the concern for restrictive effects).

Setting up a pool is a long and complex process. A first question, discussed by Verbeure and Ullrich, is when to start preparing for a pool. Pools often are the result of joint research and development by the pool partners, and cannot easily be transformed *ex post* in mere clearing arrangements.[107] That is why it might be wise, as has been demonstrated in the SARS corona virus pool by Correa,[108] to start setting up a pool early on in the process.

Another problem brought to the fore by Verbeure, Goldstein and Horn, is that of so-called 'holdouts'. A holdout is a patent owner who,

[104] See Verbeure, Chapter 1 of this volume. Also see, Correa, Chapter 3 of this volume; Horn, Chapter 2 of this volume. Whether this means only open and non-discriminatory access by third parties to the acquisition of licenses, or also their admission to the pool as members is not quite clear, see Ullrich, Chapter 22 of this volume.

[105] Ullrich, Chapter 22 of this volume.

[106] Ibid. Biotechnology may offer some examples, in particular in the field of gene research for medical purposes.

[107] Ibid.; Verbeure, Chapter 1 of this volume.

[108] Correa, Chapter 3 of this volume.

by choice or inadvertedly, gets left out.[109] The former, a so-called purposeful holdout, does not want to contribute an essential patent to the patent pool and has the ability to hold up the formation of the pool. Horn[110] and Goldstein[111] believe that the holdout problem is uniquely acute in the field of genetics. In terms of solution, Verbeure points to a grant-back clause or a compulsory licence.[112] In turn, Goldstein argues that medical standards may ameliorate the holdout problem, on top of the recent *eBay* decision.[113, 114] Burk analyses the holdout phenomenon through a totally different lens, namely the options and information theory, and suggests that in such situations liability regimes may offer an adequate solution.[115]

Transposition to genetics

The use of patent pools in biomedicine and biotechnology is in its infancy. As yet, the patent pool concept has hardly been applied in daily practice in the genetic field, but there are a few operational examples. The Golden Rice pool is an instructive case in the field of agriculture and a nice example of how private and public organizations, in a combined effort, dealt with the patent thicket by creating a non-profit, humanitarian and, therefore, an atypical patent pool.[116] As Goldstein confirms, it is indeed not to be expected that such ingenious solutions will also be available or that the players involved will act in such smooth unison in other, more competitive, areas of modern biotechnology.[117] The SARS corona virus pool is a recent case in the biomedical field.

[109] George, G. D., 'Note: What is Hiding in the Bushes? *Ebay*'s Effect on Holdout Behaviour in Patent Thickets', **13** *Michigan Telecommunications and Technology Law Review,* 2007, 557–76. Here, we focus on holdouts that purposefully decide to go at it alone.

[110] Horn, Chapter 2 of this volume.

[111] Goldstein, Chapter 4 of this volume.

[112] Verbeure, Chapter 1 of this volume.

[113] US Supreme Court, *eBay, Inc. v. MercExchange, L.L.C eBay, Inc.* v. *MercExchange, LLC*, 126 SCt 1837, 2006

[114] Goldstein, Chapter 4 of this volume.

[115] Burk, D.L., 'Critical analysis: property rules, liability rules and molecular futures. Bargaining in the shadow of the cathedral', Chapter 19 of this volume.

[116] Graff, G. and Zilberman, D., 'Towards an Intellectual Property Clearinghouse for Agribiotechnology', **3** *IP Technol. Today*, 2001, 1–12; Graff, G. D., Cullen, S. E., Bradford, K. J., Zilberman, D. and Bennett, A. B., 'The Public–Private Structure of Intellectual Property Ownership in Agricultural Biotechnology', **21** *Nature Biotechnol.*, 2003, 989–95; Parish, R. and Jargosh, R., 'Using the Industry Model to Create Physical Science Patent Pools Among Academic Institutions', **15** *J. Assoc. Univ. Technol. Managers*, 2003, 65–79. Also see Van Overwalle et al., 'Models for Facilitating Access to Patents on Genetic Inventions', 2006; Verbeure et al., 'Patent Pools and Diagnostic Testing', 2006. For an update on the Golden Rice pool, see Verbeure, Chapter 1 of this volume.

[117] Goldstein, Chapter 4 of this volume.

Correa explains that a myriad of patent applications, incorporating the genomic sequence of the SARS corona virus, had been filed by a number of organizations. By placing the scattered patent applications in a pool, the interested constituencies hoped that uncertainty about ownership could be reduced at the end of the day.[118] Goldstein critically remarks that it remains to be seen whether legal uncertainty indeed provides an additional impetus for creating a pool.[119] The Green Fluorescent Protein (GFP) pool is sometimes also listed as a patent pool.[120] Verbeure argues, however, that upon closer analysis, the GFP pool is rather an example of aggregation of patent rights with subsequent out-licensing technology.[121] The Single Nucleotide Polymorphisms (SNP) consortium has been referred to as a pool too.[122] Verbeure notes, however, that it might rather be qualified as an IP pool, than as a proper patent pool.[123]

Biopharma and genetics are usually perceived as fundamentally different from the electronics and telecommunications sectors, particularly as the generation of standards, seen as a strong incentive for setting up a patent pool, is missing.[124] Both Verbeure[125] and Goldstein[126] evangelize that standards, in principle, may be an important trigger to establish a pool in the genetic sector. Differing from the conventional way standards are viewed, a standard in the genetic field could present itself as a set of genes or mutations to be screened, which are recognized

[118] Correa, Chapter 3 of this volume. Also see Simon, J., 'Dealing with Patent Fragmentation: The SARS Patent Pool as a Model', in G. Van Overwalle (ed.), *Gene Patents and Public Health,* Brussel, Bruylant, 2007, 115–120; Verbeure, Chapter 1 of this volume and the references cited there.

[119] Goldstein, Chapter 4 of this volume.

[120] See http://www6.gelifesciences.com/aptrix/upp00919.nsf/Content/drugscr_applications%7Edrugscr_applic_technol%7Edrugscr_gfp%7Egfp_licenses?OpenDocument&hometitle=DrugScr.

[121] Verbeure, Chapter 1 of this volume.

[122] Holden, A.L., 'The SNP Consortium: Summary of a Private Consortium Effort to Develop an Applied Map of the Human Genome', **26** *Biotechniques Supplement*, 2002, 22–4

[123] Verbeure, Chapter 1 of this volume. See also this chapter at p. 446.

[124] Organization for Economic Co-Operation and Development (OECD), *Genetic Inventions, Intellectual Property Rights and Licensing Practices,* Report of a workshop organized by the OECD Working Party on Biotechnology, 2002 (available at www.oecd.org/dataoecd/42/21/2491084.pdf). Also see Organisation for Economic Co-operation and Development (OECD), *Draft Guidelines for the Licensing of Genetic Inventions*, Organisation for Economic Co-operation and Development web site, 2005 (see www.oecd.org/sti/biotechnology/licensing. In the same sense, Correa, Chapter 3 of this volume; Horn, Chapter 2 of this volume.

[125] Verbeure et al., 'Patent Pools and Diagnostic Testing', 2006.

[126] Ebersole, T.J., Guthrie, M.C. and Goldstein, J.A. 'Patent Pools and Standard Setting in Diagnostic Genetics', **23** *Nature Biotechnology*, 2005, 937–8.

by the international scientific community, or which reflect national or international best practice guidelines for genetic testing for a particular disease, and which could serve as an authoritarian guidance for the determination of essentiality.[127] However, in the genetics field, standards serve the role of quality control of testing services, rather than guaranteeing interoperability, and they are dictated by natural occurrence, rather than by human choice.[128] This leads Verbeure to conclude that it is not likely that such a standard could play a similar role in the setup of a patent pool as it does for ICT. Goldstein is more optimistic and believes that the establishment of a standard for diagnostic testing of polymutationally correlated diseases will decrease the propensity of the market leaders to want to go at it by themselves, i.e. to play holdout and that most if not all diagnostic labs will still want to offer the best test possible if it is recommended by respected medical authorities.[129] Another reason for Goldstein's optimism is the recent *eBay* decision of the Supreme Court,[130] which teaches that a holdout, who can no longer automatically count on a permanent injunction, will see his leverage decreased.[131]

Patent pools may be an efficient model to deal with patent thickets in the field of diagnostics. Cases where a disease is caused by various mutations in one gene, or by one or more mutations in any one of several possible genes are likely to give rise to patent thickets.[132] An example case of poly-mutational or multi-gene-based diseases relates to the diagnosis of Hereditary Non-Polyposis Colorectal Cancer (HNPCC).[133] Possibly, overlapping patents may emerge on the genetic data necessary in testing for HNPCC as various patent holders filed patents.[134] Might a patent

[127] Van Overwalle, et al., 'Models for facilitating access to patents on genetic inventions', 200; Verbeure et al., 'Patent Pools and Diagnostic Testing'.

[128] Verbeure, Chapter 1 of this volume. In the same sense, Goldstein, Chapter 4 of this volume ("the standards are arbitrary and not functional"), ("a medical standard informs a 'best' medical practice").

[129] Goldstein, Chapter 4 of this volume.

[130] US Supreme Court, *eBay, Inc. v. MercExchange, L.L.C eBay, Inc.* v. *MercExchange, LLC*, 126 SCt 1837, 2006.

[131] Goldstein, Chapter 4 of this volume.

[132] Shapiro, 'Navigating the Patent Thicket', 2001; Scherer, F. M., 'The Economics of Human Gene patents', 77 *Acad. Med.*, 2002, 1348–1367. Also see Van Overwalle, et al., 'Models for facilitating access to patents on genetic inventions', 2006 and Verbeure et al., 'Patent Pools and Diagnostic Testing', 2006.

[133] For details, see Verbeure, Chapter 1 of this volume.

[134] European patent applications have been identified for example for MSH2, MLH1, PMS2 and MSH5. Patent holders include Human Genome Sciences, John Hopkins University, Oregon Health Sciences University and Dana-Farber Cancer Institute.

thicket arise, an HNPCC pool encompassing the essential gene patents could help to eliminate the thicket and render proprietary genomic data more accessible for use. In line with poly- or multi-gene-based diseases, other developments are abound in the field of genetic diagnostics that may give rise to a patent thicket – to name only two, pharmacogenomics and DNA array technology.[135] When it comes to the totally different field of drug development, however, Horn is somewhat more reluctant and refers to targets, such as signalling protein or cellular surface protein pathways for purposes of developing agonists to stimulate desirable reactions or antagonists to block undesirable ones.[136]

In further refining the problem and finding the right solution, Verbeure has suggested to distinguish between vertical and horizontal patent thickets.[137] Following this distinction, we conclude that the optimal patent pool model in genetics might well be a patent *platform* where individual patent pools are narrowly defined around single genes comprising vertically oriented patents, thereby providing access to horizontally oriented thickets.[138] However, it will take quite a while before such a platform may be operationalized. Meanwhile, efforts should concentrate on patent pools set up around single genes or gene panels. Patent pools are of no help in the case of one – mainly exclusively licensed – blocking patent.[139]

Clearinghouses

Somewhat lesser attention has been paid to another new licensing arrangement: the clearinghouse. Does the clearinghouse model make

[135] See Van Overwalle et al., 2006; Verbeure et al., 'Patent Pools and Diagnostic Testing', 2006; Verbeure, Chapter 1 of this volume; Ebersole et al., 'Patent Pools and Standard Setting in Diagnostic Genetics', 2005. Goldstein claims he has anecdotal evidence from commercial enterprises who stopped further work in the field of gene microarrays and where the existence of one or more unlicensable gene patents have prevented the production and commercialization of an array containing multiple genetic sequences useful for the diagnosis or evaluation of patients' gene profiles (Goldstein, Chapter 4 of this volume).

[136] Horn, Chapter 2 of this volume, with reference to Grassler F. and Capria, M.A., 'Patent Pooling: Uncorking a Technology Transfer Bottleneck and Creating Value in the Biomedical Research Field', **9** *Journal of Commercial Biotechnology*, 2003, 115.

[137] Verbeure, Chapter 1 of this volume.

[138] Verbeure, Chapter 1 of this volume. For the notion of patent *platform,* see Verbeure, Chapter 1 of this volume. Also see Bekkers et al., 'Patent Pools and Non-Assertion Agreements: Coordination Mechanisms for Multi-Party IPR Holders in Standardization', 2006; Goldstein and Kearsey, *Technology Patent Licensing: an International Reference on 21st Century Patent Licensing, Patent Pools and Patent Platforms,* 2004, 67–79.

[138] Goldstein, Chapter 4 of this volume; Verbeure, Chapter 1 of this volume.

proprietary genetic inventions more easily accessible for further use? The authors in Part II and V have examined clearinghouses from a variety of approaches to test whether this model might resolve problems resulting from intense gene patenting. Let us take a closer look at their findings.

General concept and framework

The term clearinghouse is derived from banking institutions and refers to the mechanism by which cheques and bills are exchanged among member banks to transfer only the net balances in cash. Nowadays, as Van Zimmeren points out,[140] the concept has acquired a broader meaning and refers to any mechanism by which providers and users of goods, services and/or information are matched.[141] The key feature of any clearing mechanism is matchmaking between providers and users; what exactly is exchanged (goods, services, information etc.) is of secondary significance.

Already from the very beginning of scholarly reflection on clearinghouses and their appropriateness in a genetic context, categorizations have been put forward.[142] Van Zimmeren et al. have built further on this literature and refined the classification on the basis of the objectives pursued and services offered in a clearinghouse dealing with proprietary genetic inventions.[143] Van Zimmeren et al. have introduced a basic distinction between clearinghouses merely aiming at facilitating 'access'[144] to (proprietary) inventions, and clearinghouses aiming at facilitating 'access *and* (standardized) use' of (proprietary) inventions. Within this basic division, various subtypes may be discerned. Clearinghouses facilitating access include information clearinghouses and technology-exchange clearinghouses: the first provide 'simple' information related to technology or patents and the latter additionally provide information on the availability of technologies for licensing. Both models of clearinghouses may operate free or for

[140] van Zimmeren, Chapter 5 of this volume. Also see Van Overwalle, et al., 'Models for facilitating access to patents on genetic inventions', 2006.

[141] Krattiger A.F., 'Financing the Bioindustry and Facilitating Biotechnology Transfer', **1** *IP Strategy Today*, 2004, 1–45.

[142] Ibid.

[143] See van Zimmeren, E., Verbeure, B., Matthijs, G. and Van Overwalle, G., 'A Clearinghouse for Diagnostic Testing: the Solution to Ensure Access to and Use of Patented Genetic Inventions?', *Bulletin of the World Health Organization*, 2006, 352–9. Also see van Zimmeren, Chapter 5 of this volume.

[144] Aoki also applies this same distinction, although she prefers to use the term 'exchange', see Aoki, Chapter 23 of this volume.

a fee.[145] Clearinghouses focusing on access *and* use encompass open access clearinghouses, standard licences clearinghouses and royalty collection clearinghouses: the first offers access on a royalty-free, open access basis; the second does so via standard licences and the third offers collection and distribution of royalties, monitoring and enforcement, and dispute resolution on top.[146]

Examples of information clearinghouses vary from general search engines, such as Google,[147] to specialized biodiversity information networks, such as the Global Biodiversity Information Facility (GBIF).[148] Examples of information clearinghouses in the patent area include Espacenet[149] and Google Patent Search,[150] which are free, and Delphion[151] and Micropatent,[152] which are fee-based. Examples of technology-exchange clearinghouses may include global platforms, such as BirchBob[153] and yet2.com.[154] As van Zimmeren and Avau illustrate, BirchBob is an Internet-based platform that brings together offers and demands for innovations, and provides services dedicated to finding and facilitating contacts between technology holders and technology seekers.[155] Examples of technology-exchange clearinghouses in the field of healthcare include specific healthcare technology-exchange platforms such as Pharmalicensing[156] and TechEx.[157] These portals provide online partnering support enabling companies in the biopharmaceutical and biomedical industry to find licensing partners and conclude licensing contracts. A well-known example of an open access clearinghouse is the SNP Consortium.[158] An example of a standard licence scheme is offered by Science Commons.[159] Science Commons examines standard licensing formats to facilitate wider access to scientific subject matter, as Creative Commons has been doing in the area of copyrighted

[145] Van Zimmeren et al., 'A Clearinghouse for Diagnostic Testing', 2006. Also see van Zimmeren, Chapter 5 of this volume.
[146] Merges, 'Contracting into Liability Rules', 1996. Also see van Zimmeren, Chapter 5 of this volume.
[147] See www.google.com.
[148] See www.gbif.org. Also see Edwards, J.L., 'Case 3. The Global Biodiversity Information Facility. An example of an information clearinghouse', Chapter 6 of this volume.
[149] www.ep.espacenet.com. [150] www.google.com/patents.
[151] www.delphion.com. [152] www.micropatent.com/static/index.htm.
[153] www.birchbob.com. [154] www.yet2.com.
[155] See van Zimmeren, E. and Avau, D., 'Case 4. BirchBob: An example of a technology exchange clearinghouse', Chapter 7 of this volume.
[156] www.pharmalicensing.com. [157] www.techex.com.
[158] See also the subsection 'Categorisations and Definitions. What's in a Name?' of this chapter, p. 446.
[159] http://sciencecommons.org.

material.[160] Classical examples of royalty collection clearinghouses include copyright collection societies, such as the American Society of Composers, Authors and Publishers (ASCAP),[161] or the Belgian (SABAM),[162] French (SACEM),[163] United Kingdom (ALCS) or German (GEMA)[164] Societies. Typical for this model, as Corbet underlines, is that the owners of rights authorize the collective management society to administer their rights and negotiate with users, deliver licences, collect fees and distribute them, and monitor unlicensed uses.[165] The most common method for collecting the fees is the 'blanket licence'.[166]

Clearinghouses do have certain benefits, but may exhibit shortcomings and have certain disadvantages when applied in the patent area. At a cursory glance, Dedeurwaerdere concludes that a clearinghouse is essentially an information sharing device which contributes to the reduction of transaction costs and facilitates the enforcement of the formal and informal rules which are adopted.[167] Aoki finds that clearinghouses facilitating access are advantageous because they reduce transaction costs, and that clearinghouses facilitating access and use are interesting because they provide access to a large catalogue of IP.[168]

In an attempt to sketch an in-depth and nuanced picture, van Zimmeren systematically weighs the pros and cons of the various clearinghouse subtypes against their potential to deal with three recurrent obstacles: transactions costs, royalty stacking and blocking patents from non-cooperative patent holders. Other authors complement this image.

Information clearinghouses can be extremely valuable in view of their potential to disclose data and share information, and thus serve political and scientific interests, Edwards indicates.[169] Van Zimmeren, however, is rather sceptical in view of the restricted potential to offer a remedy for the recurrent obstacles.[170]

Technology exchange clearinghouses are useful as they offer a basis to evaluate whether a technology is available for deployment and assist

[160] http://creativecommons.org. [161] www.ascap.com. [162] www.sabam.be.
[163] www.sacem.fr. [164] www.gema.de.
[165] See Corbet, J., 'Case 7. The collective management of copyright and neighbouring rights. An example of a royalty collection clearinghouse', Chapter 10 of this volume.
[166] Under a 'blanket licence' the user is entitled to make use of any or all works or other protected material in the organization's repertoire for the purpose, and within the period indicated in the license.
[167] Dedeurwaerdere, Chapter 24 of this volume.
[168] Aoki, Chapter 23 of this volume. In the same line, van Zimmeren, Chapter 5 of this volume.
[169] Edwards, Chapter 6 of this volume.
[170] van Zimmeren, Chapter 5 of this volume.

in connecting providers and users of that technology, as Bennet and Boettiger suggest.[171] Van Zimmeren agrees but notes that technology clearinghouses do not offer a remedy for the aforementioned obstacles either.[172]

Open source clearinghouses tackle the problem of transaction costs and royalty stacking pretty well, stemming from the fact that the inventions are available at no cost. However, as van Zimmeren points out, the overall success of this model appears to be rather limited, as this scheme does not offer any opportunity to recoup high research and development investments preponderant in genetic research.[173]

Standard licence clearinghouses have important benefits for science policy, as delays or inability/failure to conclude negotiations may result in lost time, productivity and research opportunities, as we learn from Nguyen.[174] Van Zimmeren[175] and Aoki[176] take the view that standard clearinghouses significantly reduce transaction costs, whereas Spence doubts this suggestion and encourages the use, not of standard licence *agreements*, but of standard *clauses* which can be readily assembled into a variety of alternative agreements.[177]

Royalty clearinghouses can achieve a reduction of transaction costs, as they ease the bargaining process and lead to decline in enforcement costs resulting from the collection of royalties, in the view of van Zimmeren and Corbet.[178] However, van Zimmeren also voices some criticism, hereby sided by Spence. First, the pricing of the total fee would be far from straightforward[179] and the royalty clearinghouse might give rise to certain competition law problems. Second, only small players

[171] See Bennett, B. and Boettiger, S., 'Case 5. The Public Intellectual Property Resource for Agriculture. A standard license public sector clearinghouse for agricultural IP', Chapter 8 of this volume.

[172] van Zimmeren, Chapter 5 of this volume.

[173] Ibid.

[174] See Nguyen, T., 'Case 6. The Science Commons Material Transfer Agreement Project. A standard license clearinghouse?', Chapter 9 of this volume.

[175] van Zimmeren, Chapter 5 of this volume.

[176] Aoki, Chapter 23 of this volume.

[177] Choosing and picking *clauses* takes place in much the same way that software subroutines and modules can be assembled into functionally more comprehensive software systems that are suited for particular applied tasks for licenses, see David, P. A. and Spence, M., *Towards Institutional Infrastructures for E-Science: The Scope of the Challenge* Oxford, Oxford Internet Institute Research Report No. 2, 2003, 98.

[178] van Zimmeren, Chapter 5 of this volume. Similarly, Corbet, Chapter 10 of this volume: "It is generally accepted that collective management of copyrights and neighbouring rights is not only useful for the rights owners but is also to the advantage of users, who would otherwise be confronted with unbearable transactional costs."

[179] Spence, M., 'Comment on the conceptual framework for a clearinghouse mechanism', Chapter 11 of this volume.

might be willing to join the clearinghouse and there may be too little incentive for the holders of the most valuable patents to join, resulting in an 'asymmetric'[180] or 'incomprehensive'[181] library of patents. Third, the exchange of complementary know-how might be hampered.[182] Fourth, this type of clearinghouse can no more than the others force an unwilling patent holder to participate, although van Zimmeren believes that a reciprocal positive comity or a grant-back clause may be imposed in the standard licences to bring the unwilling patent holder into the scheme, even though competition law requires caution here.[183] Last but not least, not to be neglected is the fact that the administration of royalty collecting clearinghouses would be expensive and require considerable expertise.[184]

Examining clearinghouses through property theory, leads Dedeurwaerdere to argue that a clearinghouse is not linked to any specific ownership regime: it can be part of the reconstructed commons (as in the case of the SNP Consortium), the exclusive ownership regime (as in the case of patent clearinghouses), or be a hybrid of both (as in the model of PIPRA clearinghouse)[185].

Looking at clearinghouses from a management perspective, a clearinghouse could be administered either as a voluntary scheme or as a statutory framework on a compulsory basis. There is a need to consider incentives that trigger the voluntary participation of the stakeholders in the clearinghouses.

Transposition to genetics

Various national and international advisory bodies and experts have suggested that a clearinghouse should be set up in the field of patents related to genetic inventions in order to solve the problem of patent thickets.[186] Patent clearinghouses have not widely been applied in daily practice in the genetic field yet, but there are a few examples.

An example of an information clearinghouse focusing on biodiversity is the Global Biodiversity Information Facility (GBIF).[187] As Edwards explains, GBIF collects primary scientific biodiversity data from a

[180] van Zimmeren, Chapter 5 of this volume.
[181] Spence, Chapter 11 of this volume.
[182] van Zimmeren, Chapter 5 of this volume; Spence, Chapter 11 of this volume.
[183] van Zimmeren, Chapter 5 of this volume.
[184] Ibid.; Spence, Chapter 11 of this volume. [185] See p. 446–47.
[186] See Van Overwalle, et al., 'Models for facilitating access to patents on genetic inventions', 2006. Also see Nuffield Council on Bioethics, *The Ethics of Patenting DNA: A Discussion Paper,* Nuffield Council on Bioethics, 2002, 109 pp.
[187] See www.gbif.org. Also see Edwards, Chapter 6 of this volume.

worldwide network of data providers and indexes the data allowing users to search all the information at once for free, instead of having to go individually to each data provider's site. The data themselves, as well as the related IP remain with the data providers.[188] Although different terms are in use – Edwards refers to a 'distributed network of information',[189] whereas others speak of 'a federated data repository'[190] – it is clear that GBIF can be qualified as a free information clearinghouse. GBIF is not a technology-exchange clearinghouse, as it does not provide any brokerage services to link data providers with users. Nor is GBIF an open access clearinghouse, as it provides information on a free and open access basis, but cannot guarantee free use of that data, as the IP remains with the provider and prior consent and/or remuneration might be needed for the use of the data. A specific biotechnology information patent clearinghouse is Patent Lens, a fully text-searchable database of US, European, Australian and international agricultural and life-science patents, established in the framework of BiOS.[191] An additional information clearinghouse for open source biotechnology is BioForge.[192]

A specific biotechnology technology exchange platform is the Public Intellectual Property Resource for Agriculture (PIPRA).[193] As Bennett and Boettiger explain, a major activity of PIPRA is the provision of information on public/non-profit patented agricultural technologies and on the licensing status of each technology. PIPRA also facilitates bringing scientists and technology transfer offices together, which is made possible by its collaborative working relationships with the owners of the technologies.[194] These characteristics lead Bennet and Boettiger

[188] Ibid. [189] Ibid.

[190] Reichman, J.H. and Uhlir, P.F. 'A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment', **66** *Law and Contemporary Problems*, 2003, 315–462.

[191] www.bios.net/daisy/bios/patentlens.html. For more details, see Berthels, N. 'Case 8. CAMBIA's Biological Open Source Initiative (BiOS)', Chapter 13 of this volume.

[192] For more information on BioForge, see Berthels, Chapter 13 of this volume.

[193] www.pipra.org.

[194] See Bennett and Boettiger, Chapter 8 of this volume. Dedeurwaerdere suggests that exactly this investment of time and money in building a good reputation and extended confidence has played an important role in the case of PIPRA, where the reputational benefits gained by creating facilitated access to gene technologies for developing nations outweigh the market benefits to be expected from this niche (see Dedeurwaerdere, Chapter 24 of this volume, with reference to Rai, A. K., 'Proprietary Rights and Collective Action: The Case Of Biotechnology Research With Low Commercial Value', in K. Maskus and J. Reichman (eds.), *International Public Goods and Transfer of Technology*, Cambridge, Cambridge University Press, 2005, 288–306).

to believe that PIPRA is an information clearinghouse,[195] whereas van Zimmeren qualifies these PIPRA activities as a technology exchange clearinghouse.[196] An additional activity within PIPRA is the design of research tools in its own laboratories, and the distribution thereof to the broader research community on the basis of pre-negotiated licences to the pooled set of proprietary technologies incorporated in the research tool vectors. This activity, leads Bennet and Boettiger to conclude that PIPRA is also a standard licence clearinghouse,[197] which is debatable.[198] Anyhow, it is beyond doubt that PIPRA "fundamentally [is] an IP clearinghouse that operates on several levels".[199]

The key example of an open access clearinghouse in genetics is the SNP Consortium, a non-profit entity aiming to identify and collect single nucleotide polymorphisms (SNPs) and to create and make freely publicly available the SNP map of the human genome, without any proprietary rights.[200, 201]

An example of a standard licensing clearinghouse facilitating access to and use of proprietary genetic inventions is somewhat difficult to picture. As Nguyen points out, a major initiative within Science Commons is the Material Transfer Agreement (MTA) Project, which focuses on the transfer and (re)use of unique tangible research resources, such as biological materials and reagents, by setting up an infrastructure for listing, locating and licensing such materials, by way of standard contracts for intra-academic material transfer and transfer between academia and industry.[202] The MTA project within Science Commons

[195] See Bennett and Boettiger, Chapter 8 of this volume, more in particular p. 140, where the above services are described at length.

[196] van Zimmeren, Chapter 5 of this volume. See also pp. 446–47.

[197] Bennett and Boettiger, Chapter 8 of this volume.

[198] These activities cannot justify to qualify PIPRA as a standard clearinghouse, as a it misses out on one of the main characteristics of a clearinghouse, namely to act as an intermediary platform to exchange services between (a variety of) provider*s* and (a variety of) users. In the PIPRA model there is a direct exchange between *one* provider and a variety of users. Might PIPRA start offering more than just its own technology through standard licenses to the users, it might probably be qualified as a standard license clearinghouse. See also pp. 446–47.

[199] See Bennett and Boettiger, Chapter 8 of this volume.

[200] http://snp.cshl.org. For more details, see Verbeure, Chapter 1 of this volume; van Zimmeren, Chapter 5 of this volume.

[201] For the very reason that the SNP initiative does not employ its patents to enforce a specific license behaviour one would be inclined to say that the SNP Consortium may well be termed 'open access', but does not qualify as 'open source'. (On the importance of patents in an open source context, see the section on 'credible commitment' in Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume).

[202] See Nguyen, Chapter 9 of this volume. The vast majority of the materials are unpatented and the basis for the agreements is located in traditional property law.

can definitely be qualified as a standard licensing clearinghouse, but one focusing on access to biological material, rather then on facilitating access to patents.

At present no working example of a royalty collection clearinghouse in genetics exists, as the Global Bio-Collecting Society (GBS) did not materialize.[203] The GBS was designed to be an efficient, fair and equitable model for the exchange of indigenous knowledge between knowledge holders (indigenous groups) and knowledge users (the life-science industry) in the commerce of biodiversity. Although the GBS model was constructed to encourage arrangements between merely non-IP holders (indigenous groups) and IP holders, the concept could be applied to the more classical IP holder (patentee) and IP user (licensee) situation.[204]

What type of clearinghouse should be ultimately contemplated in genetics to facilitate access and use of patented genetic inventions? Will a standard licensing clearinghouse do the job? According to van Zimmeren, a differentiated and standardized licence regime might meet the need to decrease search and bargaining costs and prevent royalty stacking in an adequate manner in genetic diagnostics.[205] Spence is very critical about the idea of standardized clearinghouses in genetics and argues it may be impossible to develop an appropriate library of standardized licences for all but a limited range of uses of a limited range of inventions, such as patented DNA sequences and mutations, and a handful of commonly used diagnostic tools.[206] However, this critique indirectly amounts to an approval of van Zimmeren's plea for a standardized licence regime in genetic diagnostics.

Will a clearinghouse encompassing royalty collection, disbursement accounting, monitoring and enforcement bring an optimal solution? Van Zimmeren points out that some of the peculiar characteristics of current copyright societies cannot be transposed to the patent arena as such and recommends further reflection on the relation between the society and its *members* (e.g. singers) (more specifically the role of the society to represent members' interests vis-à-vis the users and act as trustees, rather than proceeding as an independent intermediary)[207]

[203] Drahos, P., 'Indigenous Knowledge, Intellectual Property and Biopiracy: Is a Global Bio-Collecting Society the Answer?', **20** *European Intellectual Property Review*, 2000, 245–50.

[204] Van Overwalle, et al., 'Models for facilitating access to patents on genetic inventions', 2006, 146; van Zimmeren, Chapter 5 of this volume.

[205] van Zimmeren, Chapter 5 of this volume.

[206] Spence, Chapter 11 of this volume.

[207] van Zimmeren, Chapter 5 of this volume. In the same sense, Spence, Chapter 11 of this volume.

and on the peculiar relation between the society and its *users* (e.g. radio-stations) (more in particular the use of so-called 'blanket licences' whereby the users acquire unlimited access to the repertoire of the members by a single licence for a fixed royalty,[208] and the transfer of the rights of the right holders to the society in an exclusive and definitive manner[209]). Van Zimmeren concludes that the time is not ripe yet for a patent royalty collection clearinghouse with an elaborate package of services.[210] Spence claims that any analogy of a patent clearinghouse and a copyright collecting society is very inexact and false, as there are too many differences in purpose and context.[211] He argues that a one-stop-shop is not only unachievable, but also potentially undesirable, as clearinghouses may even exacerbate, rather than relieve current problems.[212]

The institutional and managerial make up of a patent clearinghouse for genetics may take different forms. It could be established as a neutral public agency or as a private initiative, on a non-for-profit or profit basis, on a national, regional, international or nodal scale, and as a voluntary scheme or a statutory framework on a mandatory basis. Van Zimmeren favours private initiatives or public–private partnerships over a statutory, compulsory regime. Spence argues that the issue here is whether the clearinghouse would operate "to squeeze as much return as it could" or attempt "to fulfil a public duty by maximizing activity in the biomedical sciences".[213]

In conclusion, the establishment of a fully fledged patent royalty collection clearinghouse is probably 'too big a leap forward' for the time being, as van Zimmeren remarks. Following the positive evaluation of standard clearinghouses in genetic diagnostics, major efforts should probably be directed in the coming years towards setting up patent standard clearinghouses in genetic diagnostics and tuning them to the varied needs of this branch of genetics, as well as to the characteristics of the biotech business sector, while continuing further study of the patent royalty collection clearinghouse, possibly in a wider field of application. The ultimate touchstone for an acceptable clearinghouse – whatever its shape and function – will be the way in which it facilitates

[208] van Zimmeren, Chapter 5 of this volume. [209] Ibid. [210] Ibid.

[211] To name only one: it is pretty clear that gene patents are most frequently for upstream inventions, while copyright usually protects works that are finished products; if a collecting society wrongly prices a work, at most a particular use of the work is frustrated; for a gene patent, a whole project may be frustrated and technical progress hindered – see Spence, Chapter 11 of this volume.

[212] Ibid.

[213] If experience of the copyright collecting societies is any guide at all, the first objective is more likely.

access to and use of patented genetic inventions in a commercially sustainable way, while responding to concerns on equitable access to healthcare.

Open source models

Another model to deal with patent proliferation and fragmentation and opaque and complex patent landscapes is open source. Is open source indeed a model that facilitates cumulative technology development by removing IP-related barriers and facilitate freedom to operate? Does open source maximize access and use of proprietary genetic inventions? The authors in Parts III and V have explored open source in depth to verify whether this model indeed offers a solution of the current problems in patent law.

General concept and framework

The term 'open source' has several layers of meaning. In her concept paper, Hope refers to a set of *licensing* criteria to define open source. A licence is open source if "it allows anyone, anywhere, for any purpose, to copy, modify and distribute the software (where distribution takes place either for free or for a fee) without having to pay royalties to the copyright owner",[214] it being understood that the software program includes source code.[215] According to Rai, emphasizing the licensing component is "excessively formalistic".[216] Rather than referring to the legal architecture and the details of licences to characterize open source, she prefers to point to a mode of *production*, centering around "open and collaborative

[214] Hope, Chapter 12 of this volume with reference to Rosen, L., *Open Source Licensing: Software Freedom and Intellectual Property Law*, New Jersey, Prentice Hall, 2004. As to distribution, the Open Source Definition provides the following: "1. Free Redistribution: The license shall not restrict any party from selling or giving away the software as a component of an aggregate software distribution containing programs from several different sources. The license shall not require a royalty or other fee for such sale" (see http://opensource.org/osi3.0/node/4).

[215] As to source code, the Open Source Definition provides the following: "2. Source Code. The program must include source code, and must allow distribution in source code as well as compiled form. Where some form of a product is not distributed with source code, there must be a well-publicized means of obtaining the source code for no more than a reasonable reproduction cost preferably, downloading via the Internet without charge. The source code must be the preferred form in which a programmer would modify the program. Deliberately obfuscated source code is not allowed. Intermediate forms such as the output of a preprocessor or translator are not allowed." (see http://opensource.org/osi3.0/node/4).

[216] Rai, A.K., 'Critical commentary on 'open source' in the life sciences', Chapter 15 of this volume.

research".[217] Taubman recognizes that the call for open source can refer to both approaches: "licensing structures … granting access on the condition of reciprocal access" (= open source as a model or template), as well as "a general pattern for structuring networks of … researchers" (= open source as a metaphor).[218]

Whatever the definition selected, the phrase 'open source' as applied to patents results in a kind of misnomer, as an essential function of the patent system is to ensure openness in the sense that the information about the invention (cf. the 'source code') is made available through disclosure or deposit (of physical specimens of micro-organisms).[219] Rather does the term 'open source' in a patent context refer to a certain philosophy of access, improvement, production and public use.

'Open source' software should be distinguished from 'free' software. The term 'free' software refers to the fact that the technology is publicly available or accessible without restraint upon modification, examination or redistribution[220] without payment of royalties to the licensor,[221] not necessarily in the sense that a licensor cannot sell a product making use of open source.[222] Because of the confusion which may arise from the term 'free', it has been suggested to abandon the term.

Open source is characterized by three essential elements in the opinion of Hope, namely (1) credible commitment, (2) competition and, optionally, (3) copyleft. Credible commitment means that to be open source, a technology must be protected by IP or other proprietary rights and distributed on terms that are perceived to be legally enforceable.[223] As various observers have remarked, this is by far the most striking – and unexpected – feature of the open source model: open source is *based* on IP, in order to ensure adherence to the terms of the licence.[224] A technology that is made available under the open

[217] Rai, 'Open and Collaborative Research: A New Model for Biomedicine', 2005, 131. A model is open – and Mertonian – in the sense that "scientists work openly without secrecy and the usual sorts of exclusionary proprietary rights"; a model is collaborative – and goes beyond Merton – if it requires that "scientists [to] work closely with others outside their own lab or small firm". As Rai points out, the term 'open and collaborative' was invoked in a letter to the WIPO (available at www.cptech.org/ip/wipo/kamil-idris-7july2003.pdf), but does not specify the terms.

[218] Taubman, Chapter 16 of this volume. Taubman refers to two additional levels of meaning, more in particular open source as a cultural community (open source as a meme) and open source as affirmation of an inherent value in certain behaviour (open source as a badge of ethical approval).

[219] Boettiger, S. and Burk, D., 'Open Source Patenting', **1** *JIBL*, 2004, 221; Taubman, Chapter 16 of this volume.

[220] Boettiger and Burk, 'Open Source Patenting', 2004, 223.

[221] Hope, Chapter 12 of this volume. [222] Ibid. [223] Ibid.

[224] See Yochai Benkler, 'Coase's Penguin, Or, Linux and the Nature of the Firm', **112** *Yale L.J.*, 2002, 369–446; Rai, 'Open and Collaborative Research: A New Model

source model is indeed not in the public domain,[225] but is owned by the licensor, who makes a legally enforceable promise via the licence agreement not to interfere with others' freedom to use, improve or circulate the technology[226] and thus not to lock them in a web of IP. Competition refers to a level playing field between the licensor and the licensees of open source technologies with respect to the legal freedom to use and commercialize both the technology itself and any downstream innovations.[227] In that regard, an open source licence may not impose field-of-use or territorial restrictions, nor may it prevent a licensee to start a new branch of collaborative development ('fork the code'). Copyleft imposes an obligation on the licensee to make any downstream innovations that it chooses to distribute beyond the boundaries of its own organisation available under the same terms as the original technology.[228]

Open source licences can be divided into two categories. A first subset includes licences that disclose source code but impose few if any requirements on recipients.[229] A second subset pertains to 'copyleft' licences. A licence is 'copyleft' if it carries the additional obligation to make improvements to the software available to other users on the same open source terms as the recipients received it.[230]

The archetypal open source copyleft licence is the General Public License (GPL), originally written by Richard Stallman in 1989 to develop a complete Unix-like operating system in the framework of the GNU project, launched in 1984.[231] The GPL was later adopted by Linus Torvalds for the Linux kernel in 1992.[232] The GPL allows anyone to use the licensed program, to study its source code, to modify it, and to distribute (un)modified versions to others, under the same terms as the initial licence.[233] As Hope points out, it is this

for Biomedicine', 2005 (131), 137. Absent an IP right, restrictions must be imposed entirely through contract, which might do more damage than good, as the HapMap project has shown, see Rai, Chapter 15 of this volume.

[225] Similarly, Jefferson, R., 'Science as a Social Enterprise. The CAMBIA, BiOS Initiative', **1** *EconPapers,* issue 4, 2006, 13–17. Contra, Rai, Chapter 15 of this volume: "… various other flavors of open source essentially amount to a dedication of source code to the public domain. Those who improve upon source code distributed under BSD licenses may feel a [social] norm-based obligation to contribute their improvements back, but they are under no legal obligation to do so".

[226] Hope, Chapter 12 of this volume. [227] Ibid. [228] Ibid.

[229] See Rai, Chapter 15 of this volume.

[230] Hope, Chapter 12 of this volume; Rai, Chapter 15 of this volume.

[231] See www.gnu.org/.

[232] Linux is the contraction of Linus' Minix (Minix was a version of UNIX which Linus Torvalds enhanced). The name Linux was chosen by the developer (Linus Torvald) to refer to the *kernel* of the 'GNU/Linux' operating system.

[233] See www.gnu.org/licenses/gpl.html.

final proviso that makes the GPL a copyleft licence, giving it its 'viral' character.[234]

Open source models may have various advantages for both the owner-user and the follow-up users.[235] Addressing the issue of uncertainty of innovation is one of them. As Aoki clarifies, open source functions as a form of incomplete contract when there is uncertainty and informational problems, because knowledge is part of ongoing cumulative innovation.[236]

But open source models may also entail some risks. Ullrich warns that open source models may lead to antitrust concerns.[237] Whether open source models always follow a free access rationale rather than a business strategy, needs to be examined more closely.

Transposition to genetics

Applying the open source approach to the life sciences, immediately raises a question of terminology. Some authors prefer to speak of 'free biology' or 'open access biology',[238] but this phrase is subject to criticism. Because of the confusion which may arise from the term 'free',[239] the term 'open source biology' is to be preferred. Adapting the open source approach to the genetic milieu and particularly to patent licensing in genetics, raises a series of other, more important issues as well, as the genetic sector is perceived to be quite different from the software sector. In the open source sector, the technology at hand is software code, the major IP instrument deployed is copyright, the capital costs of development tend to be lower, the prevailing industry culture is thought to be less proprietary and innovations are typically protected using different sets of exclusive rights.[240]

Notwithstanding the sectorial differences, some working examples of open source have emerged in the life sciences, mainly in the field of

[234] Hope, Chapter 12 of this volume. Similarly, Boettiger and Burk, 'Open Source Patenting', 2004.

[235] Hope, Chapter 12 of this volume.

[236] Aoki, Chapter 23 of this volume. Also see Hope, Chapter 12 of this volume, referring to free revealing users and user-owners.

[237] See Ullrich, Chapter 22 of this volume and the references cited there, amongst which Böcker, L., 'Mit freier Software gegen den Wettbewerb? Die General Public License (GPL) als horizontale Wettbewerbsschränkung', *Festschrift F. Säcker*, Berlin, 2006, 69.

[238] For more details, see Boettiger & Burk, 'Open Source Patenting', 2004, 225.

[239] See Hope, Chapter 12 of this volume.

[240] Hope, Chapter 12 of this volume. Similarly, Boettiger & Burk, 'Open Source Patenting', 2004, 223; Boettiger, S. and Wright, B.D., 'Open Source in Biotechnology: Open Questions', *Innovations,* 2006, (45), 48; Taubman, Chapter 16 of this volume.

agricultural biotechnology. A prominent example is the Biological Open Source (BiOS) License from the Centre for Applications of Molecular Biology in International Agriculture (CAMBIA), a private non-profit research institute located in Canberra.[241] Founded by molecular biologist Richard Jefferson about fifteen years ago, CAMBIA pioneered, and subsequently patented the GUS[242] and TransBacter[243] technology serving as a prominent research tool in agricultural biotechnology. The BiOS initiative was launched in 2004[244] and is intended to make these biological research tools widely available. Improvements made to these enabling tools are to be shared under the BiOS License regime, but the products or materials made, created, or obtained by using them, do not fall under this provision and can be commercialized on a competitive and proprietary market under non-open source conditions.[245] Indeed, the BiOS initiators are not averse to users of these tools filing patents on products made by use of the tools, the intention is to preserve public access to the initial tools and later improvements and modifications.[246]

Another example is the open source style licence policy promoted by Diversity Arrays Technology (DArT) Proprietary Limited, discussed at length by its founding father Andrzej Kilian in his chapter.[247] Initially set up by Kilian in 2001 as a wholly owned subsidiary from CAMBIA

[241] See www.bios.net. Also see Berthels, Chapter 13 of this volume.

[242] The GUS technology relates to the β-glucuronidase (GUS) gene fusion system and to the cloning and characterization of the β-glucuronidase and glucuronide permease genes of *Escherichia coli*. Because of the abundance and availability of useful substrates for β-glucuronidase enzyme, GUS gene fusions may serve as a superior reporter gene system as well as an effective means of altering cellular phenotype. There are also implementations in conjunction with recombinant glucuronide permease, which may be used to render host cells permeable to β-glucuronidase substrates (see www.cambia.org/daisy/cambia/2539.html). Also see R.A. Jefferson, R.A., Kavanagh, T.A. and Bevan, M.W., 'GUS Fusions: Beta-Glucuronidase as a Sensitive and Versatile Gene Fusion Marker in Higher Plants', **6**(13) *European Molecular Biology Organization Journal,* 1987, 3901–7. For information on patents on the GUS technology, see footnote 251.

[243] The Transbacter technology relates generally to technologies for the transfer of nucleic acids molecules to eukaryotic cells. In particular non-pathogenic species of bacteria that interact with plant cells are used to transfer nucleic acid sequences. The bacteria for transforming plants usually contain binary vectors, such as a plasmid with a vir region of a Ti-plasmid and a plasmid with a T-region containing a DNA sequence of interest (see www.cambia.org/daisy/cambia/2538.html). For information on patents on the TransBacter technology, see footnote 251.

[244] Dennis, C., 'Biologists Launch "Open-Source Movement"', **431** *Nature (News)*, 2004, 30 September 2004, 494.

[245] Berthels, Chapter 13 of this volume.

[246] See Boettiger and Burk, 'Open Source Patenting', 2004, 221.

[247] See Kilian, A., 'Case 9. Diversity Arrays Technology Pty Ltd.: applying the Open source philosophy in agriculture', Chapter 14 of this volume.

to deliver the Diversity Arrays Technology (DArT),[248] the company separated from CAMBIA in 2003 to become an independent privately owned entity.

Do the three key objectives of open source licensing (credible commitment, competition and, optionally, copyleft) constitute insurmountable obstacles to the translation of open source software principles into the life sciences? Although the phrase 'credible commitment' might not always be employed, this feature seems to be well understood by entrepreneurs active in the realm of biotech: "The idea of using patent licences not to extract a financial return from a user of a technology, but rather to impose a covenant of behaviour, is the single feature of BiOS that is most resonant with Free and Open Source Software."[249] As Berthels confirms, it is crucial to BiOS and the owners of technology "to enforce patents and litigate infringers who are not agreeing to the BiOS licence. BiOS therefore has to ascertain substantial financial means to obtain and enforce their patent portfolio".[250] Both in the BiOS and the DArT case an IP platform was present,[251] allowing the IP owners to impose an open source behaviour on the licensees. Hope also indicates that the credible commitment requirement does not seem to raise a principle problem, apart from the fact that the price for obtaining IP – mostly patents – may be relatively (prohibitively?) high.

The competition requirement has proven to be rather problematic to implement in the genetic field. According to Hope, a major concern with regard to the BiOS licence is that the initial innovators seem to use their IP in the seed technology to retain control over its ongoing development or to insist on special rights, leading to insufficient freedom to 'fork the code'.[252] CAMBIA accepts such criticism as indicative of

[248] Wenzl, P., Carling, J., Kudrna, D., Jaccoud, D., Huttner, E., Kleinhofs, A. and Kilian, A., 'Diversity Arrays Technology (DArT) for Whole-Genome Profiling of Barley', **101** *PNAS*, 2004, 9915–20.

[249] Jefferson, R., 'Science as a Social Enterprise. The CAMBIA, BiOS Initiative', **1** *EconPapers,* issue 4, 2006, 13–17.

[250] Berthels, Chapter 13 of this volume.

[251] As to BiOS, the core IP for GUS technology is embedded in three US patents (US 5.268.463, US 5.432.081 and US 5.599.670) and for the TransBacter technology, patents are pending in the US (US 2005/0289672, US 2005/0289667) and in Europe (EP 1781082) (For more information on these (pending) patents, see www.cambia.org/daisy/cambia/2539.html and www.cambia.org/daisy/cambia/2538.html, www.espacenet.com or www.uspto.gov/patft/index.html). As to DArT, the critical formal IP for practicing DArT technology was encapsulated in one patent family (US Patent 6.713.258 B2) initially owned by CAMBIA, but reassigned from CAMBIA to DArT Pty Ltd during the preparation of the case study for the present book (see Kilian, Chapter 14 of this volume).

[252] Hope, Chapter 12 of this volume.

a naïve expectation that one size fits all.[253] It is argued that as biological innovation, biotechnology and software are drastically different in many aspects, a different approach regarding open source licensing could be justified.[254] [255] Rai argues that as a practical matter, this divergence from open source may be more apparent than real, as forking in open source software is rare in any event.[256]

The final key element, copyleft, has equally raised concern in a life sciences context. In conventional biotechnology licensing non-exclusive grant back of licensee improvements are well known.[257] The BiOS License bears resemblance to such grant back provisions, which brings Hope to say that such arrangements – even though considered harmless by competition authorities – establish a 'club atmosphere', a 'tit for tat' approach where the licensor gains a special privilege, and are therefore not open source.[258] As DArT is equally based on the idea that improvements to the technology should be subject to a grant-back provision from licensees,[259] the same critique might apply. However, the critique towards DArT might be somewhat toned down as DArT does not claim to be 'open source', but rather to deliver an 'open source-*style*' licence[260] which is 'loosely' [261] based on open source principles.

[253] See Berthels, Chapter 13 of this volume. [254] Ibid.

[255] Hope's critique might stem from the fact that the BiOS arrangement claims to be 'open source' (BiOS stands for 'Biological Open Source', see www.cambia.org), whereas the BiOS license does not fulfill the necessary criteria to apply this term. It remains to be seen to what extent the critique from Hope would hold, if BiOS no longer described itself as an 'open source' arrangement, but rather as an 'open source-*like*' initiative.

[256] Rai, Chapter 15 of this volume, with reference to Raymond, E., 'The Magic Cauldron', 1999 (available at www.catb.org/~esr/writings/magic-cauldron/magic-cauldron.html).

[257] See Boettiger and Burk, 'Open Source Patenting', 2004, 221.

[258] Hope, Chapter 12 of this volume. Also see Hope's detailed critique on the BiOS License posted on the Bioforge website on 16 November 2006 (see www.bioforge.net/forge/message.jspa?messageID=1219#1219). Cf. infra, pp. 446–47.

[259] "Open Source principles mean that improvements to the technology made by any licensee are shared between all licensees. A key requirement of any sub-license under those principles is the 'grant-back' obligation: all sub-licensees agree to grant to CAMBIA, at no cost, the rights to use any Improvement of the technology, and CAMBIA will grant those rights at no cost to all licensees and sub-licensees" (see www.diversityarrays.com/intellectualproperty.html). "Improvements shall mean any method, improvement or variant of Diversity Arrays Technology that, but for the license granted, would infringe the Licensed Patent and is protected by Intellectual Property Rights. All licensees and sub-licensees agree to provide Grant Back Intellectual Property Rights to CAMBIA, at no cost, for Improvements as defined above. CAMBIA will license the Grant Back Intellectual Property Rights at no cost to all licensees and sub-licensees" (see www.diversityarrays.com/intellectualproperty.html). Also see Kilian, Chapter 14 of this volume.

[260] Kilian, Chapter 14 of this volume. [261] Ibid.

An unsettled issue that calls for further reflection is what will happen when an improvement is developed *independently* from the original research tool made available under open source conditions. Might the resulting patent on the improvement not create a blocking situation? Can recourse on the initial tool be taken on the basis of prior use? This situation seems to be different from the one where the improvement *is based* on an open source tool with a proprietary technique. In other words, when a new (improved) research tool is developed, starting from an open source material and mixed with some proprietary technology. In the latter case, it has been suggested that improvements on open source tools can be patented and commercialized, but should be subject to a grant-back licence.

An interesting question is how an open source model can be economically and commercially sustainable. A distinction should be made between 'seed money' to establish the core technology and start up an open source company, and revenues to keep the open source company viable in the long run.[262]

As to the set-up money, CAMBIA received a grant from the Rockefeller foundation as well as computer utilities from IBM to establish the BiOS initiative.[263] In the case of DArT, seed money to develop the DArT technology was collected from government funding, philanthropic donations and research grants.[264] Since CAMBIA relied on grants from foundations to develop the technology rather than on volunteers, some wonder whether the BiOS approach can still be regarded as pure open source.[265] However, it is difficult to imagine that volunteer work would be a prerequisite for open source. And what is 'pure' open source?

As to the generation of revenues, various approaches have been put to work, as Hope illustrates. A first strategy is to use open source technology to enhance the appeal of a complementary product.[266] Closely looking at the BiOS License project, suggests that revenue is indeed also yielded from the sale of research tools, such as transformation vectors and plasmids.[267] A second way is to provide accessory services.[268] As has

[262] Hope mainly seems to focus on the second question (see Chapter 12 of this volume).
[263] Berthels, Chapter 13 of this volume, with reference to Dennis, 'Biologists Launch "Open-Source Movement"', 2004.
[264] See Kilian, Chapter 14 of this volume.
[265] See 'The Triumph of the Commons: Can Open Source Revolutionise Biotech?' *The Economist*, February 10, 2005, cited in Berthels, Chapter 13 of this volume.
[266] Hope, Chapter 12 of this volume.
[267] See the 'Technology Support Services Subscription Agreement', entitling BiOS licensees to receive licensed material and aiming at recovering some of the costs involved.
[268] Hope, Chapter 12 of this volume.

been clearly demonstrated by Kilian in the DaRT case, the majority of revenue is generated by providing value-added genotyping services and genetic testing, including data production and downstream processing.[269] A third possibility is to use the open source technology as a market positioner, in building an organization's brand and reputation.[270]

Although translating open source from software to genetics is unlikely to be straightforward and will be more than "simple cutting and pasting",[271] Hope convincingly argues that transferring open source principles from their original milieu to biotechnology is possible and that a copyleft-style open source licence in relation to diagnostic tests based on gene patents is feasible.[272] However, three remarkable observations might tune down the optimism from Hope. First, as Rai indicates, too much focus on legal architecture and the licensing component will fail to accommodate the diversity in open source projects and contexts.[273] Second, it remains to be seen to what extent open source licensing can indeed deal with cumulative technology and subsequent patent fragmentation.[274] The DArT case clearly demonstrates that the open source licence model is a viable commercial strategy through the provision of accessory genotyping services in the context of the DArT technology package, but it is unclear to what extent the DArT open source-style licence offering access to the core DArT technology has facilitated and simplified uptake of this technology.[275] Third, as Kilian himself remarks, the DArT experience seems to suggest that the open source philosophy will be difficult to be put to practice in market segments aiming at the largest potential profit margins, such as the biomedicine sector, unless a specific niche can be identified, likely in an area of

[269] For details, see Kilian, Chapter 14 of this volume.
[270] Hope, Chapter 12 of this volume. [271] Rai, Chapter 15 of this volume.
[272] Hope, Chapter 12 of this volume. [273] Rai, Chapter 15 of this volume.
[274] Boettiger and Wright, 'Open Source in Biotechnology: Open Questions', 2006, 45–63.
[275] This conclusion is based on Kilian, Chapter 14 of this volume: "Under this [the present] arrangement, CAMBIA offers *DArT* [technology] through its BiOS initiative while we at DArT PL are offering a licence to practise the technology in the context of a *complete technology package* … as the list of BiOS licensees is not publicly available it is impossible to judge the extent of DArT's uptake or development through this channel." And it is also founded on Kilian, Chapter 14 of this volume: "Interestingly, a few years after the separation of DArT PL from CAMBIA the level of interest in licensing just *the right to practise the technology in general* is very low (practically non-existent), while at the same time the level of interest in our *genotyping services and technology provision* in general is rapidly increasing." [Our italics]

limited financial opportunity, where competition with 'mainstream' companies would be less intense.[276]

In conclusion, diagnostic testing might possibly qualify as an area fit to introduce and apply the open source principles in the near future. However, further research is necessary to examine whether the open source approach can provide alternative and viable business models and can contribute to preserving freedom to innovate in the genetic sector at large.

Liability regimes

So far, we have mainly focused on patent thickets as one of the major problems observed in upstream genetic research. We have explored mechanisms designed to facilitate access to and use of patented genetic inventions. On top of this, problems in downstream product development have been reported relating to the translation of early-stage genetic inventions into applications. The liability regime has been put forward as a candidate construction to tackle this problem. Do liability rules indeed assist in bridging the gap between upstream and downstream research? In Part IV, the authors have interrogated the liability regime and its capacity to facilitate translation of basic inventions into products.

General concept and framework

The notion of 'liability rules' finds its origin in the entitlement theory articulated by Calabresi and Melamed in their epoch-making contribution 'Property Rules, Liability Rules, and Inalienability: One View of the Cathedral'.[277] Entitlement theory distinguishes between entitlements protected by property, liability or inalienability rules. An entitlement is protected by a property rule if someone must buy it from its holder in a voluntary transaction in which the value of the entitlement is agreed upon by the seller. Property rules involve a state decision as to who can be given an entitlement, but not as to the value of the entitlement. An entitlement is protected by a liability rule, if someone may use or destroy the initial entitlement if he is willing to pay an objective determined value for it. Liability rules thus involve additional

[276] Cf. Kilian, Chapter 14 of this volume.

[277] Calabresi, G. and Melamed, A.D., 'Property Rules, Liability Rules, and Inalienability: One View of the Cathedral', **85** *Harv. L. Rev.*, 1972, 1089–1092. This title refers to Claude Monet's series of paintings of Rouen Cathedral, implying that the authors' academic analysis is but one look at a subject that can be considered from various points of view.

state intervention: the state does not only decide whom to entitle, but determines the value of the transfer or destruction. Or, as Merges puts it, property rules are 'absolute permission rules': one cannot take the entitlements without prior permission of the holder. Liability rules are 'take now, pay later' rules: others can use the entitlement without permission of the owner, so long as they adequately compensate the owner later.[278] In translating the Calabresi–Melamed concepts to the IP arena, Reichman describes a liability rule as a rule "that takes the form of an automatic licence without the power to exclude".[279] The major difference between a liability rule and an IP right is that a liability rule, in contrast to an IP right, does not allow to control follow-on applications: a liability rule allows companies within a defined period of time, to borrow one another's innovation, on the condition they contribute to the costs of development.[280]

A distinction can be drawn between two types of liability rule regimes. A first type, the *contractually constructed* liability regime, may be created when "contracting parties start with property rule entitlements, and wind up subject to a collectively determined liability rule".[281] Transferred to an IP setting, this happens when stakeholders voluntarily seek to obtain private arrangements with outcomes that differ from what the default rules of IP law might otherwise provide.[282] A second type, the *codified* liability rule comes into being when the legislature imposes entitlements compensation for certain uses *ex ante*.[283]

[278] Merges, 'Contracting into Liability Rules', 1996, (1293), 1302.

[279] See Reichman, J.H., 'Of Green Tulips and Legal Kudzu: Repackaging Rights in Subpatentable Innovation', **53** *Vanderbilt Law Review*, 2000, 1743–98. Also see Reichman, J.H. and Lewis, T., 'Using Liability Rules to Stimulate Innovation in Developing Countries: Application to Traditional Knowledge', **337** *International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regime*, K.E. Maskus and J.H. Reichman (eds.), 2005, 337–366.

[280] See Reichman, 'Of Green Tulips and Legal Kudzu: Repackaging Rights in Subpatentable Innovation', 2000. Also see Reichman and Lewis, 'Using Liability Rules to Stimulate Innovation in Developing Countries: Application to Traditional Knowledge', 2005.

[281] See Merges, 'Contracting into Liability Rules', 1996 (1293), 1303, who called the process of creating "contracting into liability rules", and the resulting organizations "private liability rule organizations".

[282] See Reichman and Uhlir, 'A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment', 2003, from whom the term 'contractually constructed liability regime' has been drawn. Also see Reichman, 'Of Green Tulips and Legal Kudzu: Repackaging Rights in Subpatentable Innovation', 2000. Also see Reichman and Lewis, 'Using Liability Rules to Stimulate Innovation in Developing Countries: Application to Traditional Knowledge', 2005.

[283] Rai, A.K., Reichman, J.H., Uhlir, P.F. and Crossman, C., 'Pathways across the valley of death: novel intellectual property strategies for accelerated drug discovery',

Both subtypes have in common that they aim at converting a property rule into a liability rule. Both subtypes differ, however, in the way this transition is achieved: in the first type the initiative is taken by private parties, contrary to the second subtype where the legislator is the driving force. This results in some additional differing features: in the first model the value of the transfer or destruction of the entitlement is determined by private parties, in the second the value is set by the state; in the first subtype the impact of the measure might be rather limited in terms of people involved, whereas the effect in the second type might be more extended in terms of people affected.

Examples of *contractually*-constructed liability regimes include the liability regime which two-tiered public–private partnerships may carry along, as further elucidated by Rai et al. A leading example of a *codified*, government-determined liability regime might well be the compensatory liability regime described in Reichman's trendsetting paper 'Of Green Tulips Green Tulips and Legal Kudzu', which seems to have been originally designed as an alternative reward system for subpatentable innovation, to be enacted by the legislature as an autonomous, codified regime.[284] Another example of formal liability rules is the codified compulsory licence regime and the prior use rights mechanism which can be found in various countries, as Burk indicates.[285] Last but not least, Ullrich turns our attention to the patent pool regime and suggests that requiring an open, non-discriminatory licensing policy to everyone in third-party licensing via pooling as a matter of competition law, tends to convert the exclusivity principle of patent protection into a mere liability system, i.e. into a reward-by-compensation rule.[286] It is not clear, however, whether a pool set up by private parties and subject to governmentally imposed FRAND rules should be labelled as a contractually constructed or a government-determined liability regime, or as an intermediate between the two. Further research is needed to look into this issue, and the consequences of different labelling.

In an attempt to evaluate pros and cons of liability regimes, Aoki indicates that contractually constructed liability models are helpful in cases where the outcome of innovation is uncertain and where informational problems occur. More in particular, in cases where it is unknown

Chapter 17 of this volume.

[284] Reichman, 'Of Green Tulips and Legal Kudzu: Repackaging Rights in Subpatentable Innovation', 2000.

[285] Burk, Chapter 19 of this volume. Burk notes that in the US, liability regimes are occasionally created as judge-made law.

[286] Ullrich, Chapter 22 of this volume.

a priori which molecule is most likely to succeed or which researcher will be most effective.[287]

Transposition to genetics

Translating the liability regime in a biological sphere is a rather unseen exercise. One key example of the application of a liability regime in the biological arena can be found in the mechanism approved in the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA).[288] Article 12.4 of the ITPGRFA provides that facilitated access under the Multilateral System (MLS)[289] shall be provided pursuant to a Standard Material Transfer Agreement (SMTA).[290] Under the SMTA a recipient commercializing a product shall pay 1.1 % of the sales of the product. No payment shall be due on any product that is available without restriction to others for further research and breeding.[291] As Henson-Apollonio highlights, the Treaty imposes an *ex ante* entitlement for compensation on those who make commercial applications derived from public-domain seeds.[292]

The liability regime has also been implemented in the biological milieu in the context of translational development of new drugs. To overcome the impasse IP protection may cause in downstream research in genetics, various suggestions have been put forward and several initiatives have been taken in an effort to surmount current barriers in translational research. One way that has been reported to facilitate the interaction between basic research and clinical medicine is the establishment of translational research centres such as the Regional Translational Research Centres' Initiative set up in the framework of the National Institutes of Health (NIH) Roadmap:[293] an integrated vision to optimize NIH's research portfolio and identify the most compelling research opportunities.[294] A specific response to the valley of death problem in biological research is the Molecular Libraries Initiative (MLI) undertaken in the NIH Roadmap context several

[287] Aoki, Chapter 23 of this volume.

[288] 3 November 2001, www.fao.org/ag/cgrfa/itpgr.htm.

[289] See art. 10.4 ITPGRFA.

[290] In its Resolution 1/2006 of 16 June 2006, the Governing Body of the ITPGRFA adopted the Standard Material Transfer Agreement (SMTA).

[291] See point 1, A*nnex 2*. Rate and Modalities of Payment under Article 6.7 of the ITPGRFA.

[292] Henson-Apollonio, V., 'Case 10. The International Treaty on Plant Genetic Resources for Food and Agriculture: the Standard Material Transfer Agreement as implementation of a limited compensatory liability regime', Chapter 18 of this volume.

[293] See http://nihroadmap.nih.gov/clinicalresearch/rtrc.

[294] See http://nihroadmap.nih.gov/. For an overview of other, similar initiatives, see Moran, 'Public Sector Seeks to Bridge 'Valley of Death', 2007.

years ago: an initiative to use public funding to advance research on targets (small molecules) to a stage that elicits industry interest to develop products (drugs).[295] An alternative way which has recently received much attention is the creation of contractually constructed public–private partnerships including a subsidiary liability regime. In their concept paper, Rai et al. propose a novel public–private collaboration that would help move upstream academic research on promising genes, proteins and biological pathways across the valley of death that separates upstream research from downstream drug candidates, and that would equally bridge the public–private divide. Rai et al. believe that successful translation of upstream research into potential drugs can be achieved through intensive, large-scale collaboration between academics, who possess unique skills in designing assays that can determine whether a particular protein is a promising target, and pharmaceutical firms that hold refined libraries of potentially useful small molecules as trade secrets, which are largely off limits to these same academic scientists. Rai et al. take the view that conventional patent-based strategies are unlikely to trigger such an alliance between academic researchers and private firms, as under current default rules universities might patent targets and/or associated assays and a private firm might obtain an exclusive licence to the patented target or assay to carry out the additional work. Given venture capitalists' current reluctance to invest in relatively early-stage patents, these exclusive licences may not suffice.[296] A contract-based approach that makes small molecules available without comprising future patents, might foster possible academic–private intensive collaboration more adequately.

The partnership proposed is based on a two-tiered regime, as Rai et al. explain. At Tier 1, both academic external researchers and participating companies are operating *behind* a 'veil of ignorance':[297] although the researchers may possess some information about a potentially interesting assay and the participating companies may hold some basic information about their molecules, information on both sides is relatively inchoate and precompetitive in nature. First-tier access is governed by *standardized* licences, forbidding information disclosure, misappropriation and patenting. Once a 'hit' has been identified and the academic has chosen a partnering

[295] See http://nihroadmap.nih.gov/molecularlibraries/.
[296] Rai and Reichman et al., Chapter 17 of this volume.
[297] Rai and Reichman et al., Chapter 17 of this volume, with reference to Rawls, J., *A Theory of Justice,* The Belknap Press of Harvard University Press, 1971.

company, second-tier negotiations commence. At Tier 2, qualified researchers and participating companies move *beyond* the 'veil of ignorance' and receive all relevant information. *Custom-made* contractual arrangements specify relations between the academic and the partnering company and the distribution of expected royalties from the (then patented) lead compound. In the event overlaps occur between molecules from the partnering company and other, initially participating, firms, a supplementary system of royalties automatically comes into play, governing compensation to any firm that had provided structural information about molecules leading to a hit, even though that firm was not chosen by the researcher as final partner. In other words, participating firms would be contracting into a subsidiary set of 'take and pay rules' or liability rules, rather than relying entirely on exclusive property rights.[298] Central to the public–private partnership is the trusted intermediary. The intermediary hosts the pharmaceutical firms' molecules and conducts the high-throughput screening of the assembled molecules against the academics' assays. The intermediary would thus be the only party to the collaboration that possesses full knowledge and plays a pivotal role in handling confidential information. The intermediary would assume responsibility for the day-to-day management and administration of the pool of molecules as well.

The design of a two-tiered public–private framework has various benefits. Rai et al. point to a significant increase in public–private cooperation as the major advantage. Academic–company collaborations on small molecules, assay development and target validation have been established in the past on a limited, ad hoc basis. The first tier public–private partnership would provide an opportunity for the systematic formation of many more second tier relationships than currently exist.[299] On top of that, Rai et al. suggest that this model significantly reduces transaction costs.

However, a two-tiered partnership might also entail certain problems. A possible complication could arise if a Tier 2 partnership is formed and then dissolved. Another problem is that firms might be tempted to contribute only 'bad' molecules, out of fear or misappropriation. Rai et al. argue that restricting participation to academic scientists, and restricting screening to the trusted intermediary only, should prove attractive and reassuring.[300]

[298] Rai and Reichman et al., Chapter 17 of this volume.
[299] Ibid.
[300] Rai and Reichman et al., Chapter 17 of this volume.

In an attempt to evaluate the promise and potential of the proposed two-tiered partnership, Burk has investigated the Rai et al. model through the lens of options and information theory.[301] Apparently, the incentive structure of liability rules is equivalent to that of a 'call' option – the right to purchase an asset at a pre-defined price – in futures markets.[302] Liability rules, like call options, obligate the owner of the asset to a transfer of all or part of the rights in an asset for a pre-determined price. The recognition that liability rules operate as call options, raises the possibility that the 'put' option – the right to sell an asset at a pre-defined price – may play a role as well, but this should be explored further.[303]

The potential of the Rai et al. public–private collaborative partnership cannot be evaluated as yet as the model has not been put into practice. It might stimulate large-scale interaction between basic and clinical science and accelerate translational development of new drugs, biomarkers and treatment strategies from the laboratory bench into testing. It remains to be seen, however, whether the model will not turn out to be too complex in practice and whether it will yield desirable outcomes. From a more conceptual perspective, it is interesting to note that the two-tiered public–private partnership arrangement triggers an additional liability regime under Tier 2, when a 'hit' is found with a molecule coming from multiple firms.[304]

Comparison of problems and solutions

Having zoomed in on new collaborative licensing models and the related findings from academic and practical experts, let us now return to the major question around which the present book revolves. The current patenting and licensing landscape in human genetics has led to concerns with regard to the potential adverse effect of patents. The exponential growth of patents claiming human DNA sequences may

[301] Burk, Chapter 19 of this volume.

[302] Morris, M., 'The Structure of Entitlements', 78 *Cornell Law Review*, 1993, 440; Krier, J. and Schawb, S., 'Property Rules and Liability Rules: The Cathedral in Another Light', 70 *NYU Law Review*, 1995, 440.

[303] Burk, Chapter 19 of this volume, and the references cited there.

[304] See their contribution, section entitled 'The option of a contractually-constructed liability regime' (Chapter 17 of this volume, pp. 271–72): "In addition to the structure outlined above, participating firms might also agree on a supplementary system of royalties that would govern compensation to any firm that had provided structural information about its molecules to a researcher deciding among promising 'hits.' In other words, firms would be contracting into a subsidiary set of 'take and pay rules,' or liability rules, rather than relying entirely on exclusive property rights".

result in patent thickets and royalty stacking. Exclusive or unreasonable licensing of gene patents may lead to blocking patents. The cumbersome translation of early-stage genetic inventions into useful applications may lead to underuse of potentially useful inventions and form a valley of death. In order to remedy those problems in an adequate way, various models have been explored, from a variety of perspectives. Time has come to evaluate the suggested institutional models in view of their potential to solve the alleged problems. In other words, as Ullrich rightly observed, to find out "which exactly is the problem that needs to be solved, and which institutional arrangement is best suited to bring about the solution".[305]

Analysing the various *problems* in the current genetic patent landscape in more depth indicates that the impasses observed differ in various ways (see Table 25.2).

First, the impasses occur in a different stage of the innovation development chain. Patent thickets and blocking patents mainly raise substantial barriers in upstream research. However, it has been suggested that problems may also be expected in downstream development, for instance in the design of DNA microarrays.[306] The valley of death phenomenon typically emerges in downstream research.

Second, the obstacles observed differ in nature. Patent thickets and blocking patents do not challenge the access to patented technology as such, as under patent law the disclosure requirement provides easy access to the description of the invention at stake. Rather, obstacles are experienced with regard to the swift use of patented technology for (research and) development. Downstream translation problems are connected with both access (disclosure is lacking) and use for research and development.

Third, the various problems relate to the exchange of different types of subject matter. Patent thickets and blocking patents relate to the problematic access and use of intangible material (patents on genetic inventions), whereas the translational gap relates to the difficult access to tangible material (small molecules). As recent studies have revealed, these transactional barriers for material transfer of biological material may ultimately have more impact on the productivity of basic laboratory science than concerns related to patents or other IP.[307]

[305] Ullrich, Chapter 22 of this volume.

[306] See Verbeure, Chapter 1 of this volume; Warcoin, Chapter 21 of this volume; Matthijs and Van Ommen, Chapter 20 of this volume.

[307] Walsh, J., Cho, C. and Cohen, W., 'View from the Bench: Patents and Material Transfers', 23 *Science*, 2005, 2002–2003.

Table 25.2 *Differences in problems and solutions for mastering patent thickets and translational gaps in genetics*

PROBLEM					SOLUTION				
	Stage	*Nature*	*Subject matter*	*Regime responsible for impasse*	Collaborative rights model	*Objective*	*Subject matter*	*Open to*	*Presupposes*
Patent thicket	Upstream Downstream	Use	Intangible (use of genetic patents)	Patents	*Patent pool Clearinghouse Open source*	*Direct*: facilitate (repeated) patent use; *Indirect:* enhance development pts and pcss	Intangible assets (use of genetic patents)	All	Patent ownership
Translational gap	Downstream	Access and use	Tangible (access and use of small molecules)	Trade secrets	*Multi-firm public–private collaboration + (optional) liability regime*	*Direct*: consolidate develop-ment pts	Tangible + intan-gible assets (access and use of small molecules + know how)	Some	No patent ownership; Physical ownership molecules

Fourth, the impasses in the current genetic landscape are caused by different IP regimes. Patent proliferation – and to a certain extent blocking patents – may be seen as the (indirect) result of the patent system offering expanded protection to accommodate inventions related to biological subject matter. Transnational problems mainly seem to result from exercising trade secret protection over small molecules.

Overlooking the various problems and their features, it becomes clear that patent thickets and blocking patents have more characteristics in common than translational gaps. A clear divide becomes apparent between the constituting elements and features of patent thickets and blocking patents on the one hand, and translational gaps on the other hand. However, the phenomena observed all have one characteristic in common. Patent thickets, blocking patents and translational gaps may all frustrate the use of technology and ultimately stifle the development of health care products and services to the detriment of patients. In that regard, they all point to a failure in current patent law in achieving its primary objectives (foster innovation and public health interests) and in fulfilling its regulatory function.[308]

Comparing the measures and models suggested by the authors in the present volume to discipline and master the exercise of patent rights in genetics suggests that also the *remedies* differ in many respects (see Table 25.2). Before analysing those remedies, it is important to note that most authors have concentrated on resolving problems resulting from patent thickets, rather than on mitigating the impact of (a single) blocking patent(s).

First of all, the models differ in the objectives pursued. The direct purpose of patent pools, more advanced forms of clearinghouses and open source models is to facilitate access and use of patents. The direct purpose of the public–private collaboration model developed by Rai et al. goes far beyond that. It not just aims at facilitating access and use, but at establishing firm, steady, long lasting and fruitful multi-party collaborations for the production of new goods and services. Of course, the ultimate, indirect objective of measures designed to facilitate access and use is to enhance the production of goods and services as well, but the development of such goods and services not necessarily takes place in a collaborative endeavour.

[308] Patent thickets and blocks result from an inadequacy of patent law to accommodate the 'diffusion/innovation dilemma'. Interface problems result from an inability of patent law to provide an appropriate response to the 'exploration/exploitation dilemma', see Dedeurwaerdere, Chapter 24 of this volume.

Second, the subject matter of the transactions differs as well. The subject matter of the transaction in patent pools, clearinghouses and to a great extent in open source is intangible in nature. Pools, clearinghouses and open source models are mainly designed to facilitate the exchange of IP rights. The subject matter of the transactions in the public–private partnership is tangible in nature and relates to small molecules (although later on the transfer of related intangible knowledge is aimed at as well). One of the examples discussed under the standard clearinghouse model, namely the Science Commons Material Transfer Agreement (MTA) Project,[309] in fact also belongs here as it mainly aims to facilitate the transfer of tangible research resources (such as biological materials and reagents) by way of standard contracts. Although MTAs often include IP clauses, they do not primarily focus on minimizing IP bottlenecks.[310]

Third, the ability and desire to participate[311] in a collaborative model varies. In principle, the patent pool, the clearinghouse and the open source model, do not employ a threshold and anyone (patent holders and third parties alike) can request access to and use of one or more patented inventions. It may well be though, that a kind of member fee has to be paid to start negotiations, as is the case in some commercial clearinghouses. In contrast, the two-tiered public–private partnership is only open at Tier 1 to a restricted number of qualified public sector researchers, acting 'behind the veil'. At Tier 2 the circle of happy few is reduced and only an even more limited number of academics may act behind the veil.

Fourth, the collaborative institutions differ in the IP portfolio they require at the outset. Patent pools, patent clearinghouses and open source patent models, presuppose the existence of patents, in order to compel user-licensees to contribute or act in a certain way, for example pay a royalty (in the patent pool and clearinghouse model) or distribute the (improved) invention to others (in the open source model). The public–private ownership is based on physical ownership of molecules

[309] See Nguyen, Chapter 9 of this volume.

[310] Rai and Reichman et al. indirectly voice some criticism on the Science Commons MTA project. Although standard agreements are a mechanism for reducing transaction costs in transfers of (drug-related) materials between academics and the private sector, full standardization will be difficult to achieve and even if standardization were successfully created and implemented, the problem of insufficient numbers of transactions might remain. See Rai et al., Chapter 17 of this volume.

[311] Participating here does *not* refer to the ability to establish a collaborative institution, but to the ability to enter into negotiations once the collaborative mechanism has been set up. In other words, not participation as an owner/holder (of IP), but rather as a user (of IP).

(from industry) or assays (from academia), and it is even forbidden to patent any material after having been granted access under Tier 1.

Fifth, the arrangements differ in their effect on exclusive ownership. As Ullrich indicates, patent pools requiring as a matter of competition law an open licensing policy (i.e. non-discriminatory licensing to everyone) tend "to convert the exclusivity principle of patent protection into a mere liability system, i.e. into a reward-by-compensation rule".[312] Clearinghouses, on the other hand, maintain the ownership dogma and "the property rationale of the patent system, i.e. its principle of exclusivity-based individual exploitation".[313] Burk also points to this phenomenon.[314] The paradoxical effect of collaborative mechanisms on entitlements should not totally come as a surprise though, as Merges already pointed to this effect a long time ago.[315]

Overlooking the various solutions, it becomes apparent that patent pools, clearinghouses and open source models have much more in common than the public–private Rai et al. model. A clear divide emerges between the characteristics of pools, clearinghouses and open sources on the one hand, and the small molecule public–private partnership, on the other hand. All models have in common that they may be implemented on a voluntary or a non-voluntary basis.

25.5 Testing the research hypothesis

In order to reach a final conclusion on what institutional design (most) adequately solves the problems observed, it seems appropriate to evaluate the proposed measures against the postulated goals and to verify the four additional assumptions with the findings of the various authors in the present book, taking into account the differences in objectives, features and effects of the various models (as represented in Table 25.2).

Starting goals

The presupposed goals set forth at the start (see p. 397–98) are to promote solutions within the boundaries of the patent system that mitigate possible harmful effects of patents in diagnostic genetics. In other words, it is assumed in the present volume that what has to be achieved is (a) to maintain the positive effects of patent law (incentive

[312] Ullrich, Chapter 22 of this volume.
[313] Ullrich, Chapter 22 of this volume.
[314] Burk, Chapter 19 of this volume.
[315] Merges, 'Contracting into Liability Rules', 1996, (1293), 1302.

for the production of drugs and therapies important in health care) and (b) to design measures to remedy some of the hindering effects in the field of genetics and in diagnostics in particular (c) within a reasonable time frame. If these are the goals, then opting for the creation of tools which optimize the negotiation of a multitude of (blocking) patents seemed most adequate. In other words, the best way to remedy current obstacles in the genetic patent landscape is to work on the horizontal regulatory function of patent law[316] by designing formal rules of contract.[317]

The authors of this book differ in opinion on this point of departure. A minority of authors explicitly refute this idea, bringing up two major arguments.

A first argument is that the hindering effects patents may cause in genetics directly relate to the *existence* of patent claims on human genes. The authors suggest that the patent regime for human genes has to be reassessed and that patent rights for genes should be forbidden or at least narrowed down significantly. Matthijs and Van Ommen, herein anticipated by other fellow geneticists, support this approach and favour the abolition of patents on genes, on individual mutations in known disease genes and on the link between a (defect in a) genetic sequence and a disease. As to the latter, they argue that the establishment of an association between a monogenic disease and a gene or an individual mutation is a discovery and thus not patentable[318, 319] (even though they are willing to admit that this clear-cut reasoning becomes blurred in the case of multifactorial diseases), and that only patents on diagnostic methodology should be allowed. Their views are echoed in the recently adopted Recommendations of the European Society for Human Genetics.[320] Along the same line, Spence suggests that serious thought must be given to whether the potential problem of the anticommons is not, after all, that too many gene patents are granted.[321] Warcoin equally argues that the best way to proceed is to establish statutory limitations upstream,

[316] For the distinction between the vertical and the *horizontal* regulatory function of patent law, see pp. 394–96.

[317] For the distinction between formal *legal* rules and formal rules of *contract,* see Dedeurwaerdere, Chapter 24 of this volume.

[318] This would be naturally achieved if this association was regarded as a discovery, not an invention (Matthijs and Van Ommen, Chapter 20 of this volume). Similarly, Andrews, L., Paradise, J., Holbrook, T. and Bochneak, D., 'When Patents Threaten Science', 314 *Science – Policy Forum*, 2006, 1395–1396.

[319] With the current technology, there is arguably no inventive step and a lack of novelty, which would exclude them from patenting under current patent law (Matthijs and Van Ommen, Chapter 20 of this volume).

[320] European Society of Human Genetics, 2008.

[321] Spence, Chapter 11 of this volume.

including the limitation of patentable subject matter.[322] This viewpoint has also stricken a sympathetic chord amongst some US judges.[323] Worthwhile as it may be,[324] carving out gene patents from patent law is not an option in view of the goals set out at the start, and more in particular the temporal element.[325]

A second argument which has been put forward is that collaborative clearing models focusing on the *exercise* of patents are unfeasible and undesirable. Warcoin claims that such initiatives are difficult to realize.[326] Spence argues that the establishment of some collaborative measures is not only unachievable, but also potentially inconvenient as it may worsen rather than diminish the problem and even risk having a perverse effect. [327] Clearinghouses may exacerbate, rather than relieve the problem. In the same line, Ullrich states that the problem of patent thickets "is…a self-created one, which does not necessarily justify power-building through pooling, on the contrary".[328] He claims that "a liberal attitude on pooling invites even more patenting, thus aggravating the problem". Relevant as this thoughtful critique may be, the adverse effect of models facilitating access on the proliferation of patents has not been widely documented yet. Therefore, and in view of the goals set out at the start, modelling mechanisms to mitigate the adverse effects of gene patents is accepted to be the best option for now.

The majority of authors in the present collection indeed share the view that solutions to the current impasses in gene patenting should concentrate on the *exercise* of patent rights related to human genes. They agree – implictly or explicitly, in subdued voice or loudly speaking – that the current legal framework is the result of a long, cumbersome and legitimate decision-making process, which outcome cannot be undone overnight, and should therefore first and foremost be addressed by alternative, contractual measures eventually complemented by legal measures.

[322] Warcoin, Chapter 21 of this volume.

[323] Cf. Justice Breyer (dissenting) in Supreme Court of the United States, Laboratory Corporation of America Holdings, Labcorp, Petitioner *v.* Metabolite Laboratories, Inc. et al, on writ of certiorari to the United States Court of Appeals for the Federal Circuit, 22 June 2006. Cf. Andrews et al., 'When Patents Threaten Science', 2006.

[324] We have supported the exclusionary option for a long time (see Van Overwalle, 'Reshaping Bio-Patents: Measures to Restore Trust in the Patent System', 2007) but prompted by some pragmatism we have shifted our attention from (pre-grant) patentability issues to measures resolving potential negative (post-grant) effects of gene patents.

[325] This chapter, pp. 397–98.

[326] Warcoin, Chapter 21 of this volume.

[327] Spence, Chapter 11 of this volume.

[328] Ullrich, Chapter 22 of this volume.

Research assumptions

Four assumptions have further been articulated to refine this option (see p. 399–403). These four assumptions will now be tested against the findings of the experts.

Contractual and collaborative shape

The first assumption of the present book is that, in the current state of affairs, the access and use of (patented) inventions in the genetic field in general, and in the field of genetic diagnostics in particular, would best be served by contractual, collaborative efforts and institutions, taking the form of patent pools, clearinghouses, open source licences or liability regimes.

Concepts and cases

The conclusion that collaborative models may assist patent law in dealing with current limits, calls for some nuance. The conclusion is based on a thorough examination of conceptual features and applicable law, but not on a wide empirical analysis of existing cases, as hardly any of those models has been put to practice in the genetic field (yet). The conclusion therefore has to be toned down a little.

Categorizations and definitions. What's in a name?

The categorization set forth at the start (see Table 25.1) is mainly based on the legal *structure* and the variety in underlying legal *agreements* which characterize the models. From a legal perspective, a patent pool is a collaborative model where access is regulated on the basis of a set-up agreement between the rights holders, and where the later transactions can come about through an intermediary or not. A clearinghouse is a model where access is institutionalized without a set-up agreement between the right holders, and where the exchange takes place through an intermediary. Another way to categorize the models is by looking through the window of competition law, which is, as Ullrich says, mainly focusing on the *effects* of collaborative models on *competition*. Competition law "is not interested in the form of institutions or of organizational arrangements, but in the distortion of competition, which choosing and adopting such an arrangement actually produces".[329] Yet another way of assessing the models is through economic theory, as Aoki does. Aoki looks at the *effect* of the various institutions on *exchange,* rather than the legal set up of the models.

[329] Ullrich, Chapter 22 of this volume.

As another criterion is used a different categorization results. From a legal perspective, a patent pool is quite distinct from a clearinghouse, as a pool is established through a set-up agreement amongst all patent holders. From an economic perspective, however, patent pools may be regarded as quite similar to (a subtype of) clearinghouses, namely copyright collection societies, as they both aim at providing a bundle of goods and benefiting from network effects.[330] Still other lenses may be deployed to analyse the institutional arrangements at stake, such as the options and information theories, as suggested by Burk.[331]

The definitions employed at the start[332] to characterize the various models have been drawn from prevailing scholarly literature. It is remarkable to see, however, how various authors have applied different labels when qualifying the same arrangement or institution. One example is the SNP Consortium. In the view of Holden, cited by Verbeure, the SNP Consortium is a patent pool.[333] According to van Zimmeren, the SNP construction can be qualified as an open access clearinghouse,[334] whereas Burk argues that it is a put "at an exercise price of zero".[335] Another example is PIPRA. When clarifying that PIPRA provides information and matches scientists and technology transfer offices, Bennet and Boettiger suggest that PIPRA is an information clearinghouse. Van Zimmeren, however, qualifies PIPRA as a technology-exchange clearinghouse in this regard. When it comes to the design and distribution of research tools in its own laboratories, Bennet and Boettiger conclude that PIPRA is also a standard licence clearinghouse, which is debatable as well.[336] Yet another example is the BiOS arrangement. It is generally accepted that BiOS is an open source initiative. Hope has argued, however, that the BiOS construction has a "club character",[337] which might lead to believe that BiOS resembles a patent pool,[338, 339] or is a hybrid between open source and patent pools.

[330] See Aoki, Chapter 23 of this volume. [331] See Burk, Chapter 19 of this volume.
[332] Supra, see pp. 405, 413, 422, and 431. [333] Verbeure, Chapter 1 of this volume.
[334] See van Zimmeren, Chapter 5 of this volume.
[335] More in particular, where the holder of the technology can essentially require the public to take the invention, electing not to hold it as a trade secret or pursue a patent, see Burk, Chapter 19 of this volume.
[336] Supra, p. 419. [337] Hope, see Chapter 12 of this volume.
[338] More in particular the pool construction achieved after the cross-licensing of patents amongst patent holders in the set-up agreement.
[339] Concluding that BiOS resembles a pool would be incorrect in view of the economic literature on club goods. A patent pool (after the set-up agreement) may probably be qualified in terms of 'jointly owned club goods' or as 'jointly owned private goods'. The BiOS model rather seems to comply with a 'common pool good' concept. For a definition of these concepts '(jointly owned) club goods', '(jointly owned) private

And the critique that there is insufficient freedom to "fork the code", suggests that BiOS is not open source at all.[340] Last but not least, there is the figure of the trusted intermediary in the Rai et al. model. Analyzing the components of the two-tier collaboration arrangement, and screening the role and the set up of the trusted intermediary, makes one wonder whether the trusted intermediary, should be seen as the broker of a clearinghouse or as an independent administrator governing a pool. The trusted intermediary in the Rai et al. model is probably neither of the two.

Categorizations are helpful intellectual tools to refine the analysis on institutional models and to further legal scholarship on the complexities of applying collaborative measures in a genetic context. Different labels might be the result of unclear definitions of the basic concepts. Varying qualifications may also appear in cases where the models are not totally mutually exclusive or where different interpretations of the same definition may occur. Discrepancies in labelling could be the subject of further examination. However, the categorizations put forward in this book are not sacrosanct and the definitions employed are not unassailable. The debate on collaborative action should not be led astray by semantic subtleties and incongruities. What counts is the effect these measures achieve in fulfilling the objective of accessibility and sharing in practice, disregarding the way in which the arrangement can or should be qualified.

Upstream and downstream

The statement that differing collaborative measures might be needed to take care of upstream and downstream problems, has not been confirmed. Verbeure, Goldstein, van Zimmeren, Spence and Hope suggest that patent pools, clearinghouses and open source might assist to clear patent thickets, one of the major problems said to appear in upstream research. However, some of the recent technical developments, such as DNA microarrays, suggest that patent thickets may equally emerge in downstream development, and that patent pools, clearinghouses and

goods' and 'common pool good', see Polski, M., 'The Institutional Economics of Biodiversity, Biological Materials, and Bioprospecting', 53 *Ecological Economics*, 2005, 543–557.

340 The critique from Hope might stem from the fact that the BiOS arrangement claims to be 'open source' (BiOS = Biological Open Source, see www.cambia.org), whereas the BiOS license, strictly speaking, does not seem to fulfill all the necessary criteria to apply this term. It remains to be seen to what extent the critique from Hope would hold, if BiOS described itself as an 'open source-*like*' arrangement, rather than an 'open source' initiative.

open source might be helpful to traverse the scattered patent landscape downstream as well. The Rai et al. model merely seems adequate to solve the problem of translation in downstream research.

The reservation that collaborative measures will not be adequate to mitigate the problems resulting from one or more patents belonging to a single, uncooperative or patent holder, was confirmed. Verbeure, Goldstein, Horn and Warcoin agree that patent pools will have limited potential in solving the problem of holdouts. In the same line, van Zimmeren and Spence suggest that clearinghouses will most probably not be able to deal with unwilling patent holders. Rather compulsory licences schemes and informal norms of fair licensing might be helpful to solve the effect of blocking patents.[341]

From diagnostics to genetics

Collaborative models might indeed help to cut through the patent thicket, with regard to upstream (and downstream) genetic diagnostics. Verbeure, van Zimmeren and Hope all underline that patent pools, clearinghouses and open source models, might be accommodated to remedy hindering effects of patents in the diagnostic sector. This conclusion is based on the specific characteristics and features of the diagnostic testing sector, tipped as the number one candidate falling victim of a patent thicket in genetics. However, prudence is in order when extending their conclusion to the whole sector of genetic research and innovation at large.

Public or private

It has been argued in literature that it is the role for public sector and governance structures in particular to govern collaborative models, such as patent pools.[342] However, as the proponents admit, this suggestion might have a limited field of application, as not all areas of

[341] See G. Van Overwalle (ed.), *Gene Patents and Public Health* Brussel, Bruylant, 2007, and more in particular the contributions of Debrulle, J., De Cort, L. and Petit, M., 'La licence obligatoire belge pour raisons de santé public' (161–198) [with a translation into English: 'The Belgian Compulsory License for Public Health' (199–209)], Germann, C., 'The Swiss Approach to Compulsory Licensing for Diagnostic Products and Processes' (149–157), van Zimmeren, E. and Requena, G., 'Ex-Officio Licensing in the Medical Sector: The French Model' (123–147). Also see Van Overwalle, G., 'The Implementation of the Biotechnology Directive in Belgium and its Aftereffects. The Introduction of a New Research Exemption and a Compulsory License for Public Health', 37 *IIC*, 2006, 889–920.

[342] Caulfield, T., Einsiedel, E., Merz, J.F. and Nicol, D., 'Trust, Patents and Public Perceptions: The Governance of Controversial Biotechnology Research', **24** *Nature Biotechnology*, 2006, 1352–54.

research or all forms of patents lend themselves to this kind of governance scheme.

Conversely, it has been suggested that it is the role of the private sector to develop the models, and the challenge for the public sector to scale them up.

> Like the business innovators who come up with major innovations for the marketplace, social innovators are the mad scientists as it were – working away in their organizations that act like social innovation laboratories. They test and perfect different approaches, and when they come up with the most effective and efficient ones with the greatest impact, it should be government and the corporate sectors' respective roles to celebrate the innovation, take it up, learn from it and help scale it so that all can benefit. Ultimately, the innovation lies in the models devised for service and product delivery all along the supply chain – not in the provision of the good itself. It is those models that others need to take up and replicate.[343]

Only a few authors in the present book have focused on the possible role of public and/or private actors in setting up and/or managing collaborative models. Van Zimmeren favours private initiatives or public–private partnerships over a statutory, compulsory regime.[344] Spence underlines that institutions should "fulfil a public duty" by maximizing activity in the biomedical sciences.[345] Following Dedeurwaerdere, one of the major lessons of this book is that a whole range of actors – ranging from academic scientists, technical experts patent attorneys, commercial enterprises to NGOs – may have an interest in applying innovative contractual models and in setting up collaborative mechanisms in genomic research.[346]

IPR based

The second assumption at the start of our explorative *tour d'horizon* was that contractual, collaborative models are based on the pre-existence of IP law in general, and patent law in particular. This assumption is confirmed in the patent pool, clearinghouse and open source models. This finding came as quite a surprise for the open source model, once

[343] Schwab and Hartigan, 'Social Innovators with a Business Case. Facing 21st Century Challenges. One Market at a Time', 2006, 7–11.

[344] van Zimmeren, Chapter 5 of this volume.

[345] Spence, Chapter 11 of this volume.

[346] Cf. Dedeurwaerdere, Chapter 24 of this volume: "We will focus on one of the main lessons of this book from the point of view of institutional analysis: the involvement of the scientific and the user communities in innovative contractual and licensing agreements has proven to be successful in alleviating some of the collective-action problems that are raised by genomics research".

it became clear that 'credible commitment' is key and that the success of the open source concept depends on the existence of a strong IP power platform. As Taubman indicates, the open source experience in the life sciences demonstrates the positive role IP may play: "Exclusive or proprietary rights can be used to leverage access, to promote dissemination, to safeguard downstream use rights; the notion of promoting access through rights that exclude is indeed the underlying paradox of IP law and policy".[347] The second assumption has not been confirmed with regard to the downstream collaborative public–private partnership construction put forward by Rai et al. Indeed, the starting up of this model is not based on IP protection as it is forbidden to patent potential hits under Tier 1. It has to be noted, however, that under Tier 2, patent protection can come into play as from this moment patent applications are allowed.

So, patents fulfil a different role in the *set-up* phase of new, collaborative licensing models. In patent pools, (standards and) patents seem useful to bring knowledge/technology holders together on a (more or less) equal footing and start negotiations. In contrast, in the public–private partnership model patents are not perceived as helpful in triggering collaboration between the various technology/knowledge holders and the set up of a pool of libraries (or as Burk puts it "a semi-commons"[348]) of small molecules. Patents also seem to play a different strategic role *later on*, once the models are in place. In patent pools, patents are important to raise revenue from the user-licensees. In open source models, patents are not important to collect money, but to enforce a certain sharing behaviour from the user-licensees. In the public–private partnership, patents will also be operational in gathering rent from user-licensees, once a product is developed from the initial hint. Further research is needed to explore the role of (intangible or tangible) ownership in triggering collaboration in the set-up phase of new licensing models and in sustaining the models established.

A distinct observation is that collaborative models have a different *effect* on ownership. It has been suggested that collaborative models, once operational, turn patent rights and ownership rules into mere liability regimes.[349] However, the research on this point mainly reported on patent pools and royalty collecting societies, and has hardly looked into open source models. Would it also be correct to assume that collaborative measures reshape the patent and exclusive ownership regime

[347] Taubman, Chapter 16 of this volume. [348] Burk, Chapter 19 of this volume.
[349] Supra, pp. 431–34.

into a 'reconstructed commons'[350] or 'positive commons'?[351] This is probably true for open source regimes, but what about patent pools and clearinghouses? The change in entitlement regime, provoked by collaborative models, merits further attention.

Economically viable

The third assumption that the models designed should be viable in a not-for profit, as well as in a for-profit, context has been answered in different ways. Verbeure points to some advantages for for-profit players to enter into a patent pool, but as yet it is unclear whether these arguments will be convincing enough. Van Zimmeren clearly demonstrates that most clearinghouse models substantially reduce transaction costs[352] and may therefore be attractive in a for-profit, market context as well. Rai et al. equally argue that the public–private partnership substantially reduces transactions costs, and that pharmaceutical firms stand to risk little and gain a great deal through participation.[353] Hope and Dedeurwaerdere go along with the idea that collaborative models display certain benefits in a for-profit, market context.[354]

Looking at the BiOS initiative, Berthels admits that costs associated with innovation using biotechnology are currently high and that it is likely that funding from philanthropic organizations and governments to address agricultural and health problems in developing countries

[350] The term 'reconstructed commons' is drawn from Reichman and Uhlir, 'A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment', 2003, 315. Also see Van Overwalle, G., 'Octrooien op maat? Naar een evenwicht tussen publieke opdracht en privaat goed' ['Patents Fit All? Towards an Equilibrium Between Public Mission and Private Good'], in B. Pattyn and G. Van Overwalle (eds.), *Tussen Markt en Agora. Over het statuut van universitaire kennis* [*Between Market and Agora. About the Status of Academic Knowledge*], Leuven, Peeters, 2006, 181–214.

[351] A positive commons is "a common in which resources are jointly owned and so use of those resources by any one commoner depends on all the commoners having consented", see Drahos, P., 'The Commons, The Public Domain and (Monopoly) Commerce', paper presented at the conférence *The Politics and Ideology of IP*, organized by the Transatlantic Consumer Dialogue (TACD) Brussels, 20–21 Mars 2006 (www.tacd.org/events/intellectual-property/p_drahos.ppt); Drahos, P., 'A Defence of the Intellectual Commons', **16** *Consumer Policy Review,* May/June 2006, 3–5. Also see Van Overwalle, G., 'L'intérêt général, le domaine public, les *commons* et le droit des brevets d'invention', in M. Buydens and S. Dussolier (eds.), *L'intérêt général et l'accès à l'information en propriété intellectuelle*, Brussel, Bruylant, 2009, 149–75.

[352] Transaction costs include search costs, bargaining costs and enforcement costs.

[353] Rai and Reichman et al., Chapter 17 of this volume.

[354] "Even in markets well served by the profit motive, a science commons can in some circumstances improve efficiencyfor example, when many disparate firms can draw on a common clearinghouse of knowledge and data, rather than having to construct the same information firm-by-firm (resulting in substantial duplication costs)", Dedeurwaerdere, Chapter 24 of this volume.

remains vital. However, open source biotechnology approaches of transparency and leverage through creation of platform public resources may make such expenditures more efficient and effective, and ultimately may drive such costs down.[355] Some thoughtful observers do not share this optimism and remain very concerned about the sustainability of the BiOS model.[356] The DArT case clearly demonstrates that the open source licence model is a viable commercial strategy, but it is questionable whether this model can stand the test in market segments aiming at the largest potential profit margins, such as the biomedicine sector.[357] It remains to be seen whether indeed an open source approach will be viable in the genetic sector at large. Further economic research is needed to provide a more refined and robust answer to this question.

Restoring trust and halting ignoring the norm

The fourth assumption that collaborative models will reduce the negative social impact of patents and will help to restore trust in the patent system, as a mechanism to foster both private *and* public interest encompassing both economic *and* social welfare, is probably the most difficult one to prove. A definite answer is difficult to give. Dedeurwaerdere, in a more general fashion, concludes that "the more general discussion of the different legal models for reconstructing the commons in this volume shows that a variety of social goals can benefit from a robust scientific commons in genomics: these include advancing science, improving public health, improving food security, contributing to understanding and conserving biological diversity, and contributing to industrial R&D and commercialization". Caulfield et al. suggest that mainly governance structures are fit to help maintain public trust and argues that an independently public/privately governed patent pool might be one example mechanism to do so.[358] Additional empirical research is needed on the effect of different collaborative structures on trust. Further theoretical analysis is necessary on the concepts of trust and social impact, on ways to evaluate them and on underlying values.

The related assumption that collaborative models might reduce 'ignoring the patent norm' amongst users, is also difficult to prove at this point in time. Spence and Warcoin are both critical about the desirability of

[355] Berthels, Chapter 13 of this volume.

[356] Boettiger, S. and Wright, B.D., 'Open Source in Biotechnology: Open Questions', **1**(4) *Innovations*, 2006, (45), 53.

[357] Cf. Kilian, Chapter 14 of this volume.

[358] Caulfield et al., 'Trust, Patents and Public Perceptions: The Governance of Controversial Biotechnology Research', 2006.

such an effect.[359] The recent Recommendations of the European Society for Human Genetics (ESHG), however, give evidence of a change of attitude. The ESHG urges its members, and the genetic community at large, "to respect the patenting and licensing rules – once they are acceptable".[360] Such a recommendation displays wide sympathy for a transition from tacit infringement as a working solution to proper royalty payments as a default strategy.

25.6 Final conclusion

The current patent landscape for human genomic science has refuelled the debate on human gene patents. Expressed in figurative language, *concerns* are raised that patent thickets and blocking patents will lead to a tragedy of the anticommons, and that new genetic inventions might not find their way into products as a translational gap might widen to form a valley of death, thus frustrating new treatments in health care. Even though the problems may not paralyse commerce as yet, all authors of this book – lawyers, economists, patent experts, geneticists – in unison agree that the problems reported in current patent law and practice in the field of genetics are real and merit further attention, especially in the area of genetic diagnostics, which seems to be most prone to suffer from patent discomfort in the near future. The problems in genetic diagnostics are expected to grow with the turn from monogenetic testing to multifactorial testing (multiplex diagnostics) and the availability of bio-chips and microarrays. Difficulties might dramatically increase with the paradigm shift from monogenetic and multifactorial diagnostics based on Mendelian causality to diagnostics based on genome-wide association studies driven by the high-throughput of SNP platforms and the next-generation sequencing possibilities.

The central *question* around which this book revolves is what measures should be taken to render patented human genes accessible for further use. This question is constricted to what measures should be contemplated to safeguard research and development in genetic diagnostics, as this area is most prone to fall victim of patent thickets.

When exploring such measures, it is presupposed in this book that the ultimate *goal* of any measure is to maintain the function of patent law as incentive for the production of drugs and therapies important in health care and to remedy some of the adverse effects patent law

[359] Spence, Chapter 11 of this volume; Warcoin, Chapter 21 of this volume.
[360] European Society of Human Genetics, 2008.

may have in the field of diagnostics, within a reasonable period of time. Creating tools which optimize the negotiation of a multitude of (blocking) patents in diagnostics seems to be a better option to meet this goal, rather than reforming patent law and carve out gene patents. In other words, the best way to deal with current obstacles in the genetic patent landscape is to remedy the horizontal regulatory function of patent law by designing formal rules of contract, rather than addressing the vertical regularity function by enacting or modifying formal legal rules.

Four *assumptions* have been put forward to make this point more exacting. The *first* assumption is that in the current state of affairs, the problems created by patent law in genetic diagnostics are best served by contractual, collaborative measures. The specific features of the collaborative models and the nature of the subject matter exchanged therein, suggest that patent pools, clearinghouses and open source models are most fit to traverse the patent landscape in genetic diagnostics and thus meet the starting goal. Successful as it may be to solve the translation of small molecules, the plasticity of the public–private partnership with optional liability regime appears rather limited in this area and it is difficult to imagine to what extent the model can be applied to other contexts.

Consideration of prerequisites, benefits and disadvantages of the various models leads us to believe that the optimal patent pool model in diagnostic genetics might well be a patent platform where individual patent pools are narrowly defined around single genes comprising vertically oriented patents, thereby providing access to horizontally oriented thickets. It will take quite a while before such a platform may be operationalized and meanwhile efforts should concentrate on patent pools set up around single genes or gene panels. The optimal clearinghouse might well be a fully fledged patent royalty collection clearinghouse. Since this is probably too far fetched for the time being, major efforts in the coming years should focus on setting up patent standard clearinghouses in genetic diagnostics, tuned to the varied needs in this branch of genetics and tailored to the specific characteristics of the biotech business sector. As to open source models, translating open source from software to genetics and introducing copyleft-style open source licence in relation to diagnostic tests based on gene patents seems also feasible, but might not be unproblematic.

The remaining *three* assumptions are that contractual, collaborative models will come into being and function properly in the long run, if they are based on the pre-existence of patent rights, if they prove to be commercially sustainable and economically viable without overriding

social motives, and if they contribute to restoring trust in the patent system.

Testing the findings of the various authors against this additional set of assumptions, teaches us the following. First, the pre-existence of patent rights is indeed quintessential for the establishment of patent pools, clearinghouses and open source models. Second, all the models display certain benefits in a for-profit, market context. Additional economic research is necessary to provide a more refined and robust assessment of their economically viability and commercial sustainability in the long run. Further research is also required to identify incentives for the establishment of such models, and to ascertain that the models attract valuable patents and distribute usage rights efficiently rather than create "markets for lemons".[361] Third, the various arrangements also offer a unique opportunity to restore trust in both the private and public interest objectives of the patent system pertaining to economic and social welfare, and to discontinue ignoring the patent norm. Further empirical research would be helpful to test this last assumption. All in all, normative analysis, based on normative intuitions and ethical theory, is also needed to make the underlying objectives and values of patent law, the goals assumed by different stakeholders and the solutions presented more explicit.

REFERENCES

Akerlof, G.A., 'The Market for "Lemons": Quality Uncertainty and the Market Mechanism', **84**(3), *Quarterly Journal of Economics*, 1970, 488–500.

Andrews, L., Paradise, J., Holbrook, T. and Bochneak, D., 'When Patents Threaten Science', **314** *Science – Policy Forum*, 2006, 1395–6.

Aoki, R., 'Access to genetic patents and clearing models. An Economic Perspective', Chapter 23 of this volume.

Aoki, R. and Schiff, A., 'Promoting Access to Intellectual Property: Patent Pools, Copyright Collectives and Clearinghouses, **38**(2), *R&D Management*, 2008, 189–204.

Baldwin, T., 'Ethics and Patents for Genetic Diagnostic Tests', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 45–59.

Bekkers, R., Iversen, E. and Blind, K. 'Patent Pools and Non-Assertion Agreements: Coordination Mechanisms for Multi-Party IPR Holders in Standardization', Paper for the EASST 2006 Conference, Lausanne, Switzerland, August 23–26, 2006 (available at http://www2.unil.ch/easst2006/Papers/B/Bekkers%20Iversen%20Blind.pdf)

[361] Akerlof, G.A., 'The Market for "Lemons": Quality Uncertainty and the Market Mechanism', **84**(3), *Quarterly Journal of Economics*, 1970, 488–500.

Bennett, B. and Boettiger, S., 'Case 5. The Public Intellectual Property Resource for Agriculture. A standard license public sector clearinghouse for agricultural IP', Chapter 8 of this volume.

Berthels, N., 'Case 8. CAMBIA's Biological Open Source Initiative (BiOS)', Chapter 13 of this volume.

Bird, W., 'Using the EPO Opposition Procedure as a Strategy Against Patents on Diagnostic Methods', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 73–83.

Böcker, L., 'Mit freier Software gegen den Wettbewerb? Die General Public License (GPL) als horizontale Wettbewerbsschränkung', *Festschrift F. Säcker*, Berlin, 2006, 69.

Boettiger, S. and Burk, D., 'Open Source Patenting', **1** *JIBL*, 2004.

Boettiger, S. and Wright, B. D., 'Open Source in Biotechnology: Open Questions', **1**(4) *Innovations*, 2006, 45–63.

Burk, D. L., 'Critical analysis: property rules, liability rules and molecular futures. Bargaining in the shadow of the cathedral', Chapter 19 of this volume.

Calabresi, G. and Melamed, A. D., 'Property Rules, Liability Rules, and Inalienability: One View of the Cathedral', **85** *Harv. L. Rev.*, 1972, 1089–92.

Carlson, S. C., 'Patent Pools and the Antitrust Dilemma', **16** *Yale Journal on Regulation*, 1999, 359–99.

Caulfield, T., Bubela, T. and Murdoch C. J., 'Myriad and the Mass Media: the Covering of a Gene Patent Controversy', **9** *Genetics in Medicine*, 2007, 850–855.

Caulfield, T., Cook-Deegan, R. M., Kieff, F. S. and Walsh, J. P., 'Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies', **24** *Nature Biotechnology*, 2006, 1091–4.

Caulfield, T., Einsiedel, E., Merz, J. F. and Nicol, D., 'Trust, patents and public perceptions: the governance of controversial biotechnology research', **24** *Nature Biotechnology*, 2006, 1352–4

Cho M. K., Illangasekare, S., Weaver, M. A., Leonard, D. G. B. and Merz, J. F. 'Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services', **5**(1) *Journal of Molecular Diagnostics*, 2003, 3–8.

Claes, E., Devroe, W. and Keirsbilck, B., 'Introductory Chapter – The Limits of the Law', in E. Claes, W. Devroe and B. Keirsbilck (eds.), *Limits of the Law*, Springer, 2009, 1–24 (For the Dutch version, see : E. Claes, W. Devroe and B. Keirsbilck, 'Grenzen van (rechtsstatelijk) recht', **69** *Rechtskundig Weekblad*, 2006, 1203–17).

Clark, J., 'Patent Pools: A Solution to the Problem of Access in Biotechnology Patents?' White Paper Commissioned by Q. Todd Dickinson, the Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office, 2000 (available at www.uspto.gov/web/offices/pac/dapp/opla/patentpool.pdf)

Cook-Deegan, R. and Dedeurwaerdere, T., 'The Science Commons in Life Science Research: Structure, Function and Value of Access to Genetic Diversity', **188** *The International Social Science Journal*, 2006, 309–12.

Corbet, J., 'Case 7. The collective management of copyright and neighbouring rights. An example of a royalty collection clearinghouse', Chapter 10 of this volume.

Correa C., 'The GATT Agreement on Trade-related Aspects of Intellectual Property Rights: New Standards for Patent Protection', *European Intellectual Property*, 1994, 327–31.

Correa C. E., 'Case 2. The SARS Case: IP fragmentation and patent pools', Chapter 3 of this volume.

Cowan, R., van der Eijk, W., Lissoni, F., Lotz, P., van Overwalle, G. and Schovsbo, J., *Policy options for the improvement of the European patent system*, Report commissioned by STOA (Scientific Technology Options Assessment) of the European Parliament, 2007, 67 pp. (www.europarl.europa.eu/stoa/publications/studies/stoa16_en.pdf)

David, P. A. and Spence, M., *Towards Institutional Infrastructures for E-Science: The Scope of the Challenge* Oxford, Oxford Internet Institute Research Report No. 2, 2003, 98 pp.

Debrulle, J., De Cort, L. and Petit, M., 'La licence obligatoire belge pour raisons de santé public', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 161–98.

Dedeurwaerdere, T., 'The role of law, institutions and governance in facilitating access to the scientific research commons. A philosopher's perspective', Chapter 24 of this volume.

Dennis, C., 'Biologists Launch "Open-Source Movement"', **431** *Nature (News)*, 2004, **30** September 2004, 494.

Depoorter, B. and Vanneste, S., 'Putting Humpty Dumpty Back Together: Experimental Evidence of Anticommons Tragedies', **3** *Journal of Law, Economics & Policy*, 1–25.

Drahos, P., 'A Defence of the Intellectual Commons', **16** *Consumer Policy Review*, May/June 2006, 3–5

'The Commons, The Public Domain and (Monopoly) Commerce', paper presented at the conférence *The Politics and Ideology of IP*, organized by the Transatlantic Consumer Dialogue (TACD) Brussels, 20–21 Mars 2006 (www.tacd.org/events/intellectual-property/p_drahos.ppt)

Drahos, P., 'Indigenous Knowledge, Intellectual Property and Biopiracy: Is a Global Bio-Collecting Society the Answer?', **20** *European Intellectual Property Review*, 2000, 245–50.

Dykman, H. T., 'Patent Licensing within the Manufacturer's Aircraft Association', **46** *Journal of the Patent Office Society*, 1964, 646.

Ebersole, T. J., Guthrie, M. C. and Goldstein, J. A. 'Patent Pools and Standard Setting in Diagnostic Genetics' **23** *Nature Biotechnology*, 2005, 937–8.

Edwards, J. L., 'Case 3. The Global Biodiversity Information Facility. An example of an information clearinghouse', Chapter 6 of this volume.

Eisenberg, R., 'Science and the Law: Patent Swords and Shields', **299** *Science*, 2003, 1018–9.

European Society of Human Genetics, 'Patenting and Licensing in Genetic Testing. Recommendations of the European Society of Human Genetics', **16** *Eur J Hum Genet*, 2008, 405–11.

Fleischhauer, K. and Hermerén, G., *Goals of Medicine in the Course of History and Today*, Stockholm, Kungl. Vitterhets Historie och Antikvitets Akademien, 2006, 480 pp.

George, G. D., 'Note: What is Hiding in the Bushes? *Ebay*'s Effect on Holdout Behaviour in Patent Thickets', **13** *Michigan Telecommunications and Technology Law Review*, 2007, 557–76.

Germann, C., 'The Swiss Approach to Compulsory Licensing for Diagnostic Products and Processes', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 149–57.

Goldstein, J. A., 'Critical analysis of patent pools', Chapter 4 of this volume.

Goldstein, L. M. and Kearsey, B. N., *Technology Patent Licensing: an International Reference on 21st Century Patent Licensing, Patent Pools and Patent Platforms*, Aspatore, 2004, 576 pp.

Graff, G. and Zilberman, D., 'Towards an Intellectual Property Clearinghouse for Agribiotechnology', **3** *IP Technol. Today*, 2001, 1–12.

Graff, G. D., Cullen, S. E., Bradford, K. J., Zilberman, D. and Bennett, A. B., 'The Public–Private Structure of Intellectual Property Ownership in Agricultural Biotechnology', **21** *Nature Biotechnol.*, 2003, 989–95.

Grassler F. and Capria M. A., 'Patent Pooling: Uncorking a Technology Transfer Bottleneck and Creating Value in the Biomedical Research Field', **9** *Journal of Commercial Biotechnology*, 2003, 115–32.

Heller, M. A., and Eisenberg, R. S., 'Can Patents Deter Innovation? The Anticommons in Biomedical Research', **280** *Science*, 1998, 698–701.

Henson-Apollonio, V., 'Case 10. The International Treaty on Plant Genetic Resources for Food and Agriculture: the Standard Material Transfer Agreement as implementation of a limited compensatory liability regime', Chapter 18 of this volume.

Hermerén, G., 'Challenges in the Evaluation of Nanoscale Research: Ethical Aspects', **1**(3) *Nanoethics*, 2007, 223–37.

Holden, A. L., 'The SNP Consortium: Summary of a Private Consortium Effort to Develop an Applied Map of the Human Genome', **26** *Biotechniques Supplement*, 2002, 22–4.

Holman, C. M., 'The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation', **76** *University of Missouri-Kansas City Law Review*, 2007, 295–362.

Hope, J., 'Open source genetics. Conceptual framework', Chapter 12 of this volume.

Hopkins, M. M., Mahdi, S., Patel, P. and Thomas, S., 'DNA Patenting: The End of an Era?', **25** *Nature Biotechnology*, 2007, 185–7.

The Patenting of Human DNA: Global Trends in Public and Private Sector Activity (A Report for the European Commission – PATGEN Project – 6th FP-2003- LifeSciHealth-II), Brighton, Science and Technology Policy Research (SPRU) – University of Sussex, 2006, 57 pp. (available at: www.sussex.ac.uk/spru/documents/patgen_finalreport.pdf).

Hörig, H., Marincola, E. and Marincola, F., 'Obstacles and Opportunities in Translational Research', **11** *Nature Medicine*, 2005, 705–8.

Horn, A. L., 'Case 1. The MPEG LA® Licensing Model. What problem does it solve in biopharma and genetics', Chapter 2 of this volume.

Hovenkamp, H., Janis, M. and Lemley, M. A., *IP and Antitrust: An Analysis of Antitrust Principles Applied to Intellectual Property Law*, Aspen Publishers Online, 2002

Jefferson, R., 'Science as a Social Enterprise. The CAMBIA, BiOS Initiative', **1** *EconPapers*, issue 4, 2006, 13–17 (available at http://econpapers.repec.org/article/tprinntgg/).

Jefferson, R. A., Kavanagh, T. A. and Bevan, M. W., 'GUS Fusions: Beta-Glucuronidase as a Sensitive and Versatile Gene Fusion Marker in Higher Plants', **6**(13) *European Molecular Biology Organization Journal*, 1987, 3901–7.

Jensen, K. and Murray, F., 'Intellectual Property Landscape of the Human Genome', **310** *Science*, 2005, 239–40.

Kilian, A., 'Case 9. Diversity Arrays Technology Pty Ltd. Applying the open source philosophy in agriculture', Chapter 14 of this volume.

Klein, J. I., Business Review Letter to Gerrard R. Beeney, 1997 (available at www.usDoJ.gov/atr/public/busreview/1170.htm).

Krattiger, A. F., 'Financing the Bioindustry and Facilitating Biotechnology Transfer', **1** *IP Strategy Today*, 2004, 1–45.

Krier, J. and Schawb, S., 'Property Rules and Liability Rules: The Cathedral in Another Light', **70** *NYU Law Review*, 1995, 440.

Leonard, D., 'Gene Patents: A Physician's Perspective', Paper presented at a meeting of the US National Academies' Science, Technology and Economic Policy (STEP) Board (available at http://www7.nationalacademies.org/step/Leonard_presentation_October_proteomics.ppt).

Lipinski, C. A., 'The Anti-Intellectual Effects of Intellectual Property', **10** *Current Opinion in Chemical Biology*, 2006, 380–3.

Marincola, F., 'Translational Medicine: a Two Way Road', **1** *J Transl Med*, 2003, 1.

Matthijs, G., 'DNA Diagnostics in Practice', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 27–44.

Matthijs, G. and Halley, D. 'European-wide opposition against the breast cancer gene patents', **10** *European Journal of Human Genetics*, 2002, 783–7.

Matthijs, G. and Hodgson, S., 'The Impact of Patenting on DNA Diagnostic Practice', **8** *Clinical Medicine*, 2008, 58–60.

Matthijs, G. and Van Ommen, G.-J., 'Gene patents: from discovery to invention. A geneticist's view', Chapter 20 of this volume.

Merges, R. P., 'Institutions for Intellectual Property Transactions: the Case of Patent Pools' in R. Dreyfuss, D. L. Zimmerman and H. First (eds.), *Expanding the Boundaries of Intellectual Property*, Oxford University Press, 2001, 123–66.

'Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations', **84** *Calif. Law Rev.*, 1996, 1293–393.

'Of Property Rules, Coase, and Intellectual Property, **94** *Columbia Law Review*, 1994, 2655–73.

Merriam-Webster's Online Dictionary (available at www.merriam-webster.com)

Merz, J. F., Kriss, A. G., Leonard, D. G. B. and Cho, M., 'Diagnostic Testing Fails the Test', **415** *Nature*, 2002, 577–9.

Moran, N., 'Public Sector Seeks to Bridge "Valley of Death"', **25** *Nature Biotechnology*, 2007, 266.

Morris, M., 'The Structure of Entitlements', **78** *Cornell Law Review*, 1993, 440.

Moser, 'How Do Patent Laws Influence Innovation? Evidence from Nineteenth-Century World's Fairs', **95(4)** *The American Economic Review*, 2005.

National Research Council of the National Academies (Committee on intellectual Property Rights in Genomic and Protein Research and Innovation), *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health*, Washington, National Academies Press, 2005, 161 pp.

National Research Council of the National Academy of Sciences (Committee on Intellectual Property Rights in the Knowledge-Based Economy), *A Patent System for the 21st Century*, Washington, National Academies Press, 2004, 172 pp.

Nguyen, T., 'Case 6. The Science Commons Material Transfer Agreement Project. A standard license clearinghouse?', Chapter 9 of this volume.

Nuffield Council on Bioethics, *The Ethics of Patenting DNA: A Discussion Paper*, Nuffield Council on Bioethics, 2002, 109 pp.

Olson, M., *The Logic of Collective Action: Public Goods and the Theory of Groups*, Harvard Economic Studies, 1965, 108 pp.

Organisation for Economic Co-operation, and Development (OECD), *Draft Guidelines for the Licensing of Genetic Inventions*, Organisation for Economic Co-operation and Development web site, 2005 (see www.oecd.org/sti/biotechnology/licensing).

Organisation for Economic Co-Operation, and Development (OECD), *Genetic Inventions, Intellectual Property Rights and Licensing Practices*, Report of a workshop organized by the OECD Working Party on Biotechnology, 2002 (available at www.oecd.org/dataoecd/42/21/2491084.pdf).

Parish, R. and Jargosh, R., 'Using the Industry Model to Create Physical Science Patent Pools Among Academic Institutions', **15** *J. Assoc. Univ. Technol. Managers*, 2003, 65–79.

Pizzo, P., 'Letter from the Dean', *Stanford Medicine Magazine*, Fall 2002.

Polski, M., 'The Institutional Economics of Biodiversity, Biological Materials, and Bioprospecting', **53** *Ecological Economics*, 2005, 543–57.

Rai, A.K., 'Critical commentary on 'open source' in the life sciences', Chapter 15 of this volume.

'Proprietary Rights and Collective Action: The Case Of Biotechnology Research With Low Commercial Value', in K. Maskus and J. Reichman (eds.), *International Public Goods and Transfer of Technology*, Cambridge, Cambridge University Press, 2005, 288–306.

'Open and Collaborative Research: A New Model for Biomedicine,' in Robert W. Hahn (ed.), *Intellectual Property Rights in Frontier Industries: Software and Biotechnology*, 2005, 131–58.

'Regulating Scientific Research: Intellectual Property Rights and the Norms of Science', **77** *Northwest University Law Review*, 1999, 77–152.

Rai, A. K., Reichman, J. H., Uhlir, P. F. and Crossman, C., 'Pathways across the valley of death: novel intellectual property strategies for accelerated drug discovery', Chapter 17 of this volume.

Raymond, E., 'The Magic Cauldron', 1999 (available at www.catb.org/~esr/writings/magic-cauldron/magic-cauldron.html).

Rawls, J., *A Theory of Justice*, The Belknap Press of Harvard University Press, 1971.

Reichman, J. H., 'Of Green Tulips and Legal Kudzu: Repackaging Rights in Subpatentable Innovation', **53** *Vanderbilt Law Review*, 2000, 1743–98.

Reichman, J. H. and Lewis, T., 'Using Liability Rules to Stimulate Innovation in Developing Countries: Application to Traditional Knowledge', **337** *International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regime*, K. E. Maskus and J. H. Reichman (eds.), 2005, 337–66.

Reichman, J. H. and Uhlir, P. F. 'A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment', **66** *Law and Contemporary Problems*, 2003, 315–462.

Scherer, F. M., 'The Economics of Human Gene patents', **77** *Acad. Med.*, 2002, 1348–67.

Schwab, K. and Hartigan, P., 'Social Innovators with a Business Case. Facing 21st Century Challenges. One Market at a Time', **1** *EconPapers*, issue 4, 2006, 7–11 (available at http://econpapers.repec.org/article/tprinntgg/).

Lemley, M. A., 'Antitrust, Intellectual Property and Standard Setting Organizations' (see econ.tau.ac.il/papers/applied/0109037.pdf).

Shapiro, C., 'Navigating the Patent Thicket: Cross Licenses, Patent Pools and Standard Setting' in E. Jaffe et al. (eds.), *Innovation Policy and the Economy* (Vol. I), MIT Press, 2001, 119–50, (also available at http://haas.berkeley.edu/wshapiro/thicket.pdf).

Simon, J., 'Dealing with Patent Fragmentation: The SARS Patent Pool as a Model', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 115–20.

Spence, M., 'Comment on the conceptual framework for a clearinghouse mechanism', Chapter 11 of this volume.

Strandburg, K., 'Sharing Research Tools and Materials: Homo Scientificus and User Innovator Community Norms', in *Working Within the Boundaries of Intellectual Property*, Dreyfuss, R. & Zimmerman, D. (eds.), Oxford University Press (forthcoming), and the references cited there. Article on file with the editor.

Rosen, L., *Open Source Licensing: Software Freedom and Intellectual Property Law*, New Jersey, Prentice Hall, 2004.

Taubman, A., 'Several kinds of "should". The ethics of open source in life sciences innovation', Chapter 16 of this volume.

'The Triumph of the Commons: Can Open Source Revolutionise Biotech?', *The Economist*, February 10, 200.

Thomas, D., 'The EPC and the Granting Policy and Case Law of the EPO', G. Van Overwalle, (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 61–71.

Ullrich, H., 'Gene patents and clearing models. Some comments from a competition law perspective', Chapter 22 of this volume.

Van Overwalle, G., 'Human Rights' Limitations in Patent Law', in W. Grosheide (ed.), *The Human Rights Paradox in Intellectual Property Law*, Oxford, Edward Elgar Publishing Ltd, 2009 (in press).

'L'intérêt général, le domaine public, les *commons* et le droit des brevets d'invention', in M. Buydens and S. Dussolier (eds.), *L'intérêt général et l'accès à l'information en propriété intellectuelle*, Brussel, Bruylant, 2009, 149–175.

(ed) *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 241 pp.

'Setting the Scene', in G. Van Overwalle, (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 11–24.

'Reshaping Bio-Patents: Measures to Restore Trust in the Patent System', in H. Somsen (ed.), *The Regulatory Challenge of Biotechnology. Human Genetics, Food and Patents*, Cheltenham, UK – Northhampton, US, Edward Elgar Ltd., 2007, 238–56 (Proceedings of a Conference held at the University of Amsterdam 27–28 May 2004).

'The Implementation of the Biotechnology Directive in Belgium and its Aftereffects. The Introduction of a New Research Exemption and a Compulsory License for Public Health', 37 *International Review of Intellectual Property and Competition Law (IIC)*, 2006, 889–920.

'Octrooien op maat? Naar een evenwicht tussen publieke opdracht en privaat goed' ['Patents Fit All? Towards an Equilibrium Between Public Mission and Private Good'], in B. Pattyn and G. Van Overwalle (eds.), *Tussen Markt en Agora. Over het statuut van universitaire kennis* [*Between Market and Agora. About the Status of Academic Knowledge*], Leuven, Peeters, 2006, 181–214.

'Legal and Ethical Aspects of Bio-Patenting. A Critical Analysis of the EU Biotechnology Directive', in C. Baumgartner and D. Mieth (eds.), *Patente am Leben? Ethische rechtliche und politische Aspekte der Biopatentierung*, Paderborn, Mentis, 2003, 145–58.

'Klinische proeven en volksgezondheid. Naar een herijking van het algemeen belang in het octrooirecht' ['Clinical Trials and Public Health. Towards a Reassessment of Public Interest in Patent Law'], *Tijdschrift voor Privaatrecht [Journal for Clinical Law]*, 2000, 899–968.

Van Overwalle, G. and van Zimmeren, E., 'Functions and Limits of Patent Law', in E. Claes, W. Devroe and B. Keirsbilck (eds.), *Limits of the Law*, Springer, 2009, 415–42.

Van Overwalle, G., van Zimmeren, E., Verbeure, B. and Matthijs, G. 'Models for Facilitating Access to Patents on Genetic Inventions', 7 *Nature Reviews Genetics*, 2006, 143–54.

van Zimmeren, E., 'Clearinghouse mechanisms in genetic diagnostics. Conceptual framework', Chapter 5 of this volume.

van Zimmeren, E. and Avau, D., 'Case 4. BirchBob. An example of a technology exchange clearinghouse', Chapter 7 of this volume.

van Zimmeren, E. and Requena, G., 'Ex-Officio Licensing in the Medical Sector: The French Model', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 123–47.

Van Zimmeren, E., Verbeure, B., Matthijs, G. and Van Overwalle, G., 'A Clearinghouse for Diagnostic Testing: the Solution to Ensure Access to and Use of Patented Genetic Inventions?', *Bulletin of the World Health Organization*, 2006, 352–9.

Verbeure, B., 'Patent pooling for gene-based diagnostic testing. Conceptual framework', Chapter 1 of this volume.

Verbeure, B., Van Zimmeren E., Matthijs G., and Van Overwalle G., 'Patent Pools and Diagnostic Testing', **24**(3) *Trends in Biotechnology*, 2006, 115–20.

Verbeure, B., Matthijs, G. and Van Overwalle, G., 'Analysing DNA patents in relation with diagnostic genetic testing', **14** *European Journal of Human Genetics (EJHG)*, vol. I, 2006, 26–33.

Verbruggen, J. and Lorincz, A., 'Patents and Technical Standards', in **33** *IIC*, 2002, 125–32.

Vlassak, K. and Schüller, K., '*The Effect of Patents on Diagnostic Research and Kit Development*', in G. Van Overwalle (ed.), *Gene Patents and Public Health*, Brussel, Bruylant, 2007, 99–113.

Walpole, I. R., Dawkins, H. J. S., Sinden, P. D. and O'Leary P. C. 'Human Gene Patents: The Possible Impacts on Genetic Services Healthcare', **179** Medical Journal of Australia, 2003, 256–83.

Walsh, J. P., Arora, A. and Cohen, W. M., 'Effects of Research Tool Patents and Licensing on Biomedical Innovation' in W. M. Cohen and S. A. Merrill (eds.), *Patents in the Knowledge-Based Economy*, Washington, The National Academies Press, 2001, 285–340.

Walsh, J. P., Cho, C. and Cohen, W. M., 'Where Excludability Matters: Material Versus Intellectual Property in Academic Biomedical Research', **36** *Research Policy*, 2007, 1184–1203.

'View from the Bench: Patents and Material Transfers', **23** *Science*, 2005, 2002–3.

Patents, Material Transfers and Access to Research Inputs in Biomedical Research (Final Report to the National Academy of Sciences Committee [on] Intellectual Property Rights in Genomic and Protein-Related Research Inventions), Washington, National Academies Press, 2005, 172 pp.

Warcoin, J., ' "Patent Tsunami" in the field of genetic diagnostics. A patent practitioner's perspective', Chapter 21 of this volume.

Wenzl, P., Carling, J., Kudrna, D., Jaccoud, D., Huttner, E., Kleinhofs, A. and Kilian, A., 'Diversity Arrays Technology (DArT) for Whole-Genome Profiling of Barley', **101** *PNAS*, 2004, 9915–20.

World Health Organisation (WHO), *Public health, Innovation and Intellectual Property Rights*, Report of the Commission on Intellectual Property Rights, Innovation and Public Health, WHO, April 2006, 228 (available at www.who.int/intellectualproperty/documents/thereport/CIPIH23032006.pdf).

Yochai Benkler, 'Coase's Penguin, Or, Linux and the Nature of the Firm', **112** *Yale L.J.*, 2002, 369–446.

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