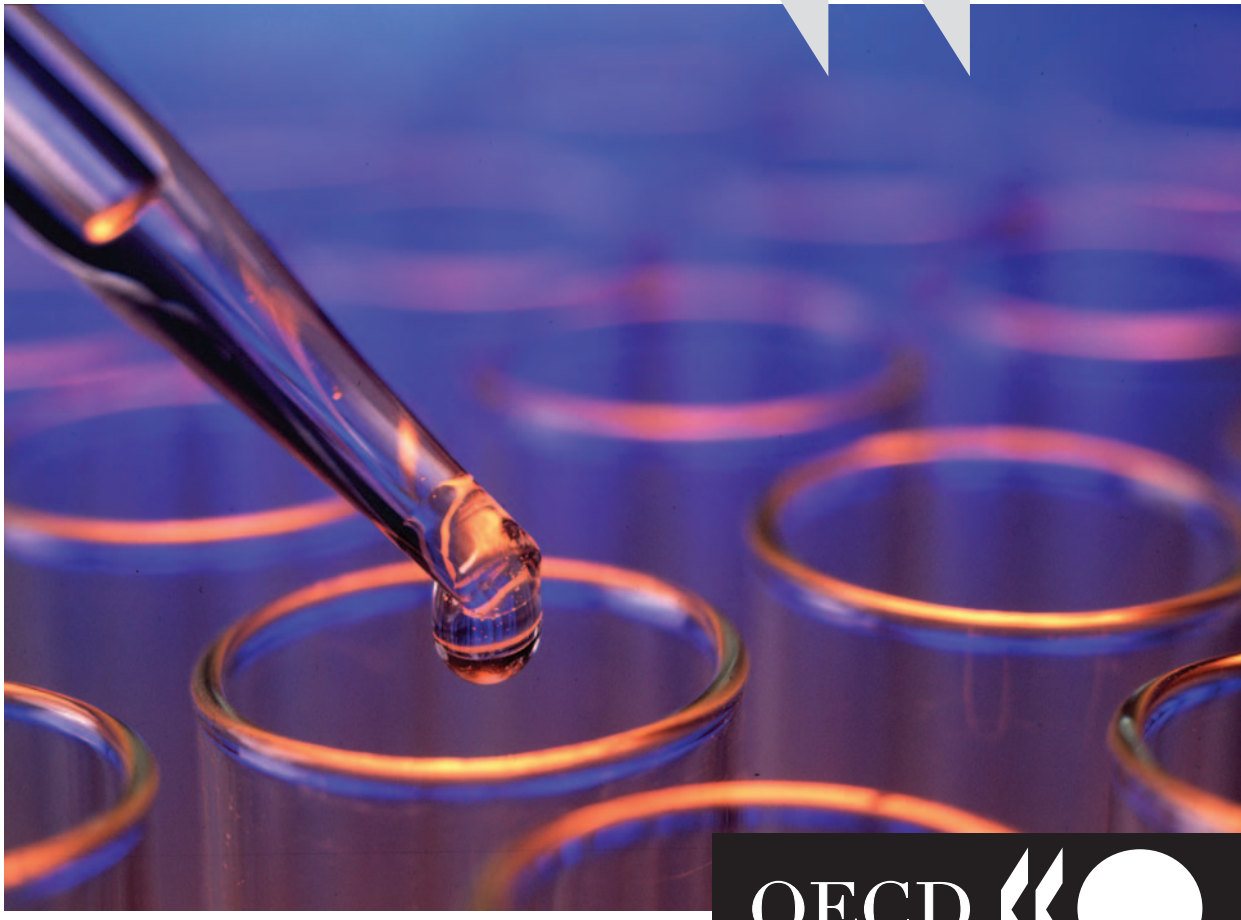
Genetic Inventions, Intellectual Property Rights and Licensing Practices

EVIDENCE AND POLICIES



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EVIDENCE AND POLICIES

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FOREWORD

On 24-25 January 2002, the OECD Working Party on Biotechnology held an expert workshop, "Genetic Inventions, IPR, and Licensing Practices", which was hosted by the German Federal Ministry for Education and Research in Berlin and opened by Minister Edelgard Bulmahn. Invited speakers included practitioners from industry, government, public research organisations (PROs) and the legal community. Over 100 private and public sector experts from 18 OECD countries attended. The meeting aimed to inform OECD member countries about:

- The challenges raised by the proliferation of patents on genes and gene fragments, and by the licensing strategies of firms, research bodies and others.
- Studies and empirical data that could shed light on the economic impact of the present system of intellectual property (IP) protection for genetic inventions, in particular studies that explore how patenting and licensing practices have influenced the research process, new product development and the clinical diffusion and use of novel treatments and diagnostics.
- The advantages and disadvantages of various policy measures, within and outside the IP regime, which could be used to address any systemic breakdowns in access to genetic inventions.

OECD member countries wish to address public concerns about systematic gene patenting. Lack of trust in the patent system and its application to genetic inventions stems from many sources. While companies and patent offices are sometimes accused of not acting in the public interest, such concerns increasingly extend to the actions of scientists, doctors, universities and government agencies. At the same time, OECD member countries recognise the important role the patent system has played in developing a vibrant biotechnology industry which contributes to the advancement of medical science and to public health.

In an attempt to address public concerns, OECD member countries have sought to identify the most pressing practical problems posed by DNA patents and the way they are licensed. The focus of this report, therefore, is the identification

of any systematic problems encountered by researchers, firms or clinical users of DNA patents in their attempts to gain legal access to genetic inventions. The report also explores solutions that might be considered remedies to specific access problems.

The present publication is an edited and amplified version of the rapporteur's report by Mr. R. Stephen Crespi. Dr. Bénédicte Callan of the OECD contributed sections of this report and incorporated improvements suggested by the Working Party for Biotechnology, the project Steering Group and outside experts. It is published on the responsibility of the Secretary-General of the OECD.

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Chapter 1

INTRODUCTION TO THE ISSUES AND QUESTIONS

Innovation in biotechnology and the rise of gene patents

Biotechnology is a fast-moving field in which new products and services are developed from an increasingly complex and cumulative set of underlying technologies. The ability to sequence genes, identify their functions and mutations, create systems to selectively express, regulate or silence genes, predict protein structures and expression, map the influence of genetic make-up on metabolism and otherwise analyse the vast amounts of genetic data has been dubbed the genomics revolution. These many technologies contribute to the rapid pace of advancement in the life sciences and offer tremendous promise for improving human health and furthering economic development.

The genomics revolution, however, has reopened debate about intellectual property rights (IPR). OECD member countries are trying to balance the need to keep information and access to genetic data open in order to encourage the diffusion of research results with the commercial need to protect inventions in order to create revenue from investments in research and development (R&D). From the start, advances in biotechnology have tested the boundaries of the intellectual property rights system. An important early legal landmark was the 1980 US Supreme Court *Diamond v. Chakrabarty* decision on the patentability of a genetically modified bacterium, after which inventions involving biological materials and some life forms were deemed patentable in the United States and later in other countries. Since then, OECD countries have had to decide on the patentability of other biotechnological inventions, and some of the most contentious debates have been about the granting of patents on genetic material.

In many OECD countries, patent protection for biotechnological inventions has been available and expanding for close to 20 years. The existing patent system's adaptability to innovations in biotechnology has contributed to the rapid

development of a new and dynamic industry. Given the commercial importance of the pharmaceutical sector and the new biotechnology industry, it is not surprising that researchers in the public and private sector increasingly took advantage of patent protection in the hopes that their inventions might have commercial applications. From 1990 to 2000, the number of patents granted in biotechnology rose 15% a year at the United States Patent and Trademark Office (USPTO) and 10.5% at the European Patent Office (EPO), against a 5% a year increase in overall patents (OECD, 2001).

A subset of these biotechnology patents covers "genetic inventions". These gene – or DNA – patents have claims that cover nucleotide (DNA or RNA) sequences that may encode genes or fragments of genes. The number of gene patents granted has risen dramatically since the second half of the 1990s. In 2001, over 5 000 DNA patents were granted by the USPTO, more than the total for 1991-95 combined. According to the USPTO, 9 456 patents that include the term "nucleic acid" in the claims have been granted, 8 334 of them since 1996.[1] In Japan, the Japanese Patent Office (JPO) has granted 5 652 such patents since 1996. Similarly, the EPO estimates it has approved several thousand patents for genetic inventions. In 2000, about 5 000 patent applications were filed at the EPO pertaining to "mutations or genetic engineering", 605 of which relate to human or animal DNA sequences. The number of gene patents will continue to grow rapidly as researchers exploit information from the recently sequenced human genome as well as other plant and animal genomes.

The OECD project on genetic inventions, IPR and licensing practices

The rise in the number of patents for genetic inventions can be a sign of dynamism in a new technological sector. Questions have been raised, however, about the potential impact of the growing web of gene patents on: *i)* the research environment; *ii)* the market dynamics for new product development; and *iii)* the clinical uptake of new tests and treatments. Since gene patents have existed for several years, the concerns they raise are increasingly about the way the patents are used and licensed (or not licensed) by their owners.

Unfortunately, policy debate about gene patenting has generally not benefited from reliable information on the licensing practices of title holders to genetic inventions. The objective of this report, therefore, is to provide OECD member countries with a better understanding of the data, cases and studies that illuminate how gene patents are actually being used by firms and research organisations; what advantages and disadvantages certain licensing practices present for users;

and what strategies are being developed in response to the proliferation of gene patents. The report documents the benefits of licensing practices and the concerns they have raised, and identifies possible policy responses to identified problems.

The body of this report is based on discussions at the OECD Expert Workshop on Genetic Inventions, Intellectual Property Rights and Licensing Practices. The Workshop addressed six major themes.

- ***The IPR system and its relevance to genetic inventions.*** This session addressed the criteria of patentability for genetic inventions, trends in gene patenting, the limits of the patent system and current debates about proposed legal, regulatory and administrative reforms affecting the patenting of genetic inventions.
- ***New surveys of patenting and licensing practices for genetic inventions.*** This session included presentations of three recent studies of bio-pharmaceutical licensing practices and examined existing data on the licensing of genetic inventions, on who licenses what to whom, and what are considered the greatest challenges and opportunities these licensing practices raise for researchers in the public and private sectors.
- ***The impact of patenting and licensing practices on public research.*** This session discussed strategies of public research organisations for the patenting and licensing of genetic inventions, the design of institutional or national policies to maintain greater legitimate public access to genetic inventions, and the invocation of research exemptions for non-commercial research.
- ***The impact of patenting and licensing practices on new product development.*** This session explored the benefits for industry of patents on genetic inventions; the challenges of patent thickets, patent dependencies, reach-through rights and royalty stacking; and the possible use of consortia, patent pools and collective rights organisations as novel private-sector strategies for maintaining access to genetic inventions and information.
- ***The impact on human health and technology uptake.*** This session focused on licensing practices and their effects on public access and costs for genetic tests, public and private strategies to obtain greater access to genetic tests and ethical considerations.
- ***Lessons to be drawn and potential strategies for ensuring access.*** This session addressed whether there were any systematic failures in the

licensing of genetic inventions; the main challenges licensing practices raise for companies, the public research sector, and health care providers/users; and what private and governmental tools could be used to meet these challenges.

These sessions aimed to help governments assess whether the current system of protection for gene-based inventions is working to achieve their social and economic goals. In the health field, these involve effective delivery of health care, including the advancement of scientific knowledge and the rapid development and uptake of cost-effective new diagnostics, methods and treatments.

Concerns about patenting genes

In many OECD countries, genetic inventions are both legally patentable and increasingly patented. The presentations at the Berlin Workshop indicate that, up to now, this has not led to a systemic breakdown of R&D or the clinical availability of new products and treatments. Many legal specialists tend to see DNA patenting as a largely "settled" issue, and remaining difficulties in the system as technical challenges best decided by the courts and patent offices.

In most OECD countries, the statutory situation of gene patents has been much clarified since the late 1990s. In the United States, for example, the USPTO decided in 1998 that gene fragments, such as expressed sequence tags (ESTs), were patentable if the patent application disclosed a genuine function. In 2001, the USPTO published its *Revised Guidelines on the Examination of Patent Applications*, which clarified that patent applications must disclose "a specific, substantial and credible utility".

In Europe, the EU Directive 98/44/EC on the legal protection of biotechnological inventions states that gene sequences with specified function are eligible for patent protection. The Directive was adopted in 1999 by the EPO and is law throughout Europe, although only five European countries have sp far ratified the directive (Denmark, Finland, Greece, Ireland and the United Kingdom, which, however, has not ratified two articles). The EC directive will unify not only European legislation but also the interpretation thereof, and in time the European Court probably will become an important actor in this field.[2]

In 2001, the Japanese Patent Office issued examination guidelines for biological inventions as well as examples of examinations for inventions related to DNA fragments, full-length cDNA, and single nucleotide polymorphisms (SNPs).[3]

In fact, the USPTO, the EPO and the JPO co-operate to try to reach similar understandings with respect to their patent examination practices for biotechnology through a trilateral commission which can ultimately help to harmonise practices worldwide.[4]

Nevertheless, in many OECD member countries the patenting of genetic inventions still raises questions of an ethical, legal and commercial nature. Despite the greater statutory clarity, debate on gene patenting has not abated and can be extremely heated. Critics of the existing system include groups as respected as *Médecins sans frontières*, which won the Nobel Peace Prize; as scientifically knowledgeable as the Human Genome Organisation and the American College of Medical Genetics; as politically influential as the Green parties in Europe, the European Parliament and some Canadian provincial governments. New actors, including patient groups for particular diseases and doctors, have also joined the policy discussions and have helped to bring the rather esoteric subject of patents for genetic inventions to widespread public attention.

The most influential critics of the present system are not against intellectual property rights, technological change and scientific advances in principle, but they feel a certain reticence about genetic inventions. For some, the issue is mostly ethical, a dislike of associating property rights with biological materials, especially if they are human.[5] To others, genes are part of the "common heritage of humanity" and should only be public property. There are arguments that DNA does not meet the legal criteria for patentability. If genes are "nature identical materials" and the identification of their utility lies more in the area of a discovery than an invention, for example, they should not be patentable. Others argue that DNA sequences are not simply chemical compounds but also strings of information and that the genome should be viewed as a huge database whose information should be available to all.[6] Still others feel that the peculiar character of the genome warrants special consideration. The finite nature of the genome – the relatively small number of human genes and the limited genetic variation between species – might call into question the assignation of property rights. It is feared that within a rather short period all of the 30 000–40 000 human genes could be patented and that their owners would be the beneficiaries of huge "reach-through rights" on the many uses of these genes yet to be discovered. Finally, gene patents are said to be special because the book of life is very hard to "invent around" making these patents stronger than in other fields.

Focusing on the practical implications of DNA patents, academic researchers, clinicians, patient groups and even pharmaceutical companies have warned about the possible side effects of a proliferation of gene patents. Their concerns have to

do with the cost, pace and efficiency of research, as well as the downstream development and uptake of new genetic technologies by commercial users and health care providers. Perhaps the best way to summarise these practical concerns is to call them "access issues". Such groups worry that the removal of research resources (*i.e.* nucleotide sequences) from the public domain will impede the follow-on research efforts necessary to make genetic information useful. In the words of a recent USPTO paper:

> "Many feel that by allowing genetic information to be patented, researchers will no longer have free access to the information and materials necessary to perform biological research. This issue of access to research tools relates to the ability of a patent holder to exclude others from using the material. Further, if a single patent holder has a proprietary position on a large number of nucleic acids, they may be in a position to 'hold hostage' future research and development efforts."
>
> J. Clarke *et al.* (2001)

Examples of access issues are described below. In several cases, it would appear that the present system of protection and exploitation of genetic inventions seems not to deliver the greatest common good. It is difficult, however, to judge whether the examples given are anecdotal, isolated accounts, typical of the learning process for the protection of new technologies, or whether they presage a more systemic failure that may require public attention.

Access issues are arranged under three headings: "research issues", where access to information or material by third-party researchers appears to have been impeded as a consequence of protection; "commercialisation issues", where access by those who would develop other commercial products has been impeded; and "clinical use issues", where protection appears to have impeded access to information or material in a clinical setting.

Many of the examples come from the United States. While similar issues are believed to be relevant in other OECD countries, there is less documentation of their frequency or impact.

Research issues

Blocking patents or overly broad patents. In theory, patents on early "foundational" discoveries, if not widely licensed, may discourage or limit the use

of these important innovations and slow the pace of R&D in a particular field. Foundational discoveries are early discoveries in a field, which are of sufficient importance that all or much that follows in that field flows from these discoveries. An example of a foundational invention is the Cohen-Boyer patent on recombinant DNA. Some researchers fear that patents granted on genes implicated in disease could have such a "blocking" effect on further research by others on the disease.

In 2000 the USPTO granted a patent to Human Genome Sciences (HGS) which claimed rights to a gene, the precise function of which was initially unknown and the utility of which was asserted to be a research reagent or material for diagnostics. When other researchers subsequently discovered the DNA sequence actually coded for the CCR5 receptor, the "docking receptor" used by the HIV virus to infect a cell, it was widely feared that this patent would have a "blocking" effect on AIDS research. Since, HGS has issued several licences for research into new drugs and does not plan to prevent academics from undertaking unlicensed research into CCR5 (Nuffield Council on Bioethics, 2002). In this case, fears about blocking appear thus far to be unfounded.

Similarly, the Wisconsin Alumni Research Foundation (WARF) was recently granted a patent on pluripotent embryonic stem cells and the method for isolating them. Human embryonic stem cells, from which many types of cells can be derived, are likely to be an important research tool. It is believed that this patent will cover any embryonic stem-cell invention. WARF awarded an exclusive licence to Geron Corporation for the commercial development of a number of cell types. Academic researchers feared that the exclusive licence could limit their access to this fundamental research tool. However, in a memorandum of understanding with the US National Institutes of Health (NIH), it was agreed that researchers at the NIH and non-profit institutions that win NIH grants will be able to access the cell lines for the cost of handling, or approximately USD 5 000 (NIH, 2001). In this case, too, a way forward seems to have been found.

Increases in secrecy and a slower pace of research. There is some evidence in the biomedical sciences that research delays (before the publication of research results) are increasing, although it is as yet unclear why this is occurring. The withholding of data, research materials and research results is reputed to be more common in genetics and especially in human genetics than in other fields (Weinberg, 1993). Delays in publishing and in sharing data with other researchers may be necessary for a limited period if researchers are to apply for patents. They may also be used to protect the proprietary value of the research or establish a scientific lead. Delays in publication of research results, however, are frequently attributed to requests by commercial R&D partners (for a survey of such practices,

see Campbell *et al*., 2002). The effect of increased secrecy might be to slow the pace of research, by making it impossible to confirm published research and by increasing duplicate research efforts (Campbell *et al*., 2002). Recognising this trend, scientists from the genome centres affiliated with the Human Genome Organisation agreed in 1996 to share the results of sequencing "as soon as possible" and to submit the data to Genbank, the public database of sequence information, within 24 hours. It is not clear what effect this commitment has had on secrecy or the pace of research.

Increased research and transaction costs. Even where patent owners are amenable to licensing, the price demanded for use of a genetic invention might pose a barrier to researchers. Different research-performing institutions may have very different perspectives on the value of a research tool (Eisenberg, 1999). Moreover, negotiations over access to technologies and materials can be long and complicated, imposing delays and administrative burdens on research. Finally, the terms of licences or material transfer agreements – restricting publication and exchange of materials, demanding reach-through rights – can be such that they ultimately make collaboration and communication with other researchers more difficult. Some public research organisations and universities are trying to develop simple, standard "materials transfer agreements" that could reduce paperwork and maximise the exchange of technologies (NIH, 1998a).

The DuPont Cre-lox case is the archetypal example of the above concerns. Cre-lox is a gene-splicing tool patented by Harvard University and under exclusive licence to DuPont Pharmaceutical Co. It allows researchers to make knock-out mice by deleting a single gene from specific cells and is very useful for identifying gene function. DuPont initially asked that public-sector researchers sign an agreement that would limit their ability to use and share the Cre-lox technique and that would subject their articles to pre-publication review by the company. In addition, DuPont wanted commercial rights to future inventions that might arise from experiments involving Cre-lox animals (*i.e.* reach-through rights). While at least 150 universities and non-profit organisations agreed to these terms (Freundlich, 1998), some prominent institutions, including the NIH, refused, claiming they created obstacles to biomedical research. The issue was resolved in the United States in 1998 with a memorandum of understanding between the NIH and DuPont (and separate agreements with academic laboratories), which simplified access conditions for the US public sector to this patented research tool (NIH, 1998b).

Increased litigation at public research organisations. As public research increasingly becomes commercially relevant and public research organisations

push to exploit intellectual property, their current exemption from litigation over patent infringement is put in jeopardy. Recently, a US patent was granted on the NF-KB messenger protein claiming rights to any disease treatment methods that affect the NF-KB pathway. Ariad Pharmaceuticals holds an exclusive licence on the patent, and it is as yet unclear whether the company will require licences for any corporate-sponsored academic research projects on the pathway (Brickley, 2002). This would seem to be a departure from the present, often tacit, corporate practice in some OECD member countries of allowing academic researchers to use patented inventions without a licence. This is sometimes called the "informal research exemption".

Commercialisation issues

Patent thickets and royalty stacking. The proliferation of gene patents, including multiple patents on various research tools, can necessitate negotiating multiple licences when developing a single product or process. Such patent thickets have the potential to raise the transaction costs of doing research and possibly the ultimate cost of products owing to stacking of royalties and, in some OECD member countries, the potential for more frequent legal disputes.[7] For example, the development of a medicine may require licences to access genomics technologies, targets such as receptors, assays and high-throughput technologies. Companies report that royalty exposure to net sales of a given product can in some cases exceed 20%.[8]

While there are few commercial data available on the density of patent thickets or the extent of royalty stacking for new products, some not-for-profit groups have revealed how they navigate patent thickets. For example, in considering the development of a malarial vaccine which could be sold at relatively low cost in developing countries, the Programme for Appropriate Technology (PATH) commissioned a study of the patents that might need to be licensed for a vaccine that would rely on the MSP-1 protein of the malaria parasite (Nuffield Council on Bioethics, 2002). From an initial patent map of close to 40 relevant patents (Galloway, 2002), PATH narrowed the relevant patents to five core US patents relating to MSP-1, a dozen patents useful in constructing vaccines, and five specialised patents for the production of MSP-1 vaccines.

Reach-through claims. Research tool patents (*e.g.* patents on markers, assays, receptors, transgenic animals) increasingly claim they cover products "identified by" the patented tool or method. If such a claim is granted, patent owners can demand royalties on the sale of a product found with the help of their

research tool. Since many different patented research tools must be used in the development of a drug, reach-through claims increase royalty stacking. A number of such patents have been granted, including: *i)* European Patent (EP) 724 637 B1, which claims the CRF2 antagonist and its use for the manufacture of a drug; *ii)* EP 680 517 B1, which claims a method for determining the toxicity of a compound, a method for decreasing its toxicity and a modified drug produced by the method; *iii)* US Patent 6 048 850, which claims a method for selectively inhibiting PGHS-2 activity in humans, and the future compounds which, when administered to humans, will selectively inhibit the activity of PGHS-2 (Grubb, 2002).

Dependency and uncertainty. There has also been concern that the rapid proliferation of gene patents will increase commercial uncertainty owing to possible dependency between granted patents. For example, if different patents are granted for inventions that claim respectively a partial gene sequence (*e.g.* an EST), the full-length cDNA or gene, and the protein encoded, it is unclear which title holder will be able to prevent the others from using his or her invention. While licensing under uncertainty about the extent of property rights is not new to the pharmaceutical industry, too much litigation could again slow progress, raise end-product costs or discourage entry to certain fields of enquiry.

Clinical use issues

Costs and terms of access. As disease-related genes are discovered, an increasing number of tests for genetic predisposition to diseases are being developed.[9] Disease gene patents generally claim "a gene sequence, one or more mutations which are found to be associated with disease or risk of disease…all uses of the chemical sequences…[and] also all methods of diagnosis of disease by identifying in a specific patient the disclosed genetic alleles, mutations, or polymorphisms" (Merz, 2000). The licensing practices of the owners of patents for certain genetic tests – for example, Myriad's BRAC1 and BRAC2 breast cancer tests, Athena's Alzheimer's (ApoE) test, and the test owned by Miami Children's Hospital for Canavan's disease – have raised concern about high costs and limited access to genetic tests.

A 1999 survey of the licensing practices of holders of patents that cover the diagnosis of genetic disorders showed that almost all the patents were being licensed exclusively; in theory, this could allow the monopolisation of genetic testing services (Schissel *et al*., 1999). The fear is that exclusively licensed patents are offered at costs that prohibit the provision of genetic testing services. In some

OECD member countries, several public agencies have stepped in to reduce the price of tests. Concerns also exist regarding terms of access, for example if licensed non exclusively. How many laboratories actually offer the test? Who is allowed to perform it? Are physicians prevented from testing their patients? How aggressive is the owner in pursuing those who use the test in research? The main issues regarding IPR and access to genetic tests are set out in Box 1.

Box 1. Access issues in genetic testing

Canavan's disease: Canavan's disease is a rare and fatal genetic disorder in which the myelin sheathing of nerves in the central nervous system degenerate in infants. In order to study the disease and develop a screening test for the gene that gives rise to it, a group of families co-operated with researchers by donating tissue samples from their children. In 1997, scientists at Miami Children's Hospital received a patent on method of diagnosis which also covered therapies potentially arising from the test. MCH subsequently sought to license the test exclusively, prompting some clinical laboratories to stop offering the test and potentially impeding research on the disease. The parents of affected families argued that the test should have been offered non exclusively and free of charge. In response to the criticism, MCH halved its per-test fee.

PXE: As a result of the experience with MCH and Canavan's disease, other patient groups have been more active in obtaining agreement on the terms of their co-operation with researchers. For example, PXE International and scientists at the University of Hawaii jointly filed a patent application in 2000 on the gene which causes *pseudoxanthoma elasticum*. The group, PXE International, created a tissue and blood bank which scientists could access to study this genetic disorder in which connective tissues calcify. Access to the bank was conditioned on signing a contract including a provision for joint ownership of any resultant intellectual property with PXE. The patient group developed this strategy to ensure that future licences for any genetic tests will be inexpensive and widely available (Smaglik, 2000; Fleischer, 2001; Spier, 2001).

BRCA1 and BRCA2: When the two genes BRCA1 and BRCA2 mutate, they are involved in 5-10% of the breast cancer cases diagnosed. Women with the BRCA1/BRCA2 mutations are seven times more likely to develop breast cancer than the general female population. Myriad Genetics has obtained exclusive rights to diagnostic tests for BRCA1 and BRCA2 in many OECD member countries. Myriad's licensing strategy has met with strong opposition. The company insisted that all testing worldwide be performed by Myriad's own laboratories, and its per-test charge is in many cases over USD 2 500. The company sent cease and desist letters to a large proportion of laboratories that had been offering the tests. The reaction worldwide was swift. In France, the *Institut Curie*, the *Assistance publique* and the Gustave Roussy Institute filed opposition to the European patents (Cassier, 2001). The Belgian Society for Human Genetics and the Danish Society for Medical Genetics filed separate oppositions. In the United Kingdom, negotiations are ongoing between the Department of Health and Myriad regarding the terms of the provision of testing for BRCA1 (Nuffield Council on Bioethics, 2002). All Canadian provinces but one are ignoring Myriad's injunctions to stop offering breast cancer genetic testing, despite Myriad's Canadian patents. Many health-care authorities and providers believe that the terms of access to the technology are too stringent, that the costs are too high, and that they may constitute an abuse of monopoly power.

Impediments to improved quality of tests. Because only licensed entities can offer patented genetic tests, if a patent-holder decides not to license, or to license exclusively, other clinical testing services are excluded from using the test. When clinical testing centres are also research laboratories investigating the genetic basis of a disease, the inability to obtain a licence impedes research and can mean that higher-quality tests may not emerge. "[T]he state of the art of genetic tests is such that much more clinical study is necessary to validate and extend the early discovery of a disease gene…the restriction of physicians from performing clinical testing will directly reduce the knowledge about these genes" (Merz, 2000). The French opposition filing at the EPO against Myriad's tests argues that the test misses 10-20% of the BRCA1 and BRCA2 mutations. Moreover, if only one organisation provides a clinical service, it is more difficult to evaluate the service or compare its quality with competing products (Caulfield *et al*., 2000).

In sum, it is very difficult for governments to assess the frequency with which such access issues arise or their impact on research, product development or clinical uptake of new technology. In other words, are the reported cases examples of systematic problems that arise in the licensing of gene patents, or do they represent occasional, acceptable or at least manageable tensions in the patenting system which can be worked out by firms, governments and research organisations? To answer this question, a more comprehensive review of licensing practices is necessary. However, the fact remains that many OECD member country governments continue to face public disquiet about the application of the patent system to genetic inventions.

The OECD Berlin Workshop: A practical focus on facilitating access

The workshop sought to address how patents are used in reality by rights holders and what the economic and social (including access) effects are likely to be. It drew together available empirical data on these issues and debated the implications of the data in order to draw conclusions about the functioning and operation of the patenting and licensing regimes of member countries.

There is already a large literature on innovation and the protection of intellectual property which focuses on the provision of knowledge as a public good and the trade-offs between its under-supply, when IP rights are too weak, and its under-utilisation when IP rights are too strong (Scotchmer, 1991). Many of these studies are concerned with devising optimal IP regimes to encourage innovation and the commercialisation of new technologies (Merges and Nelson, 1990). The importance of intellectual property protection, and particularly of

patents, to individual companies for fostering innovation and maintaining an edge over competitors varies greatly from industry to industry. The pharmaceutical and biotechnology industries are reputed to be among the most reliant on patent protection (Mansfield, 1986). In part this is because these industries invest far more in R&D than other sectors, and their innovations are easily copied by competitors (for patent protection in biotechnology, see Hirshhorn and Langford, 2001).

This report does not question the nature of the IP regime or its importance to fostering genetic inventions. The workshop quickly concluded that the patent system has in general well served the interests of commercial business, science-based industries and, more recently, the scientific research community, all of which invest significant time and money into improving health care, nutrition and agriculture, ultimately for the public's benefit. Instead, both the workshop and this report have tried to evaluate whether licensing practices for genetic inventions are working well or encountering significant roadblocks. Obviously, it is impossible to divorce the licensing of inventions from the rights conferred by patents, but the focus here is on trying to understand the strategies of firms and research organisations as they attempt to exploit their inventions and to gain legitimate access to information and technologies held by their competitors.

To this end, the most recent studies about the licensing of genetic inventions, including three new surveys of licensing practices at firms, public research organisations and hospitals, were presented. Practitioners were asked to identify the challenges they routinely face in gaining access to patented genetic inventions and whether they have had to develop new strategies to facilitate the process. It appeared that firms, governments and civil society are rapidly reorganising their approaches to dealing with the ever more complex and crowded environment of intellectual property protection. For example, public research organisations are developing model contracts for simplified material transfer, companies are negotiating new contracts to reduce the stacking of royalties, patient groups are learning to make in advance their claim to the results of any studies in which they participate.

Workshop participants identified three issues that might warrant government attention. These are:

- The clinical use of patented genetic tests. The genetic tests for breast cancer have come under particular criticism because the patent holders for these genes are refusing to license so that no others can provide testing services.

- The commercial use of patents which include reach-through claims.
- The ability of public research organisations to identify and protect their IP and research missions interests adequately, although this is not specific to the protection of genetic inventions.

Workshop debate focused on remedies that might be envisaged to address these access problems.

In the rest of this report, Chapter 2 reviews the legal framework for the patentability of genetic inventions in OECD countries. Chapter 3 discusses empirical evidence on the issuance of patents for genetic inventions and the licensing practices of title holders. Chapter 4 is the core of the report and summarises the main debates and points of consensus of the workshop. Finally, Chapter 5 re-emphasises the main policy lessons and suggests areas which might benefit from future policy attention in OECD member countries.

Chapter 2

THE PATENTING OF GENETIC INVENTIONS

This chapter provides a brief factual overview of the patenting of genetic inventions. It relates the basic principles of intellectual property protection, summarises the key issues in patent protection, and describes how patent protection for genetic inventions currently works. It also provides a brief review of the types of reform proposals being debated which would influence the patenting and licensing of genetic inventions.

The basic principles of IP protection

The essential principle of all forms of IPR is to recognise and reward the work of inventors, designers and authors because society deems that it benefits from the promotion of the useful and cultural arts. This recognition is achieved by the granting of a measure of legal protection, of a specified duration, against unauthorised use and reproduction by others of the invention, design or protected work.

When technological innovations lead to new processes and products, as is often the case with genetic inventions, patents are the form of IPR most often used to protect the invention. The laws on copyright and database rights may also apply to certain aspects of the disclosure of information in the field of gene sequences. Indeed, the rise of genomic databases, and the algorithms to analyse them, may make other forms of protection increasingly valuable in the near future (European Commission, 2001). However, patents and the licensing of patented technologies are the main concern of this study.

Objectives of the patent system

The patent system has many objectives. As mentioned above, it aims to protect inventors and those who fund their work. It also promotes the disclosure of inventions, as against secrecy, through the publication of patent applications. One condition for granting a patent is that the inventor must disclose the invention in a written description (the patent specification) which gives a skilled person adequate instructions for putting the invention to practical use. A third objective has a more implicit purpose, namely, to stimulate others to "invent around" patents. Inventions may be viewed as new solutions to technical problems. Therefore, insofar as a patent gives its holder the exclusive right to benefit from his/her particular solution, others may be induced to find alternative solutions which can be used without infringing the patent in question. The necessity to "design around" or "work outside" the patent is often the mother of further invention (see Box 2).

Box 2. Inventing around gene patents

Several companies are trying to make a market out of the legal circumvention of patents on genes or gene-related molecules. Patents on genetic inventions cannot cover a substance as it is found "in nature". Most patents, therefore, claim nucleotide sequences that have been isolated, purified and/or altered outside the plant, animal or micro-organism. This leaves open the possibility of changing the expression of the patented gene inside the body or cell, a process called "endogenous activation" or "gene switching". Companies such as Sangamo BioSciences, Athersys and Transkaryotic Therapies have developed different technologies that activate protein production and are designed to work around existing patent thickets. Whether these technical solutions will be found not to infringe existing gene patents is being tested in US courts.

Source: Stix (2002).

The patent system is designed to diffuse technical knowledge rather than maintain secrecy, while industrial or trade secrecy is the main alternative to patents for avoiding piracy or the imitation of inventions. In most countries, patent applications are published long before a decision is made to grant or refuse a patent (in many countries, this only occurs 18 months after application). For certain technologies for which secrecy might be attractive, it may be possible to exploit the invention by limiting the availability of crucial biological materials or information to one's potential partners or licensees. Examples might be genetically modified cell lines which produce monoclonal antibodies for diagnosis and therapy, or genomic databases which combine sequence data with protein structure and possible function. When secrecy is used to protect intellectual property, access to materials and information relies on the negotiation of private contracts between the parties.[10]

Those who make use of the patent system, and those who work in it professionally, see it as one form of regulating competition in a liberal economy by striking a balance between the legal protection of innovators and the freedom of other parties to operate commercially without undue limitation. The patent system, as the term is used here, means not only the laws governing the granting of patent rights but also the ways in which patent holders may exercise these rights.

Understanding patent protection

To start the discussion about the effects of patent protection on genetic inventions, it is necessary to look at the sorts of rights a patent grants, as well as how those rights are limited and enforced. The fundamental principles of the patent system are frequently misunderstood. This section therefore reviews the basic features of the patent system, before moving to a discussion about patents for genetic inventions.

The nature of patents

A patent is a property right granted by a state authority which excludes others from the use or benefit of the patented invention without the consent of the patent holder. A patent does not confer the positive right to use an invention. Freedom of use may, for example, be dependent on the existence of prior rights or on regulatory approval. Not infrequently, a patent for an improvement on a basic product or process will be subject to, or dependent on, a prior patent for the basic product or process.

The patent application

To obtain a patent, an application must be filed with the relevant national authority (*e.g.* patent office) and will be examined for compliance with legal requirements. Separate patent applications are usually necessary in each country where protection is required, though a single application at the European Patent Office covers a number of European countries.

Patentability

The principal legal requirements for patentability are that the invention is *i)* new; *ii)* involves an inventive step; and *iii)* has an industrial or other useful capability. In addition, the patent application must include a specification of the invention which contains instructions that are adequate to enable a skilled person to produce or perform the invention. In other words, the specification must be "enabling".

The invention itself is defined in the "claims" which form part of the specification. In biotechnology applications, common forms of claims involve an apparatus or device; a process or product of manufacture; and a method of treatment, testing or use. The claims are a guide to the scope of protection conferred by the granted patent.

Identifying the scope of a patent

In considering any patent, the most important task is to decide what it covers, *i.e*. the extent of the protection it gives to its owner. Identifying the "scope of the claims" (alternatively, the "breadth of the claims") will help determine whether one is working within or outside the legal scope of a particular patent. The claims constitute the legal part of the patent – as distinct from the technical description – as they define in words what is protected by the patent. Frequently, several types of claims are made. For genetic inventions, claims are usually a combination of definitions of new products, processes, methods, compositions and uses. Claims can also be directed to devices for use in genetic testing. Identifying the "scope of the claims" is a crucial issue in litigation or in any preliminary assessment of the likelihood of potential litigation and its outcome. (Box 3 gives examples of typical genetic invention patents and their claims.)

Official examination

The patent office will carry out a search of previously published documents, including the scientific and patent literature, to determine the relevant prior art. The prior art is therefore a continuously expanding corpus of knowledge which has to be taken into account when assessing patentability. The application is examined in the light of these search results. In the examination process, there are usually arguments about the specification, and especially about the scope of the claims, which may take several years to settle.

Box 3. Examples of genetic inventions and their patent claims

For genetic inventions, many different types of patent can be found. They vary as to the kinds of claims used and how the set of claims is structured. There are at least three common categories of patent in this field.

DNA coding for industrially useful expression products. The cloning of a DNA coding sequence can enable the commercial production of an important therapeutic protein, such as a blood protein. Such an achievement can represent a clear advance in pharmaceutical technology and deserve legal protection, provided the innovation meets standard criteria of patentability. Similarly, the cloning of DNA coding sequences which leads to advances in plant biotechnology, thereby improving agricultural products, practices and productivity, is patentable.

A typical claims structure in such a therapeutic product patent will cover the following:

1. DNA of specific function and/or nucleotide sequence.
2. A recombinant vector (plasmid) containing DNA of (1).
3. A genetically modified organism containing DNA of (1).
4. A method of production of polypeptide expressed by DNA of (1).
5. The expressed polypeptide per se (only if novel, *i.e.* differing in some respect from the naturally occurring protein).

Genes as diagnostic tools. The diagnosis of genes implicated in diseases typically involves the tracking down and sequencing of genes which, in the "normal" allele (the wild-type gene), confer a healthy condition on their possessor. The genes cause disease when they mutate and express the wrong product or are deleted and express none. Patents directed to such genetic testing will usually have the following claims structure:

1. The wild-type gene of defined nucleotide sequence.
2. The mutated (altered) forms of the wild-type gene (nucleotide sequences specified).
3. The DNA primers useful for amplification of the above DNA sequences.
4. Test method(s) using the above for detecting mutations.
5. Reagent kits for use with the method(s) of (4).
6. Screening methodology based on the use of the gene or polypeptide as a target for finding potential therapeutic products.

It should be noted that these different forms of claims may not all be present in a single patent; official patent regulations in certain countries may require them to be divided into two or more separate patent applications. The US patents on breast cancer genes (BRCA1 and BRCA2) and their use in diagnostic testing are illustrative examples of this practice.

Genes which control biological pathways. Research continues to identify receptors and genes involved in biological pathways. When such a gene is located, it may be possible to correlate a malfunction in the pathway with a mutation or loss of this gene. The cDNA and the encoded polypeptide would be considered targets for diagnosis and drug discovery.

One type of invention in this category would be the use of the target to discover substances which achieve some useful effect by binding to the target. This would also include substances which, by blocking the target, prevent entry of pathogens such as viruses into the cell. Typical claims are:

1. The receptor peptide or polypeptide (protein) of a defined sequence.
2. DNA coding for the receptor (1).
3. A transformed cell expressing the receptor (1).
4. An assay system comprising the transformed cell (3).
5. A method of identifying an agonist or antagonist of the receptor.
6. Agonists or antagonists of receptor (1) identified by method (5), (a claim of this type is allowed with great difficulty).

Opposition or re-examination

Even after acceptance by the patent office, a patent application or patent can in most countries be opposed by third parties who may raise objections and prior art similar or in addition to those already overcome by the applicant. This process is termed "opposition" or "revocation", depending on the country, and involves argument between the applicant/patentee and the opponent. Both have equal status as contending parties. In the United States, patent law does not provide for opposition in this sense but allows a third party to request official re-examination of the patent in the light of prior art not already considered. If this succeeds, it may result in limitation of the scope of the claims or outright revocation of the patent.

Conflicting patent applications

In some cases, two or more inventors independently seek a patent for the same invention (*i.e.* their claims cover the same ground). Most countries operate a "first-to-file" system, according to which the application with the earliest filing date usually prevails, assuming that it is effective as a proper "enabling disclosure" of the invention. The United States, however, has a "first-to-invent" system, and in the case of conflicting patent applications, the USPTO has to decide which application has priority. Provided the dates of filing their respective applications are close to one another, the USPTO will declare an "interference", a procedure based on examining laboratory notebook records and other evidence to determine the dates on which each party made the invention, and thus which was "first to invent".

Duration of a patent

The term during which a patent is valid differs from country to country. In the United States, Japan and most European countries, the term is 20 years from the application date.[11] The payment of annual official renewal fees is required in most countries to avoid lapsing of the protection.

Enforcing patent rights

For the limited period in which a patent is in force, a patent holder is allowed to exclude others from the use of the patented invention. However, a patent is not self-enforcing. When there is infringement, it is up to the patent holder to take

action to bring unauthorised use of the invention to an end. While the patent holder can seek remedy in a court of law, litigation is a last resort because it is risky and costly. In the course of litigation, for example, the validity of the patent may be challenged by the alleged infringer. While the patent may be upheld by the court, a patent holder faces the real possibility that court might revoke the patent or narrow the permissible claims.[12] Instead of going to court, a patent holder often chooses to resolve the problem by licensing the patent to the other party on reasonable terms.

Licensing patents

The patent holder may wish to be the sole provider of the product or service covered by the patent and, subject to certain safeguards, this is permitted. Alternatively, the patent holder may license the patent to others for appropriate payment, either to one other party only (an exclusive licence) or to more than one party (a non-exclusive licence). Where the patent holder is not an industrial or commercial organisation and does not wish to create a start-up company to commercialise the invention, licensing the patent to an industrial partner is the most effective way of securing a financial return on the investment in research.

Patent protection for genetic inventions

The economic value of patent protection in the life sciences, and especially in the pharmaceutical and agrochemical industries, is widely recognised. In no other fields is the relationship between patent protection and the incentives to innovate so strong. In biotechnology, where a wide variety of inventions originate in basic and applied research, the relationship between patents and research is very important. Even public research scientists and administrators, steeped as they may be in a culture of open science, have come to value the importance of patent protection in the past decades.

The legal situation

Here the focus is on patents for "genetic inventions" which are defined as all uses of new discoveries of the role of genes and related DNA or RNA molecules. Of interest in this report are genetic inventions in the health field – inventions relevant to the diagnosis and therapeutic treatment of diseases. Genetic inventions

more broadly understood also encompass agricultural, environmental and industrial uses. Claims in gene patent applications pertain, among other things, to:[13]

- Genes or partial DNA sequences such as cDNAs, ESTs, SNPs, promoters and enhancers.
- Proteins encoded by these genes and their functions in the organism.
- Vectors used for the transfer of genes from one organism to another.
- Genetically modified micro-organisms, cells, plants and animals.
- Processes used for the making of a genetically modified product.
- Uses of genetic sequences or proteins which include: genetic tests for specific genetic diseases or predisposition to such diseases; drugs developed on the basis of the knowledge of proteins and their biological activity; industrial applications of protein functions.

In this particular field, the question is whether the patent system is achieving its objectives in ways that best serve the public interest. It is useful first to summarise what sort of protection is permitted for genetic inventions under the present law as interpreted by patent offices and courts of law across OECD countries. For a review of patent protection for genes see Crespi (1999/2000).

Although the appropriateness of granting patents on DNA and other nucleotide sequences continues to be publicly debated, the position of the official patent authorities in OECD countries has been more or less stable for some time. Assuming that a DNA sequence is novel (not previously publicly known or used in a public manner) and that the other criteria of patentability are also met (utility, inventiveness/non-obviousness), the substance of the DNA itself can be patented. To be precise, the claims concern not the sequence as abstract information, but a molecule which has the defined sequence and function. This type of product claim will often be qualified in some respect, especially if the substance exists in nature. For example, in the European Community a directive of the European Council and European Parliament (EC Directive 98/44/EC) establishes that no patent can cover a substance *in situ* in the human body but only when isolated from its natural source. The policy of the USPTO is similar in intent since it requires product claims for genetic materials to be limited to the "purified" or "isolated" material.

Apart from the above restriction, a DNA sequence can be claimed as the substance *per se*, without limitation to any particular process of purification or isolation and without any limitation as to its intended use. In patent parlance this is

known as a "product *per se*" claim and it confers "absolute product protection". The potential scope of such a claim can be broad.[14]

Granting "product *per se*" patents for genetic inventions is consistent with the established practice for new pharmaceuticals and other chemical compounds. The trend in many countries over the years has been to allow such product claims, as against previous more restrictive policies of allowing claims only to the particular chemical processes described in the patent application for making end products. In fact, the World Trade Organization (WTO) Trade Related Intellectual Property Rights (TRIPS) Agreement requires patent protection to be available for process and product claims in all branches of technology, without discrimination.

Nevertheless, whether product *per se* claims should continue to be allowed for genetic inventions is a source of continuing debate. In its 2001 Guidelines, the USPTO addressed many of the arguments against the patenting of genes as products *per se*. The USPTO rejected the contentions that: *i)* genes are discoveries and not inventions; *ii)* genes are products of nature and therefore not "new"; *iii)* Congress should be consulted on this question; *iv)* genes are the basic core of humanity and should not be "owned" as property; *v)* gene patents should be limited to specific disclosed uses; *vi)* gene sequencing is routine and obvious. Likewise, the EPO much earlier stated its position as follows (EPO, 1990):

> "An initial question to be considered (…) is the protection which is conferred by a claim to a physical entity such as a compound *per se*. It is generally accepted as a principle underlying the EPC that a patent which claims a physical entity *per se* confers absolute protection upon such physical entity; that is, wherever it exists and whatever its context (and therefore for all uses of such physical entity, whether known or unknown)."

For most national patent authorities and courts of OECD member countries, product patents for genetic inventions are standard provided that they meet the requirements for patentability. The scope of such product patents can, in full legality, be quite broad and extend to areas which the inventor neither stipulated nor contemplated. Nevertheless, because genetic inventions have been among the most challenging areas of technology for patent offices, efforts have been made through the trilateral co-operation of the US, European and Japanese patent offices to harmonise their approach to the examination of patent applications in biotechnology. Much common ground has already been found for applying the main criteria of patentability to the examination of biotechnology patent applications (novelty, inventive step, adequate disclosure of the making and using

of the claimed DNA and proteins for which they code). Patent authorities have also tried to clarify the circumstances under which genetic inventions such as SNPs, ESTs and cDNA are patentable.

The appropriate scope of claims has been one of the most contentious issues. While some differences among national patent offices remain, inventors are now more aware of what is required to justify their claims internationally. Through administrative reforms, patent offices have tried to temper over-ambitious patent applicants who seek much wider protection than is justified by the contribution made in their patent disclosure. Whether patent office efforts alone are sufficient is hotly debated. For a history of the product *per se* claims in Europe, see White (2000/2001) and Crespi (2000/2001).

The public perception is that product *per se* DNA patents, and the absolute protection they confer, may reward first inventors in an inappropriately generous manner. While examples of very broad claims do exist – for example, the patents on the CCR5 receptor and on the hepatitis C vaccine – it remains to be seen how frequently potential users of these technologies are "locked out" and unable to access or license the technologies. The remainder of this report explores what evidence exists to support the concern that DNA patents may be causing significant access problems that make government intervention necessary.

Reforming the system of IP protection for genetic inventions

In discussing possible reforms to the present system of IP protection for genetic inventions, workshop participants stressed the enormous challenge of striking a new balance between the protection of inventions and the promotion of greater legal access to information and technology. Achieving this balance is the essence of all negotiations between patent attorneys and patent examiners and is at the core of most IP disputes. The arbiters of these debates are frequently the patent offices and the law courts, which decide on a case-by-case basis whether patents are valid and the extent of the claims allowed. For many users of the patent system, the slow and intermittent interpretation of statutes and precedence is perhaps costly and imperfect but adequate to the task of finding a just reward for genetic inventions that does not unduly hamper research or commerce.

However, the patent offices and the courts are simply the executors of the existing patent system. They usually do not take into account and are not competent to judge the economic repercussions of their decisions. If indeed DNA patents are found to lead to systematic and serious access problems, final authority

about whether the patent system functions for the greatest public good rests with the government. A number of proposals for reform have been put forward in an effort to "rebalance" the protection afforded genetic inventions. Some of these proposed changes are directed at the IP regime itself, and involve new legislation, while others suggest measures outside the IP regime.

The proposals under discussion can be classified into legislation (usually to amend the patent regime); regulations and regulatory bodies that would act as a check on either the patent offices or the patent holders themselves;[15] administrative reforms to change the behaviour of public bodies (*e.g.* patent offices, funding agencies, public laboratories); and efforts to encourage more self-regulation by patent holders. Examples of each type of intervention discussed at the workshop include:

- ***Judicial decisions and case law:*** legal action involving both public and private actors which results in binding decisions by courts on such issues as the validity of patents, clarification of dependency, acceptable patent scope, research exemptions.
- ***Legislation:*** to alter patent laws, for example: the introduction of grace periods; clarification of research, experimental and diagnostic use exemptions; the expansion of exclusions to patentable subject matter; and/or the addition and use of public order (*ordre public*)and morality clauses.
- ***Regulation:*** *i)* expanded use of compulsory licences and/or antitrust procedures; *ii)* creation of new regulatory bodies, or the granting of regulatory powers to existing bodies, for example to stipulate how the criteria of patentability should be interpreted for genetic inventions, or to decide on the criteria for public order and morality.
- ***Administration:*** *i)* reforming the administration of patents, for example by raising the criteria for patentability of genetic inventions (*e.g.* requiring greater proof of utility or inventive step) and how to apply these criteria; *ii)* licensing guidelines (*e.g.* for the licensing of technologies developed in public research bodies).
- ***Self-regulation:*** *i)* public funding of research with the explicit aim of putting results into the public domain (*e.g.* HUGO, the SNPs Consortium); *ii)* private-sector access initiatives (*e.g.* consortia, patent pools, or collective licensing organisations); *iii)* educational or public relation initiatives.

Each of these reform suggestions has its advantages and disadvantages. Legislative changes are enacted very slowly and are not always based on the level of expertise or subtlety needed in crafting effective policies for a fast-moving field like biotechnology. Judicial decisions can also take time, and their outcome is not directed by policy imperatives or based on economic or social analysis. Creating new regulatory authorities is costly and may be cumbersome, but in theory these could have the advantage of being insulated from interest group politics and better informed about the social and economic impact of proposed changes to IPR policies. Administrative reforms of patent offices may be quicker, and perhaps more targeted at particular problems, but they suffer from a lack of wider public legitimacy. The development of best practice guidelines through a consultative process might be able to help with the problem of legitimacy. Self-regulation and efforts to promote self-regulation are attractive because they are less likely to distort incentives to innovation, but they are less likely to garner public trust and their effectiveness in changing behaviour has yet to be proven.

Chapter 3

THE PATENT DATA

This chapter puts forward a definition of genetic inventions. The data available on patents for genetic inventions granted by the major patent offices are presented, as is some more general information on biotechnology patents, in order to put the protection of genetic inventions in a broader context. There are very few statistics available on licences for genetic inventions.

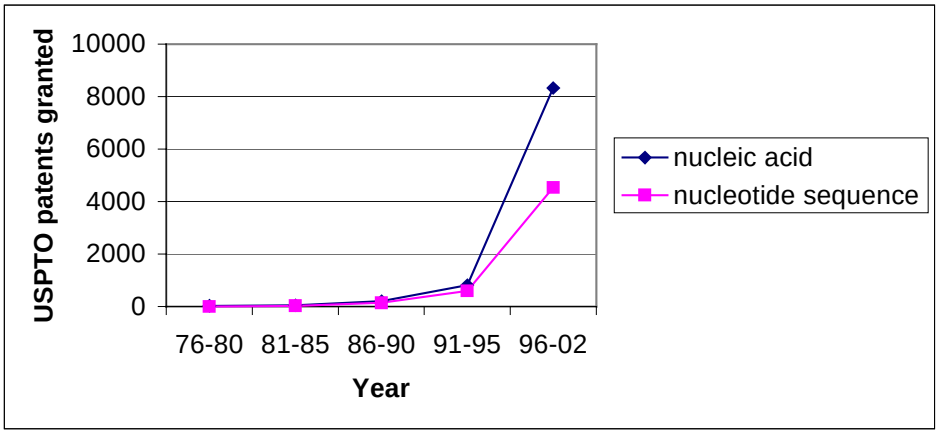
Since the sequence or partial sequence of a gene has become patentable subject matter, the protection of "genetic inventions" has been rising (Figure 1). The rapid increase in the number of DNA patents has, not surprisingly, coincided with advances in the sequencing of human and other plant and animal genomes (*e.g. H. influenza, D. melanogaster,* mouse, rice). As sequence information from many genomes accumulates, so too will the identification of genes and their functionality. The recently completed genome sequencing of the Fugu puffer fish, for example, has helped to identify close to 1 000 human genes (Wade, 2002):

> "The Fugu genome…contains essentially the same genes and regulatory sequences as the human genome, but it carries those genes and regulatory sequences in approximately only 400 million bases as compared to the 3 billion bases that make up human DNA. With far less so-called 'junk DNA' to sort through, finding genes and controlling sequences in the Fugu genome [is] a much easier task. The information [is] then used to help identify these same elements in the human genome."
>
> Preuss (2000/2001)

As understood in this report, patented genetic inventions cover all patents whose claims include nucleotide (DNA or RNA) sequences. The broader category of biotechnology patents has been growing more quickly than the rate of growth of all patents granted by the USPTO and the EPO (see OECD, 2001, for details) (see Box 4 for a description of biotechnology patents and Figure 2 for growth in

biotechnology patents). If one looks specifically at gene patents, grants have also climbed rapidly since the second half of the 1990s in the United States. One study estimates that the total number of DNA patents granted by the USPTO to date is somewhere around 10 000. In 2001 alone over 5 000 DNA patents were granted by the USPTO,[16] and it is estimated that approximately 1 500 of these patents are on human genetic material (Rivers, 2002).

Figure 1. Nucleic acid and nucleotide sequence claims in USPTO granted patents



Source: OECD, based on USPTO Patent and Full Text Image Database.

However, these numbers should be interpreted with caution. Gene or DNA patents do not coincide with a specific International Patent Classification (IPC) category. Very few groups, patent offices included, consistently track gene patent applications or grants. In addition, there is no easy way to make cross-country comparisons of patent activity, as no group has yet compiled a database of DNA-based patents worldwide (Cook-Deegan *et al*., 2000). One way around the internationally comparability problem might be to use the patent office search engines and search for patents that include nucleotide sequences in their claims. According to the USPTO search engine, for example, 9 456 patents which include the term "nucleic acid" in the claims have been granted, 8 334 of them since 1996[17] (see Figure 1).

Box 4. Biotechnology patents

Patenting biotechnology, and particularly gene patents, can differ between patent offices.

For more information on biotechnology patenting, refer to the trilateral studies (USPTO, EPO and JPO) at the Web site: www.jpo.go.jp/saikine/tws/sr-3.htm

Biotechnology patents granted by the USPTO

Patent statistics provided in Figure 2 are based on numbers of patents granted by the USPTO.

Biotechnology patents consist of class 435 of the USPTO classification system. Class 435 ("Molecular biology and microbiology") includes technologies relating to the analysis and application of the genomes of all creatures, such as recombinant DNA, genome analysis, combinatorial chemistry, clone/cloning, gene/genetic diagnosis, genetic engineering, gene amplification, gene probes, protein engineering, DNA vaccines, DNA markers, DNA sequencing, DNA synthesis, cell fusion and polymerase chain reaction (PRC). A complete definition of class 435 can be found at:
www.uspto.gov/web/offices/ac/ido/oeip/taf/moc/435.htm

Year is the year of the patent grant. *Country* is the country of residence of the inventor. For patents with several inventors from different countries, "fractional counting" was applied (the patent is shared between the concerned countries) to avoid double counting.

Biotechnology patents at the EPO by priority date

These data are for patent applications (which may or may not be granted) to the EPO and relate to the inventor's country of residence and to the priority date, which is generally considered close to the date of invention.

Biotechnology patents consist of five IPC codes:

C12M: Apparatus for enzymology or microbiology.

C12N: Micro-organisms or enzymes; compositions thereof.

C12P: Fermentation or enzyme-using processes to synthesise a desired chemical compound.

C12Q: Measuring or testing processes involving enzymes or micro-organisms.

C12S: Processes using enzymes or micro-organisms to liberate, separate or purify a pre-existing compound or composition.

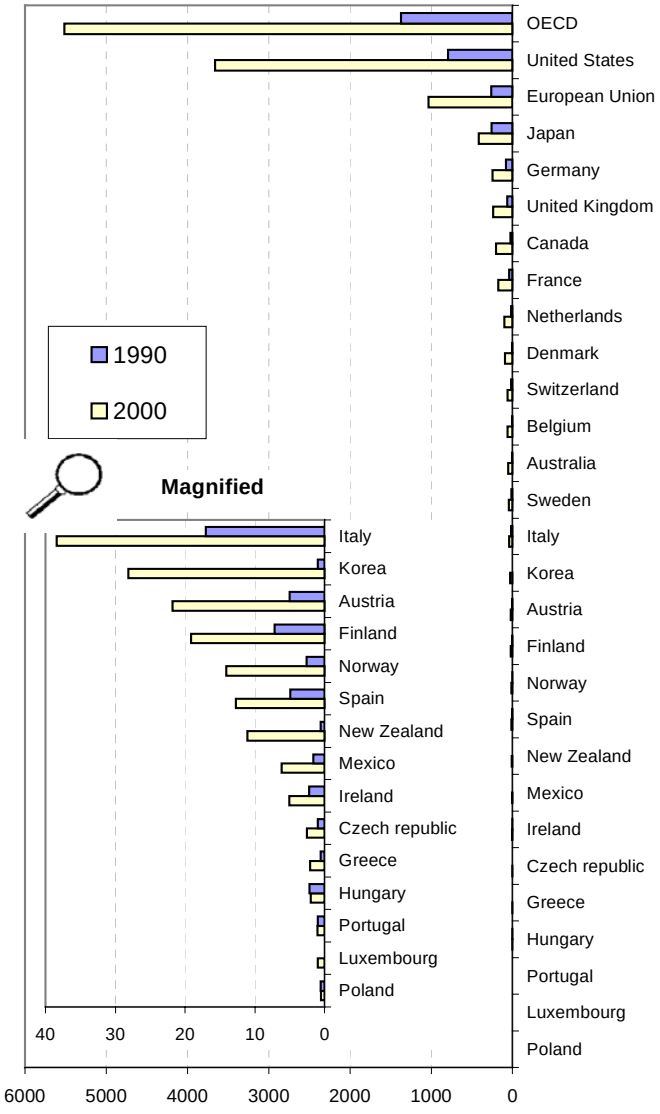
Complete definitions of these IPC codes can be found at:
http://classifications.wipo.int/fulltext/new_ipc/index.htm

Year is the priority year of the patent application. *Country* is the country of residence of the inventor. For patents with several inventors from different countries, "fractional counting" was applied (the patent is shared between the concerned countries), to avoid double counting.

Source: OECD (2001).

Figure 2a. Biotechnology and patents

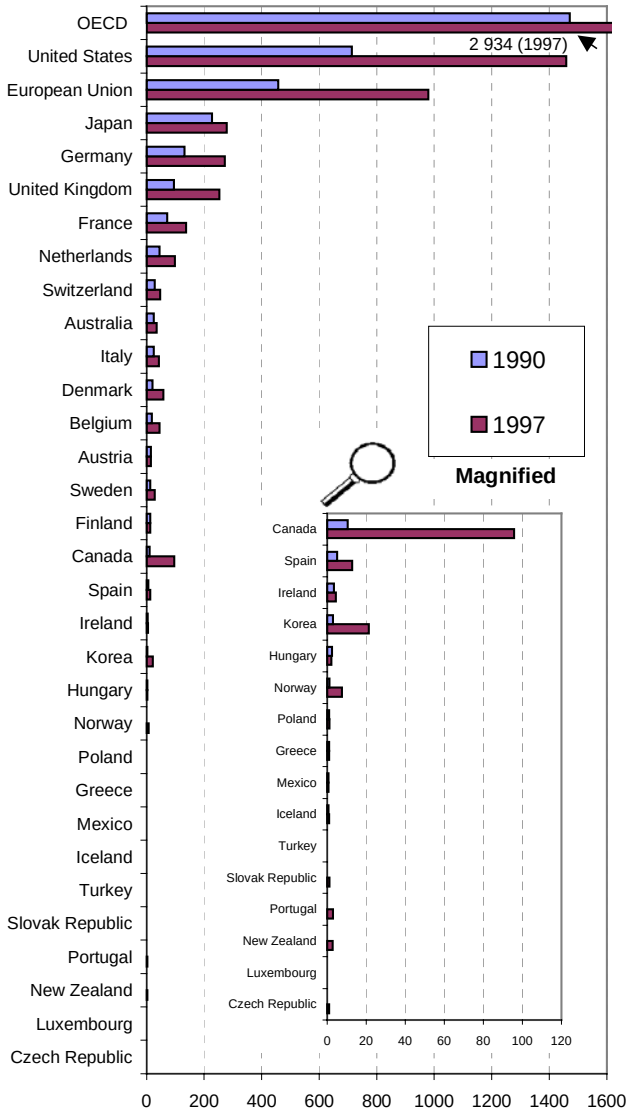
Biotechnology patents granted by the USPTO, 1990 and 2000



Source: OECD (2001), calculations based on data from the USPTO.

Figure 2b. Biotechnology and patents

Biotechnology patent applications to the EPO for priority years 1990 and 1997



Source: OECD (2001), calculations based on data from the EPO.

A similar search by the JPO found that 5 652 patents issued between 1996 and 2001 had the terms gene, nuvleic acid, DNA, RNA or genome in the claims[18] (Table 1).

Table 1. DNA patents issued by JPO 1996-2001

Year	Number of patents issued
1996	737
1997	690
1998	906
1999	1 085
2000	1 011
2001	1 223

The EPO estimates that several thousand patents that claim nucleotide sequences have been granted. However, the precise number is not known. The EPO has received around 30 000 patent applications in biotechnology since 1998, of which about 10 000 pertain to "mutations or genetic engineering". About 40% of the latter are for micro-organisms, plants and/or animals and 60% relate to human or animal DNA sequences.

The estimated number of gene or DNA patents granted, therefore, varies, according to reports, from a few thousand to tens of thousands at each of the major patent offices (USPTO, EPO, JPO). While the numbers are impressive, especially in light of the relatively small number of human genes, the figures are believed to overestimate the number of gene patents. Many of the published figures are actually on patent applications, rather than grants, and these include provisional patent applications. Furthermore, it is thought that a proportion of the patents actually granted will be found invalid.

Although reliable international figures are not yet available, it nevertheless appears that there has been a sharp rise in DNA-based patents issued in the major patent jurisdictions. Moreover, these patents are believed to be increasingly complex, both in terms of the number of claims and the transparency with which those claims are made. While it might be thought that genomics and pharmaceutical companies are best positioned to protect genetic inventions, in 1999 they represented in fact only 52% of the gene patent assignees in the United States. Universities accounted for 23% of these patents, while public or non-profit research organisations accounted for another 19% (Cook-Deegan, 2002).

As a result of the explosion of this particular type of biotechnology patent, many feel that the "freedom to operate" of companies and research organisations is more constrained. The need to sort through all possible relevant patents and their claims is increasingly time-consuming and expensive, and the transaction costs are not captured by the raw patent grant data. For this reason, the following chapter brings together information on licensing practices in order to paint a more accurate picture of the impact that these patent grants are having on the research, the economy and the health of OECD member countries.

Chapter 4

KEY POINTS FROM THE WORKSHOP SESSIONS

This chapter presents the various workshop discussions. Proceedings are summarised and reported according to the order in which debate took place. Where appropriate, opinions are attributed to the individuals concerned.

The workshop was opened by the German Federal Minister of Education and Research, Mrs. Edelgard Bulmahn, who emphasised the economic and political importance of gene patents in her country. She said that Germany's objective was to ensure that researchers are not hampered by overly broad patents and that they have access to genetic information and inventions. At the same time, Germany wants to maintain strong incentives for private-sector investment in research and development in the life sciences. Minister Bulmahn said that the 1998 European Directive on the protection of biotechnology inventions (EC/98/44), which specifies that patents should only be granted if a specific gene function is identified, is an important step in establishing this balance across Europe and should be ratified. She underlined the need to gather further information on how the patenting and licensing of inventions actually works in order to address remaining questions on the appropriate breadth of patent claims, the scope of protection offered and the effects of patent crowding. Only fact-based discussions, Minister Bulmahn stressed, can lead to specific recommendations for action for policy makers. The OECD workshop aimed to deliver such fact-based discussions.

Session 1: The IPR system and its relevance to genetic inventions

The first session of the workshop focused on how genetic inventions are protected under the present intellectual property regimes of OECD member countries. The two speakers, Mr. Ulrich Schatz and Mr. Alain Gallochat represented public bodies (EPO and the French Ministry of Research, respectively). They discussed the legal criteria for patentability of genetic inventions, the rights that patents confer and how those rights are limited, as well

as the need for non-IP regulatory structures in pursuing national policy objectives. One of their declared priorities was to dispel common misconceptions about the patent system. In particular they made the following points:

- A patent does not give its holder the exclusive right to do what is covered by the patent. Rather, a patent gives its holder the right to exclude others from doing what the patent covers.
- A patent is no bar to the circulation of information concerning the invention; in fact, through publication it enhances dissemination of this information.
- Patents turn inventions into tradable commodities which can be licensed or assigned to various parties and which foster the wider use of the invention.
- Patenting is an adversarial process in which the public examining authority has to be convinced that the conditions of patentability are met, and to decide the appropriate scope of protection. After this is settled, third parties may challenge the application or patent through formal opposition procedures in most countries.
- A patent does not bar others from carrying out research.
- Patent law in most countries makes provision for dealing with unduly restrictive practices of patent holders in extreme cases, *e.g.* national emergency, danger to health. Compulsory licences may be obtainable in some countries if justified by circumstances.

The utility criterion

From the standpoint of patent offices in Europe, especially the EPO, genetic material is not seen as a special case requiring treatment different from chemical compounds and other products. This view is shared by the patent offices of the United States and Japan. Common ground between the EPO, USPTO and the JPO has already been reached in relation to DNA sequence patents. Mere determination of a DNA sequence is not enough for patentability, but where the inventor is the first to identify a gene and its useful function, to isolate and clone the gene and thereby make synthetic copies of the gene (or more often a modified form of the natural gene) that are available for use in diagnosis or therapy, these offices accept that this is not mere discovery but the kind of invention for which a patent can be granted.

For the European Community, harmony of practice in member states on points of this kind is the objective of the Biotechnology Directive 98/44/EC on the legal protection of biotechnological inventions.[19] Although this directive is not directed to the EPO, the EPO nevertheless attaches considerable importance to the unity of patent law throughout European Patent Convention (EPC) member states (which include some countries that are not EU member states). In consequence, the EPO has amended its regulations to be in conformity with this directive for the treatment of EPC patent applications and patents.

Absolute versus limited protection

To be patentable, the utility of a DNA molecule of defined sequence must be disclosed in the patent application. This applies to whole genes or parts of genes. However, this utility, which can be expressed either as its industrial application or its biological function, is not seen as restricting the scope of the claims, the latter usually being written in terms of the nucleotide sequence or the amino acid sequence of the polypeptide (protein) for which the gene codes, *i.e.* it is a product *per se* claim. This interpretation of the scope of a claim to a genetic invention, which is similar to the scope of patents on chemical and pharmaceutical compounds, is generally accepted under EPC jurisprudence and is also implicit in the case law of other countries. It is important to recall that new uses of a particular patented gene can still be patented, giving the later inventor a bargaining position for negotiating a licence under the first patent (*i.e.* the new use patent is "dependent" on the first use patent). The new use of the patent cannot be worked by the holder of the original patent without consent of the second patent holder.

There is considerable debate, including among experts, about whether "absolute" protection granted for genetic inventions is commensurate with the inventive step disclosed in a patent. Suggestions that the scope of the protection be somehow "limited", preferably to those uses described in the patent, are being put forward by a number of organisations and individuals.[20] Confining the scope of DNA patent product claims to their use for a particular purpose, however, would require a change in the present laws of most OECD countries and, many experts consider, would probably conflict with the WTO TRIPS Agreement which calls for patents to be allowed for products and processes without discrimination as to technology [Article 27(1)]. The need for such a change in the type of protection offered genetic inventions would require considerable justification.

However, interpretation of the language of TRIPS Article 27(1) is not settled. Limiting the scope of protection that can be granted for DNA patents, or applying

different criteria to the granting of a genetic invention in addition the criteria of novelty, inventive step and industrial application/utility, is likely to be interpreted as discriminatory. It may not be discriminatory to determine how the three accepted patentability criteria should be applied to or interpreted in the case of genetic inventions, given the particular nature of those inventions.[21] In other words, patent offices may choose or be asked to apply stricter guidelines when interpreting whether an invention is novel, useful or represents an inventive step. The revised USPTO guidelines, for example, specify that utility in the case of genetic inventions has to be "specific and credible".

Self-regulation and limiting the scope of claims

The scope of claims can be limited by means other than offering the limited protection discussed above. It is important to strike a balance between the rights patents grant, the inventive effort made and the information disclosed, to avoid any public perception of an "undue scope of claims" that might lead to opposition to the patent system as a whole or gene patents in particular. Mr. Gallochat emphasised that an appropriate balance can be reached if applicants are reasonable in their requests; patent offices are diligent in their appreciation of prior art; and third parties are ready to lodge an opposition (where available) and make the patent examiners consider new elements of prior art they may not have been aware of. Governments themselves can consider lodging opposition procedures. However, it may not be realistic to expect economic actors to be "reasonable". Therefore, legal, administrative or regulatory action may be needed to change the incentives patent applicants face, so that the claims they make in their patent applications are more commensurate with the invention's real scientific or social contribution.

The limits of public order and morality

In many countries, patents cannot be granted for inventions whose commercial exploitation would be contrary to *ordre public* or morality. In Europe, this is provided for in Article 53(a) of the EPC, and equivalent provisions in European national patent laws. The moral test is to be applied only to the "publication or exploitation" of the invention and not to the research that preceded it or to the attempt to obtain patent protection. Morality is not simply to be equated with legality. Thus, Article 53(a) indicates that the use of an invention is not to be deemed immoral simply because it is prohibited by law in some or all of the EPC member states. By the same token, it would seem possible to conclude that the use

of an invention is not automatically deemed to be moral simply because it is permitted by law. This conclusion is borne out by the fact that the oppositions that have been filed against certain EPC patents have not been rejected at the outset by the EPO on this basis. In the absence of commonly agreed criteria for making moral judgements as to the application of new technology, therefore, it is difficult to apply morality provisions of this kind. In addition, the patent system is meant primarily to regulate competition, and patent examiners are not in a position to define or even interpret the basic values of society. Regulatory decisions about what is and is not lawfully traded should probably be incorporated in laws or decisions of regulatory bodies outside the IP system.

Session 2: Surveys of patenting and licensing practices for genetic inventions

The second session of the workshop examined the licensing practices of owners of genetic inventions. Speakers presented three recent studies of the patenting and licensing practices of firms and research organisations in bio-pharmaceuticals. The German government commissioned a study on "Genetic Inventions and Patent Law" by Professor Joseph Straus of the Max Planck Institute for Foreign and International Patent, Copyright and Competition Law. John Walsh presented a study on "The Patenting of Research Tools and Biomedical Innovation", a project prepared at the US National Academy of Sciences (with co-authors Wes Cohen and Ashish Arora). Finally, Professor Fabio Pammolli presented results from an ongoing project, "Markets for Technology in Biopharmaceuticals in Europe and the United States".[22]

While official statistics show that the number of patent applications and grants is on the rise, little is known about who is licensing what technologies to whom and under what conditions. Firms claim that it is increasingly difficult to assess whether they have "freedom to use" their own in-house or licensed technologies as the web of patents becomes more complex and overlapping. Whether this is really a challenge or whether it is an opportunity for industry and public research organisations remains uncertain and perhaps rather subjective.

The surveys presented here provide a base of information about the licensing of genetic inventions and about the challenges raised by the proliferation of gene patents for potential licensees. The studies by Straus and Walsh *et. al.* rely on interviews at companies and other groups involved in bio-pharmaceutical research. Professor Pammolli's study, on the other hand, maps networks of firms, relying on published announcements of inter-firm collaboration, and thus explores the role of licensing in bio-pharmaceutical industry dynamics more generally.

Germany

The purpose of the German survey on "Genetic Inventions and Patent Law", presented by Joseph Straus, was to clarify whether research organisations had encountered specific problems for the application of the special legislation on genetic engineering (*Gentechnikgestez*), in particular regarding the grant of patents on DNA sequences. The survey specifically probed the extent to which the following issues are present and problematic for German bio-pharmaceutical R&D:

- Dependency of patents on earlier inventions, resulting from a proliferation of DNA patents generally and from unduly broad claims specifically.
- Reluctance to enter fields in which genes had already been patented.
- Royalty stacking and higher transaction costs for research owing to a proliferation of patents on technologies such as research tools.
- Reach-through claims.
- Explosion of legal disputes.
- Slower publication times owing to the novelty requirements for patent applications.

Table 2. German survey of research organisations

Interviewee	Patent applications	Patents granted	Licences granted	Licences-in	Co-operation	Lawsuits
Pharmaceutical companies	100	500-1 100	N/A	N/A	Many	0-2
Biotechnology companies	25-180	0-55	0-28	1-multiple	0-many	0-multiple
Research institutions	50-100	30-110	0-83	0-10	2-91	0-4
Clinical testing institutions	1-20	1-6	0-3	0	0-5	0-1

Source: Joseph Straus *et. al.*

Interviews were conducted with four large pharmaceutical companies, nine small and medium-sized specialist biotechnology companies, seven public research institutions and five genetic testing centres. All of these organisations are

involved in patenting and licensing of biotechnological inventions (Table 2). Most respondents indicated that the above problems could be handled flexibly and, while some problems have not been solved or negotiations have failed, working solutions have been found in most cases. The following paragraphs summarise the findings of the survey.

Economic and financial value. The role and economic importance of patents differ according to the type of institution surveyed. For biotechnology firms, patents are an indicator of the company's intangible assets and they are, because of their role in the financial valuation of companies, much more important than for established pharmaceutical companies. Large pharmaceutical companies viewed patents as a mechanism for ensuring their ability to continue research in a particular field and as currency in negotiations with possible collaborators. The evaluation of the companies by the stock market is no doubt positively influenced by their patent holdings.

Research co-operation. Respondents claimed that research co-operation agreements are not unduly hampered by intellectual property issues. In most cases, parties agree prior to the start of co-operation on the distribution of intellectual property, on who should become sole proprietor of resulting patents, and the terms of licences to the other parties. It was rare for pharmaceutical companies to be reluctant to license their intellectual property. The exception to the rule, however, was the licensing of certain research tools where exclusive licences were more typically granted so that the licensee could benefit from a period of exclusivity to capitalise on his investment.

Dependency and product development. All companies indicated that they are vigilant in examining the validity of their competitor's patents. They also test whether the products they have under development internally are likely to infringe upon existing patents of competitors. Companies are reluctant to pursue fields of research that will only lead to dependent patents. Certainly, companies rarely set out to improve the inventions of their competitors, but if R&D in a field is already advanced and it appears that an invention is likely to be dependent, companies may try to license, cross-license or even buy the dominant patent.

Research tools. Patents on research tools have not had a discernible effect on the cost or pace of research in Germany, and the survey answers suggested several reasons for this. Some research tools are staple goods, like enzymes, which can be purchased without declaring their intended use. Moreover, it is difficult to detect infringement of research tools which are used behind laboratory doors. While end-products may be suspected of having been developed using a patented research

tool, many biotechnology companies do not yet have such commercialised products, making it difficult to claim infringement. Public research bodies claim that their staff are often unaware of the legal implications of using patented research tools. However, fear of litigation is low in the public sector, as research institutions usually generate no revenue through the use of the research tool and thus the patent owner has little incentive to sue. In short, many groups act as if an "informal research exemption" exists for the use of patented research tools.

Legal disputes. Licensing is widely used in Germany, except between direct industrial competitors, and lawsuits have not accumulated. In part this is because infringement can be hard to detect (especially for research tools). Also patent infringement suits result at most in the grant of reasonable royalties. The plaintiff cannot expect to reap damages. Only one of the surveyed German biotechnology companies had been involved in a legal dispute over patents, a situation unlike that in the United States. However, this number may be deceptively low, as many companies have not yet marketed any products. Germany may or may not see a rise in legal disputes over IP. A further disincentive to launching legal actions is the fact that there are few precedents in Germany that help make the outcome of patent infringement lawsuits predictable for potential litigants.

Reach-through claims. Opinions were split on the impact of reach-through claims. While some held that such claims are invalid, others have had to confront these claims and believe that the issue of validity will remain unresolved until settled at high level in the EPO or in national courts. Reach-through claims for licences, while easier to address, still make negotiations more cumbersome.

Royalty stacking is real. Licensing is often welcomed as a means of generating increased income, especially when the patent holder cannot supply all possible uses of the invention to potential markets. However, the need to take licences under numerous patents means a series of royalty payments to the respective patent holders, or "royalty stacking", and this is seen as a real problem which can only be overcome by the mutual realisation that royalty rates must be adjusted to reflect the reality of the commercial situation. Some firms include royalty stacking clauses in their licence contracts, such that the royalty rate of each individual licence is reduced if the cumulative royalty payments exceeds 10% of the turnover of the final product. On the other hand, patent pools, consortia and cross licensing were not deemed effective for increasing access to genetic inventions owing to the difficulty of assessing the contributions various parties are likely to bring to such a grouping.

Government action. The public and private sectors were divided on the need for a grace period to allow publication of research results. While companies have well-established pre-publication procedures to prevent leakage of information into the public domain, research institutions favour a grace period because scientists are not sensitive to the fact that disclosure of inventions in talks and conferences, for example, constitutes prior art and precludes future patentability. Pharmaceutical and biotechnology companies were split on the need for absolute versus limited protection of inventions, with large pharmaceutical companies seeing absolute protection as essential to cover the costs of developing a new medical drug. Biotechnology companies, on the other hand, were more equivocal and stated that claims should reflect an inventor's contribution to the state of the art. However, all interviewed believed that no special patent law for genetic inventions was necessary and that the specificities of genetic inventions would diminish in future. Moreover, the need for harmonised international laws was underlined. No one wanted guidelines for patent examiners, for example, to differ from country to country (*e.g.* regarding the genetic functionality and the possibility of including multiple members of a sequence family in a patent application).

United States

John Walsh presented the results of a recent study, "The Patenting of Research Tools and Biomedical Innovation" (Walsh *et al*., 2001). Like the German survey, this study consisted of interviews with executives and researchers at biotechnology and pharmaceutical firms and research personnel and administrators at several universities. The objective was to evaluate whether the "tragedy of the anti-commons" is indeed a reality in biomedicine and whether patent rights to certain research tools are retarding innovation.

The "tragedy of the anti-commons", a term coined by Heller and Eisenberg (1998), refers to a situation where there are numerous property right claims over the building blocks necessary for research and development. If property rights are diffusely held by multiple owners, the negotiations necessary to bring these building blocks together can fail, thus stifling follow-on innovations. The proliferation of patents on biomedical research tools or on genetic inventions could, in theory, lead to a tragedy of the anti-commons, making it difficult for researchers to pool licences on all the technologies needed for R&D.

The responses elicited in the American survey were generally in line with those in the German study. There is in fact little evidence so far of breakdowns in negotiations over IP rights or evidence that biomedical research has slowed. Indeed, much like the German interviewees, firms and research organisations in the United States reported "working solutions" which allow them to continue to innovate relatively unimpeded. Solutions include licence negotiations where necessary or the avoidance of patent obstacles by working around the claims. Firms also chose to ignore or infringe patents, to challenge patents and litigate, to move offshore or to put innovations in the public domain. It would appear that access to patented technology has rarely been blocked. Likewise, royalty stacking has very rarely put an end to a project, although a third of the respondents said it added to the costs of research.

Interviewees indicated that they have had to develop working solutions because the patent landscape has become more complex, owing to a proliferation of patents for the drug development process. The patenting of "research tools" is singled out as contributing particularly to the general complexity and as increasing transaction costs and delays. The potential for future "anti-commons" problems has not entirely been averted, but to date breakdowns have rarely happened. It still is possible to contract to have access to patents that are relevant for R&D.

For present purposes, it would be helpful to have a definition of a "research tool". The term can be used in a very wide sense, including genomics databases, DNA chips, recombinant DNA technology, PCR, combinatorial libraries, genes and receptors, and even transgenic mice. A good proportion of the entire range of biotechnology can fall under this term. It cannot be denied that these resources are all used in research but some are potentially saleable products as well. Most of these "general tools", however, are licensed broadly. Some commentators understand the term "research tool" in the more restricted sense of methodologies used in the research laboratory for identifying potential drugs through binding to receptors and other targets. There are indeed examples of broad patents on targets with specific therapeutic and diagnostic functions being licensed exclusively, and complaints about exclusion from using these targets in research are increasing (*e.g.* the CCR5 receptor and the NF-KB messenger protein). These targets are being exploited, but others are excluded from pursuing alternative "lines of attack". However, it is not yet clear whether this exclusivity entails social welfare losses.

The conclusions of the US and German studies differed in some ways. First, litigation was perceived as far more costly and time-consuming in the United States. Even in the absence of litigation in Germany, however, respondents found

that both the process of determining which potentially relevant patents are important to a research project and the negotiations for access to them can be long and costly, delaying their research projects. For this reason, US firms, like their German counterparts, tend to avoid research projects for which there are many existing patents on research tools ("crowded art"). Also, US respondents seemed more supportive of recent public policies to increase access through administrative measures, as in the changes in USPTO guidelines on the patentability of genetic inventions, and through self-regulatory mechanisms, such as the use of legal action that leads to narrower court decisions on patent claims. German respondents seemed more split in their assessment of what government responses were deemed necessary and were divided over grace periods and the introduction of limited, rather than absolute, patent protection. However, both studies concluded that there are indeed some reasons for caution and for continued monitoring of the transaction costs associated with patents in biomedical research.

The market for technology in biopharmaceuticals

The study presented by Fabio Pammolli focused more broadly on the role that licensing plays in technology transfer between universities, biotechnology firms and large pharmaceutical companies (Arora *et al*., 2001). Whereas the topic of the two previous surveys was patents on genetic inventions and research tools, this study describes the network of biopharmaceutical firms and research organisations in the United States and Europe on the basis of data on collaborative agreements.

A distinctive feature of the biotechnology industry, especially in the area of health care, is the role of the small to medium-sized specialist companies that are in the forefront of research activity. In the United States, a high proportion of drug R&D projects have been initiated by these new biotechnology firms (NBFs) whereas in Europe the large established pharmaceutical companies have played a greater role. The NBFs excel in the area of drug discovery while the larger firms have an advantage in the commercial development of these discoveries into clinically useful compounds. The combination works well for the innovation process. The NBFs perform the early exploratory stages to produce candidate drugs for subsequent evaluation, a high proportion of which fail. These differing roles may be termed exploration and exploitation.

Despite the division of labour described above, the economics literature on the market for technology suggests that the licensing of external technologies may be inferior to in-house development because: *i)* the licensor has better information about his/her technology than the potential licensee and is likely to license out less

successful projects; and *ii)* the integration of discovery and development in one organisation is more efficient. Licences are the way companies market technologies, and these types of markets for information have natural imperfections. Why then is licensing such an important part of biopharmaceutical activity?

Pammolli's study of licensing in biopharmaceuticals shows that biotechnology firms are more likely than pharmaceutical firms to develop potential drugs, but also that they have a higher early failure rate for candidate drugs (*i.e.* the selection criteria for projects are higher and more projects are terminated before they reach the clinical trial phase than in pharmaceutical firms). Pharmaceutical companies, on the other hand, have higher success rates for bringing a product through the clinical trial process, probably because of factors such as their closer links to hospitals and physicians. Moreover, during the development process, a molecule licensed in by a pharmaceutical company is more likley to move to the next phase of clinical trials than an in-house compound. In short, for pharmaceutical companies, licensed compounds have a substantially higher probability of success because they are chosen from superior projects developed initially by biotechnology firms.

Given this market dynamic, NBFs will vigorously seek patent protection as an important factor in securing outside funding and an appropriate share of the rewards that come from marketing a successful drug. NBFs usually license upstream technology to a pharmaceutical firm for development. Some NBFs in the genomics field may find alternatives to patents, for example granting access to sequence databases through private agreements rather than through patenting. However, licensing is a common practice for access to new inventions, and it works well. Patents, in short, allow a division of labour that permits contracts to develop between different research organisations.

Session 3: The impacts of patenting and licensing practices on research

The exponential growth in the number of patent applications filed and patents granted in this field testifies to the upsurge of genetic research in both the public and private sectors. Without plentiful research activity there would be not be such an abundance of patenting activity. The question is raised, however, as to the possible impact of more aggressive protection of genetic inventions on the need to make these technological advances accessible to the public in an acceptable way. It is of course in the interests of patent holders to make their products and services available as widely as possible to the research community and to public health

authorities. It may be asked whether the proliferation of patents on genetic inventions may not have a chilling effect on research and clinical use of genetic inventions owing to overcrowding and the increasing complexity of the legal situation.

Speakers on this topic were Ms. Maria Freire, Chief Executive Officer of the Global Alliance for Drug Development, an international not-for-profit organisation dedicated to the development of new medicines for infectious diseases that afflict developing countries; Mr. Christian Stein, Director of Ascencion in Germany, a technology transfer organisation serving the German Helmholtz life science research centres; and Mr. Fabirama Niang, Director of Industrial Relations for the University Louis Pasteur and head of *Réseau Curie*, a network for biomedical technology transfer.

Public research organisations

The question of maintaining public access to genetic inventions is of special concern to public research organisations that receive direct government funding. PROs are themselves prolific generators of inventions of high calibre, and they have seen the need to develop IP policies which both reflect their public mission and encourage technology transfer in a business-like manner.

The experience of one substantial PRO in the United States provides a model for balancing the interests of science and public health needs with those of commercial development. The National Institutes of Health has over the past decade developed the concept of "appropriate patenting". Patenting is one of the tools available to the NIH for transferring publicly funded technology to the market. In stark contrast with the private sector, however, the NIH believes patenting should not be undertaken when the research has generated technology that is already ready for transfer. The NIH sees patenting as critical for encouraging future or follow-on R&D investment, bowing to the private-sector view that investment in further R&D is unlikely without the prospect of patent protection. If no additional investment is needed to successfully transfer a technology, however, the NIH believes that patenting is not necessary. When this policy was put in place in the mid-1990s, the percentage of all disclosed inventions for which the NIH sought patent protection dropped from 90% to 40%.

Appropriate patenting also means that the NIH seeks patent claims that are commensurate with what has been invented and only as broad as necessary to achieve its aims. The NIH undertakes no blocking or defensive patenting.

Consequently, their current policy on gene patents is that these should only be sought for full-length genes of known utility and not for partial sequences, *e.g.* ESTs of speculative utility. The NIH was instrumental in helping the USPTO work out new guidelines for the patentability of genetic inventions.

The NIH also has a strategic licensing policy. While the NIH both licenses in and licenses out IPR as required, its licensing strategy seeks to promote public health and the dissemination of research results while encouraging market competition and attempting to obtain appropriate financial returns from technologies. In its efforts to promote market competition, the NIH prefers to grant non-exclusive licensing and to limit the licences given to firms to a particular field of use or territory. Out of approximately 1 000 licences in 2000, the NIH granted only a dozen exclusive licences. Moreover, the licences include a clause in which the NIH retains the right to use the invention for non-commercial research along with a working requirement to ensure that results are disseminated as broadly as possible.

In addition, the NIH has developed guidelines for the patenting and licensing of biomedical research tools developed with NIH funds. After 20 years of policies that fostered commercial development and the transfer of publicly funded research, the NIH has tried to balance the scale in favour of broader access. Its research tool guidelines help recipients of NIH funds to: *i)* decide what sorts of restrictions to accept as a condition of receiving access to research tools; and *ii)* determine reasonable terms and condition to impose in making NIH-funded research tools available to other scientists (NIH, 1998a). Public health considerations are best served if agreements on research tools do not unduly impede academic freedom, the ability of scientists to publish and the educational mission of many of NIH's fundees. While preserving incentives for commercial development remains very important, the NIH encourages the broad dissemination of research tools (through free access or non-exclusive licences), discourages reach-through provisions and warns against high royalty obligations.

To reduce the administrative burden and time necessary for the negotiation of access to research tools, the NIH developed a simple, one-page materials transfer agreement (the Uniform Biological Materials Transfer Agreement) which it uses itself and encourages its fundees to use. The UBMTA also militates against some of the more pernicious clauses, about reach-through provisions for example, found in some MTAs.

The NIH has also been called in to negotiate for public-sector researchers in securing access to technologies on reasonable terms. As noted earlier, the first

research tool controversy at NIH was over access to DuPont's recombinant Cre-lox mice. More recently, the NIH found itself involved in negotiating access agreements with WiCell (set up by the University of Wisconsin) over access for public researchers to its patented stem-cell technologies.

In conclusion, NIH recognises IPR as an important strategic tool provided the academic core mission is preserved. NIH policies and actions have striven to reach an appropriate balance between social benefits and the commercial benefits that can be derived from public research.

Experience at other public research organisations

PROs also include universities and other types of research institutions that receive substantial government funding for their research activities. In many countries, however, these institutions enjoy a degree of autonomy from the central government in their operation and their management of IPR. Often these organisations also espouse the academic ideals of research freedom and the importance of publication. However, many PROs in OECD member countries do not benefit from the same level of policy guidance that the NIH offers its recipients of biomedical research funds. For good or bad, most PROs have to develop their own guidelines regarding the patenting of genetic inventions and the licensing practices they deem acceptable. To the extent that a PRO has title to the innovations of its research staff, its patenting and licensing policies most probably will be developed by the institution's administration, academic staff and technology transfer office (TTO).

An almost universal issue in countries with a "first-to-file" system of establishing patent priority is the handling of disclosure of research results by academic scientists. Disclosing an invention in public in any way before a patent application is filed – even by posting a draft research paper on the Internet – constitutes prior art which renders the invention unpatentable. For this reason, the timing of filing patent applications in the public sector is almost always dictated by the need to submit papers at conferences or for publication in scientific journals. TTOs at PROs are trying to make scientists aware of the lost opportunities that early disclosure of their inventions may entail. At the same time, universities and PROs are some of the strongest advocates for the creation of a "grace period" in countries where these do not exist.

PRO patent applications are thus filed very early in the development process. Often, PRO inventions require further development before industrial interest can

be aroused, and a potential licensee will need to commit additional funding to development before the invention is commercially viable. PROs increasingly understand that patent protection for inventions is crucial to future commercial development.

Speakers contrasted the experience of German, French, and US research institutions. No obvious single pattern emerged.

Germany

In 1998, Germany enacted new regulations giving all public research institutes (*e.g.* the Helmholtz centres, the Fraunhofer Gesellschaft, Max Planck institutes) title to inventions arising from government-funded research. It was not until 2001, however, that the "professor's privilege", which granted university professors title to their inventions, was abolished. The German Employee Law now defines inventions by professors as service inventions belonging to the university. Both of these amendments were intended to help German PROs catch up with countries where technology transfer and profit maximisation in the public sector are already well-established principles.

To implement effective policies that balance the commercial and public interests of PROs, Germany is building professional TTOs. For universities, Germany is considering establishing in each *Land* (federal state) a single TTO which would serve several universities. The procurement and licensing of IP at a number of institutions might be more efficiently managed by a central body or holding company responsible for patent administration, asset management and the structuring of licensing agreements with the industry. However, hopes for earning revenue from licences should be realistic, as such revenue will certainly not cover the cost of research or, at least at the outset, the costs of the TTO.

German PROs are beginning to respond to these new incentives for exploiting publicly funded research. For example, four of the Helmholtz life science research institutions established a single IP asset management centre which aims to become a one-stop shop for technology transfer to the pharmaceutical and biotechnology industry. Many universities, however, are still disinclined to enter the complex field of IP management, particularly as their budgets cannot cover the extra expenses IP management incurs. Consequently, much remains to be done to develop a coherent IP strategy and infrastructure that would match the expertise of established university TTOs in countries such as the United States and the United Kingdom.

Given the relative novelty of IP management at German PROs, it is not surprising that there is as yet no policy on the protection of genetic inventions which takes into consideration the special needs of life science research institutions. For example, there are no codes of conduct for patenting and licensing strategies or mechanisms for protecting the access of scientists to research tools. Nor is there a standard, transparent and easy-to-use materials transfer agreement, although it would facilitate the transfer of biological material to and from PROs, encourage academic freedom and secure future IP. Such guidelines would be helpful for PROs that are facing decisions about their licensing strategies in biomedical research but are considered luxuries until TTOs are established. Nevertheless, guidelines or codes of conduct may not be enough to change incentives. The government may have to make legal or regulatory decisions about the acceptable scope of protection, the establishment of a grace period and the need for broader research exemptions, most likely in international concertation with other governments.

France

In France, public research is performed by a complex web of national PROs (such as CNRS and INSERM), universities and engineering schools. Some laboratories are shared among these institutions, and this complicates the management of their intellectual property. Although universities are autonomous, a recent Charter on Intellectual Property in Public Research and Higher Education Institutes reminds universities of their legal duty to protect and exploit the innovations of their staff. French universities have title over the inventions of their professors. Protecting IP should make it possible to choose industrial partners, provide visibility for the PRO and secure financial return at least sufficient to cover the cost of implementing IP policy. This charter is being used by the government to help universities establish TTOs that will offer the necessary skills and services required for professional IP management. Moreover, the charter establishes guidelines for the patenting and licensing of public inventions. For example, it specifies a preference for negotiating non-exclusive, time-limited licences which can be revoked in case of non-exploitation. Rights are retained for research use by the PRO, a right of public access is included for all libraries and databases, and publication is not to be inhibited. The results of basic research must be accessible to all.

Although there was no specific report of parallel experience in other countries at the workshop, it was noted that US and British universities have well-established, experienced and high-profile TTOs which handle patenting and

licensing activities, MTAs, and other contract research projects. These countries have developed patenting and licensing strategies which balance the commercial interests of PROs with the public interest in promoting health and scientific freedom. Principles such as the decision not to engage in "defensive patenting" or to disseminate research tools and results broadly through non-exclusive licensing have emerged. However, to implement such policies, professional TTOs are necessary. In many OECD member countries, efforts to establish TTOs of this calibre have just started. In Europe, it was suggested that harmonisation of technology transfer guidelines and possibly legal instruments (MTAs or research exemptions, for example) could be an impetus for more successful technology transfer. In particular, when negotiating access to IP for research purposes, strong and professional TTOs will be indispensable.

PROs and research exemptions

The impact of patents on the freedom of research is of common concern to PROs in all countries and is not limited to genetic inventions. Clearly a patent forbids the unauthorised use of the patented invention for commercial purposes. But whether use for research purposes is similarly precluded is a question on which laws vary across OECD member countries. To be precise, the research exemption holds that a product or process covered by a patent may be freely made or used to test whether the patent description is sufficient to enable one to replicate what the inventor has done and whether the product or process performs as stated in the patent. However, this is usually not what is understood as "research" by public bodies.

In policy discussion, the "research exemption" or "experimental use exemption" refers to further scientific research or experiments carried out with the use of the invention. In recent times, this exemption has been recognised by statutory or case law in some OECD member countries to permit clinical trials for the purpose of providing data to official regulatory authorities for market clearance of a medicine being promoted by a non-licensed third party but covered by a patent due to expire shortly, as is true under German and US law. However, policy discussions of "research exemptions" usually go further.

In the case law of US courts, the research exemption is considered to be narrow in scope. Thus, any use in research which is not simply for the purpose of "philosophical enquiry" or which has a commercial end in view is considered to fall outside the exemption. For this reason, when licensing out their own intellectual property, US PROs typically reserve the freedom to use the invention

for future research (for their own or academic and other institutional research) in their contracts with industrial and other licensees.

In Europe, acts "done privately and for purposes which are not commercial" and acts "done for experimental purposes relating to the subject matter of the invention" do not infringe a patent. But the term "privately" has not yet been judicially defined. The second exception is regarded by some as applying to the preliminary testing mentioned above and is usually assumed also to allow PRO research leading to improvements or variations of the claimed invention, which might be separately patented.

It should be noted that the routine use in the research laboratory of a "research tool" for the purpose for which it was invented is unlikely to be the type of experimental use that falls outside the protection of the patent. A typical example might be the identification and isolation of a particular receptor protein or channel protein involved in an important biological pathway. The cDNA coding for this protein can be used to express this protein as a target in the search for compounds that activate or inhibit the pathway and therefore may have therapeutic potential. As this is precisely the practical utility of the tool for research, the use of the protein for this research purpose likely would not be exempt from the scope of the patent and consequently would be considered by courts as an infringement.

In many cases, PROs and other bodies have recommended that the research exemption issue should be examined at international level, with a view to a more liberal interpretation so as not to stifle further research.[23] Recent instances of the restrictive policies of a few patent holders *vis-à-vis* academic and clinical research activities have brought the practical importance of this matter to light. In reinterpreting what research exemptions permit, however, it is important to recognise that too broad a research exemption might be counterproductive. One object of the patent law is to stimulate the competitive spirit and lead to further discoveries. More importantly, it has proved very difficult to define a more equitable research exemption or to draw a clear line between pure and commercial research which would help advance the debate.

Session 4: The impact of patenting and licensing practices on new product development

This session explored the impact of patenting and licensing practices on the development of new products by the private sector. In particular, speakers focused on the commercial consequences of the very large numbers of patents granted for

genetic inventions and on the increased transaction costs for integrating these rights. Representatives of pharmaceutical, genomics and biotechnology firms all emphasised the importance of protecting the fruits of innovation, but they also acknowledged that protection must be balanced to guard against a fragmentation of technology through tangled patterns of rights.

A first group of speakers addressed the impact of patent thickets, royalty stacking, reach-through rights and dependency on the freedom of companies to operate and develop new products. Mr. Philip Grubb, the Intellectual Property Counsel for Novartis, Mr. Jacques Warcoin, a patent attorney with Cabinet Regimbeau in France, and Mr. Erik Tambuyzer, of Genzyme Corporation in Belgium, discussed the views of small and large biotechnology firms. Mr. Richard Johnson, Senior Partner at the law offices of Arnold & Porter in the United States, and Mr. Lawrence Horn, Vice President MPEG LA, also in the United States, discussed possible novel approaches to IP management (*e.g.* consortia, patent pools, collective rights organisations), and whether these are likely to emerge from the private sector as self-regulatory mechanisms.

In the discussion, patent thickets, royalty stacking and reach-through rights were all recognised as real concerns for the industry, but none was seriously judged a threat to innovation in biotechnology. Many speakers felt that "working solutions", such as changes in the types of contracts negotiated, or collective actions, such as the formation of consortia and possibly patent pools, are emerging to overcome transaction costs associated with a more complex patent environment (*e.g.* the Single Nucleotide Polymorphism Consortium). The private sector is especially interested in such solutions because they usually do not require affirmative government intervention. However, other speakers, reflecting the responses in the German survey, were more sceptical of the ability or desire to co-operate in such a manner among companies and research organisation.

Nevertheless, government attention was drawn to two important issues. First, companies felt that reach-through claims in patents and the definition of non-infringement for research (*i.e.* the extent of the research exemption) were a source of commercial uncertainty and need to be clarified. Second, the situation for the private sector is likely to become more complex and challenging as IP protection in biotechnology increasingly includes not just biochemical patents but database protection, copyright and patents for software, reflecting both the chemical and informational nature of inventions. Companies may find their ability to evaluate how to protect inventions and whether or not they are free to exploit their invention more difficult. In conclusion, industry representatives strongly agreed that there was no need for new or additional laws on the patenting of genetic

inventions, and most were against limiting patent rights to the uses identified in the claims. However, they did feel that greater administrative and judicial clarity, for example decisions on the validity of reach-through claims, could help limit the number of applications filed and increase patent transparency in the medium term.

Patent thickets and royalty stacking

According to industry speakers, the high transaction costs associated with steering a path through conflicting and overlapping patents are real and should not be underestimated. At stake is the ability of firms to commercialise new products and services with a reasonable degree of freedom ("freedom to use") and certainty about the risks of exploitation. The term "patent thicket" has been coined to characterise a technological field where multiple rights owned by multiple actors may impede R&D because of the difficulty or cost of assembling the necessary rights.

Patent thickets have arisen in other technological fields – radio and telecommunications, semiconductors, and high-density polymers, for example. Pragmatic solutions have been found in these industries. In biotechnology, perhaps because of the comparatively large numbers of patents involved, there may be an initial temptation to overestimate the extent of the challenge. When companies engage in a new project, an initial study of the patent literature can sometimes reveal an apparent patent thicket: there can be dozens, sometimes more than 100 patents to consider (*e.g.* the example of the Malaria Vaccine Initiative mentioned in Chapter 1). On detailed examination by patent attorneys, however, companies often find that the thicket their project initially seemed to face is reduced to a manageable number of patents of relevance or real concern.

The most straightforward way to gain access to patented technologies is simply to license or cross-license under free market conditions. To establish one's freedom to enter a market may indeed require licences from a number of patent holders, each demanding separate royalties. One speaker noted that in the field of genetic testing, royalties for licensing in patents on genes and other "must-have" technologies run at 1-4% of net sales of a given product for non-exclusive licences (though royalties can sometimes be as high as 10%) and at 6-10% of net sales for exclusive licences (again, these can sometimes reach as high as 20%). As more and more biotechnology companies commercialise "research tools" – genomics sequencing and expression technologies, targets, screening assays – the pharmaceutical companies that develop end products must enter into multiple licensing agreements and agree to the payment of royalties to many parties. The

accumulation of such royalty agreements could reduce a firm's ultimate profits to a point where pursuing commercialisation is no longer viable,[24] thus leading to a "royalty-stacking" problem.

Industry representatives acknowledged royalty stacking as an ongoing concern, but believed that private, contractual solutions are frequently possible. Partners can often reach agreement as to the level of royalty rates that reflects business realities. For example, contracts may stipulate minimum and maximum levels of royalty rates, depending on the number of other research tools that need to be licensed and on the risk that the technologies may infringe other patents (see Box 5 for anti-stacking provisions in contracts). It is in the interest of both smaller specialist biotechnology companies and larger pharmaceutical companies to allow for an appropriate reduction in royalties when necessary. Projects are very rarely dropped because of royalty stacking alone.

Box 5. Types of anti-stacking provisions

Variable rates. Different rates apply depending on how much additional work is done by the licensee (*e.g.* analogue development). The smaller the role the technology plays, the lower the rate the licensor receives.

Joint venture expense. This model deducts any third-party royalty rate from gross revenues, prior to determination of net sales on which royalties or profit splits are made. A licensor with a 10% net sales royalty would only bear one-tenth the cost of a third-party payment under this structure.

Creditable percentage. The parties share the third-party royalty, down to a floor rate.

Maximum royalty rate. The parties put a top limit on all combined royalties. If a third-party royalty must be paid, previous rates are adjusted downwards to stay below the limit.

Royalty-free. The technology is licensed outright, with some combination of up-front and/or interim payment, but no royalties are owed downstream on products sold.

Source: Signals Magazine (1998).

Very few specific cases of how companies have resolved patent-thicket challenges are found in the literature because these solutions have an element of commercial secrecy. However, one highly instructive discussion of the problem of negotiating a path through a dense patent thicket was published in a particular field of plant genetic modification, the GoldenRice case.[25] (See also the Malaria Vaccine Initiative mentioned in Chapter 1.) GoldenRice is a technology developed to raise levels of Vitamin A in rice and thereby to respond to the nutritional needs of peoples for whom rice is the most basic food crop. Three genes were inserted into the rice plant to complete the beta-carotene biosynthetic pathway. In addition to the proprietary genes, the methodology involves the use of a number of plant

transformation vectors, promoters and antibiotic resistance markers, all of which are the subject of patents held by various owners or covered by MTAs. In consequence, over 70 items held by a dozen or so patentees were identified in the survey as requiring consideration. Most are published patent applications. The GoldenRice survey refrains from recording conclusions as to the relevance of each of these patents but points to alternative strategies for international organisations concerned with facilitating the introduction of genetically improved rice varieties into developing country agriculture.

Reach-through claims

Research tool patents are often implicated in royalty stacking. Here a research tool is a biological material (or other type of material) or a method used in the laboratory to test candidate medicinal products. The research tool might be a reagent kit for laboratory use, a gene associated with disease, a marker, an assay or a transgenic animal. Smaller biotechnology firms and universities are prolific sources of inventions of this kind. Research tool patents are on "upstream" technologies, which are used in the research process itself. Other types of patents on upstream technologies include claims to compounds identified through a method of screening, claims to compounds which potentially bind to a specific enzyme or receptor, and even methods of analysis for biological data sets. Such upstream patent claims are on the rise at the EPO and USPTO. Licences on these patents typically call for either a fixed annual fee or one based on the extent of use (numbers of tests). Normally, a research tool patent does not contain claims to products found by using the tool (reach-through claims).

However, industry speakers were critical of the increasing trend towards demanding downstream royalties from the sales of a medicinal product discovered with a research tool (*i.e.* reach-through royalties). Larger companies may on occasion agree to reach-through royalties as a short-term expedient and PROs may agree because they do not require fees up front. The concerns evoked about reach-through royalties are that they increase royalty stacking, as multiple tests and assays are needed when developing a medicinal product, that they make project management more complex and the relationship to all collaborators more delicate, and that they are costly to negotiate.

The legitimacy of claiming reach-through royalties depends to a large extent on the wording of the patent granted, and in particular on the presence or absence in the patent of a claim to "a compound identified by the method claimed above". In the absence of such wording, claiming royalties on something not in the patent

could constitute patent misuse. The challenge of reach-through claims may be satisfactorily resolved through administrative decisions by patent authorities or through the judicial process. An administrative change might include, for example, a decision that the patent offices should not permit reach-through claims to be made in patents. Judicial solutions might also help clarify the legitimacy of reach-through claims. Several important cases are already being addressed in courts or in opposition procedures (*e.g.* Rochester University vs. Pharmacia on COX-2). If they are not resolved through administrative or judicial measures, and the existence of reach-through claims proves to be detrimental to research and commercialisation, governments may have to consider alternative solutions.

Patent breadth and strength

Patents issued with what some commentators consider to be excessively broad claims, especially claims that are not deemed commensurate with the inventive step, have provoked concern and debate in recent years in pharmaceutical as well as agricultural biotechnology. Patent offices are fully aware of the concern and many have taken steps to regulate their practice. The USPTO, for one, published new guidelines in 2001 which raised the utility requirement by specifying that, to be patentable, an invention should have a "credible and specific utility".

Collaboration between the USPTO, the EPO and the JPO has produced a series of studies which indicate that they have reached a measure of harmony as to the permissible scope of claims and the requisite degree of support for the claims in patent applications.[26] The studies indicate, for example, that patent applications on partial gene sequences with inadequate disclosure of utility or function will not be granted patent protection. Patent applicants claiming utility and function for novel DNA sequences on the basis of sequence similarity with compounds of known utility in databases (DNA or protein) may be required to produce more convincing evidence of these properties when challenged by patent office examiners. The Trilateral Commission has also addressed common approaches to the problem of "reach-through" claims, and there appears to be a movement not to grant claims to compounds "identified by" a screening method or tool, especially if the efficacy of the screening method or tool has not been proved.

The patent offices' intentions as reported in these studies notwithstanding, only practice will show how these guidelines will be viewed by patent attorneys and whether they will be supported by the courts. It appears that a more rigorous practice of examining patents may result in a reduction of the numbers and breadth

of patents granted in future. However, this alone will not eliminate the problems addressed in the workshop.

Increased complexity

As a general rule, it is difficult to predict the likely outcome of patent applications for genetic inventions in this field. Not only are there more patent applications and grants, but the complexity of the claims, the rise of upstream patents, the lack of transparency in some important claims, and the sheer length of applications, sometimes reaching thousands of pages, also confound risk calculations (Allison and Lemley, 2001). Moreover, the success or failure of an application is not known for some years, owing both to the length of the examination process and potential opposition after grant in some jurisdictions. Firm decisions as to whether patent infringement will arise cannot be made until the final form of patent claims is known. In consequence, many contracts and licences have to be concluded while patent applications are pending and R&D is far from complete. In these circumstances, payments to the licensor at certain defined stages of development of the technology ("milestone payments") are now a regular feature of agreements.

Patent owners thus find that they negotiate more numerous and more complex contracts. Relationships with public research bodies are more formalised, through materials transfer agreements, and separate contracts must, in some OECD member countries, be made both with PROs and with post-doctorates or students who may participate in the project but are not considered as part of the staff. In addition, new players, such as patient groups that donate biological materials, must be considered. The Convention on Biological Diversity requires that firms also enter into agreements for access to national genetic resources with source countries. Despite the complexity, the system does appear to work: large numbers of start-up companies and pharmaceutical companies successfully conclude licences with multiple parties.

The intersection of genetic inventions and bio-informatics

From the viewpoint of the patent profession, the greatest challenge has been to respond to the increasing technical complexity and sophistication of inventions in this field. As patentability has become harder to evaluate, the professional time required to deal with most questions on which advice is required is now much longer than for inventions in earlier eras of bioscience. The problem is bound to

become even greater for inventions in the field of bioinformatics, in which patents are now being granted, especially by the USPTO. Compounds are being claimed, not in the traditional form based on chemical structure, but in terms of their ability to bind to regions of the three-dimensional configuration of target enzymes and other proteins. Enzymes and enzyme inhibitors themselves are claimed in terms of *in silico* determination of spatial numerical co-ordinates rather than by their chemical characteristics, such as their primary or secondary amino acid sequences. For such applications, patent searchers and examiners encounter difficulties for performing the necessary search and evaluation of prior art. These patent professionals are continually challenged by the rapid evolution of technology, which complicates their task of securing adequate protection for inventors on the basis of the inventive contributions made.

Patent pools

While recognising that patent thickets and royalty stacking are a problem, industry speakers noted that they mostly address these challenges through licensing and cross-licensing of patents on genetic inventions (see also Schapiro, 2001). Patent pools have been suggested as an alternative solution to the emergence of patent thickets in biotechnology. Multiple owners of significant patents enter these into a common pool in order to facilitate the licensing of all necessary technologies for new product development to each other or third parties.[27] A White Paper from the USPTO (Clarke *et al*., 2001) outlines the features of patent pools, their history and their perceived advantages and disadvantages. The authors conclude that patent pools present an effective solution to the problem of "blocking" patents and "stacking" licences in biotechnology. While patent pools can run afoul of competition law, there are cases where a favourable judicial opinion has been given on the legality of patent pools provided certain conditions are met.

When entering patents into the pool, patent holders retain ownership of their respective patents and license them non-exclusively to others, either directly or through an administrative intermediary set up for the purpose. There have been patent pools for earlier technologies (sewing machine parts in the 1850s, aircraft during World War I, radio parts in the 1920s), sometimes with government intervention, other times autonomously. However, patent pools come under close scrutiny for possible anti-trust violations and so must be able to show that the arrangement has pro-competitive effects. They can: *i)* help integrate complementary technologies; *ii)* reduce transaction costs; *iii)* clear blocking positions; *iv)* avoid

costly infringement litigation; and *v)* promote the dissemination of technology. However, there is no precedent for patent pools in bioscience.

A successful patent pool exists for the digital video compression standard, MPEG-2, which embraces 116 patent families and over 490 licensees worldwide. No attempt is made to apportion differing values to each of the pooled patents, and a standard royalty rate is applied to all patents, and the sharing of licence revenue among pool members is in accordance with the amount of patent usage by licensees. The pool is administered by a legal entity, MPEG LA, which provides professional management of legal and tax matters and monitors the operation of the pool for compliance with competition law, thus relieving individual pool members from the considerable burden which they would otherwise have to bear. The concept of the patent pool is clearly valuable for use with patents for which mutual licensing is essential to enable parties to enter the field with their own products or services.

While the concept is intriguing for biotechnology, it is questionable whether the technologies and markets for genetic inventions are amenable to pools. It is true that there is a growing interdependence among patents, that the claims of many patents are narrower, and that patents are held by multiple owners. Licensing transaction costs are burdensome and freedom of operation is restricted, thus increasing the potential for conflict among researchers. However, the pharmaceutical biotechnology industry may be fundamentally different from the electronics sector. It is not an industry in which defining standards is important, and assuring interoperability of technologies is not very important, especially not in the development of therapeutics. A company's worth is tightly tied to its intellectual property and fosters a "bunker mentality". There are likely to be disagreements among partners over the value of the different patents in a pool, and dominant players may not have a strong incentive to join the pool. If a limited field of application and essential patents can be defined, the patent pool model is worthy of consideration in biotechnology (Marks *et al*., 2001). The suitability of the patent pool for biotechnology patents certainly requires further study, as does the role of government in promoting them.

Other forms of co-operation work well in biotechnology. The SNP Consortium and Genebank are arrangements where co-operative behaviour has facilitated the pooling of research results and the development of genetic resources. The SNP Consortium is a non-profit entity whose goal is to create and make publicly available a high-quality single nucleotide polymorphism map of the human genome. In addition to the Wellcome Trust, the Consortium is made up of 11 pharmaceutical and technological companies.[28] The work on molecular genetics

supported by the Consortium is being performed at four major research centres (Stanford Human Genome Center, Washington University School of Medicine, Wellcome Trust's Sanger Centre, Whitehead Institute for Biomedical Research). These centres identify and collect SNPs into a database which is freely available to scientists. Over a million SNPs have already been mapped, and the total map will probably include 3 million SNPs which can be useful for finding genetic associations with diseases and therapies. The pharmaceutical companies hope the database will help them develop drugs to treat diseases whose genetic basis is revealed through the SNP map. Consortium members agree not to seek to patent SNPs, but they are free to patent any downstream inventions. A major difference between the SNP Consortium and proposed pools is that the aim of the former is to put upstream inventions or discoveries into the public domain rather than to create a pool for which users would pay to have access. Nevertheless, the fact that the industry has successfully joined forces in this case does suggest that alternative contractual solutions to the access problem are possible and may function well under certain circumstances.

Session 5: The impact of patenting and licensing practices on human health and technology uptake

This session focused primarily on the licensing of genetic tests, whether access to these tests has been unreasonably restricted, and the measures available to ensure their availability. In addition, the session also touched on convergence and clashes between patents and ethical considerations. Speakers included two academics who study the impact of gene patents, Mildred Cho of Stanford University in the United States and Richard Gold of McGill University in Canada. Jeffrey Kushan, a lawyer with Powell, Goldstein, Frazer and Murphy, also in the United States, discussed industry views on improving access to genetic tests. Finally, Ludger Honnefeld, of the University of Bonn in Germany, discussed why governments need to address ethical issues in order to build public trust in the legitimacy of the patent system.

The discussion made clear that genetic testing for predisposition to disease and its early diagnosis is of great public importance and that certain restrictions on the availability of such tests raise ethical issues. There is therefore a need for more empirical evidence on the extent to which patents contribute to restrictions on clinical practice.

Mildred Cho and colleagues have recently conducted two studies of laboratories in the United States at universities, hospitals and private companies engaged in testing for DNA analytes. One study showed that when patents are issued on genetic tests, a substantial proportion (65%) of the clinical laboratories had been contacted by the holders of the patent or licence for the genetic test. Among the laboratories that had been offering the test, 25% said that the patent owner or licensee prevented it from continuing its testing service and 53% that were considering developing or offering the test decided not to for patent reasons. An overwhelming proportion of responses indicated that patents had a negative impact on access, cost and quality of testing and on information sharing between researchers.

In a study of gene testing for hereditary haemochromatosis (an iron overload disease which, if untreated, causes organ failure), it was found that a large proportion of the US clinical laboratories surveyed had introduced a diagnostic test for mutations of the HFE gene, which is associated with the disease, immediately after the method was published in the scientific literature (Merz *et al*., 2002). Three US patents were subsequently issued. The history of the companies involved in exploiting the IP covering this genetic test is rather complicated. The original innovator, Mercator Genetics, went bankrupt after spending USD 10 million on research. A series of mergers, acquisitions and licence deals followed before the final terms for licensing clinical laboratories to perform the test were settled by the eventual owner of the patent. The licence fees demanded in the early stages of the test's existence were at a level unacceptable to US clinical test laboratories and many withdrew from offering the test in consequence. Of 119 laboratories that could perform the test, 36 did not do so and 22 of these claimed that the reason was the licence fees demanded (Merz *et al*., 2002). However, current licensing terms are at a much lower level and over 50 US centres now offer the test (Buckles, 2001). Merz *et al*. point out that without the potential value of the patented invention, the initial investments in research might not have been made and the gene discovery delayed. However, the authors question whether the licensing strategy adopted by the various companies that exploited the underlying patent was the best method of securing financial reward.

Public health authorities in several OECD member country have concluded that the licences on genetic tests tend to reduce access by clinical laboratories. For breast cancer screening in France, for example, the *Institut Curie*, the *Assistance publique* and the Gustave Roussy Institute are challenging the patent granted by the EPO to Myriad Genetics on the BRCA1 gene. Though the challenge will be on the technical merits of the patent granted, at the heart of dispute are the cost of the test (at USD 2 500, it is over three times more expensive than domestically offered

tests) and the fact that all DNA samples must be sent to Myriad, thus eliminating the research capacity of French clinical labs. Richard Gold also noted that the Province of Ontario in Canada has challenged Myriad's right to provide breast cancer genetic tests exclusively. Other national authorities – in Italy, Sweden and the United Kingdom – have similarly voiced concern that patents on genetic tests can lead to abusive monopoly positions and that unreasonable licensing practices pose a threat to public health by reducing access to screening procedures. However, reaction to perceived abusive practices varies considerably across countries. Clearly, at least in some cases, health authorities and business differ on what reasonable licensing terms ought to be.

Although the two studies described above call into question the patenting of genetic tests, they also highlight a breakdown in licensing owing to an inflexible attitude on the part of patent owners. More information on licence negotiations and why they fail would be helpful. It may be that some laboratories that lack experience with patents might hesitate to enter the "deep waters" of licence negotiation and withdraw rather than explore the possibility of an accommodation with the patent owner on reasonable terms. If patent owners refuse to license the tests on *any* terms, this would be an extreme case of the permissible exercise of patent rights and may result in the sacrifice of company reputation and public image. The underlying reasons for the breakdown in licensing need to be elucidated as it is a serious concern.

The above studies suggest that solutions should be sought through modification of the patent law, which at present offers a generous degree of protection when current patentability requirements are met. However, workshop participants noted the difficulty of drawing the line between what some commentators think is the appropriate or inappropriate scope of patent protection. For example, a complete embargo on gene patents, *i.e.* patents with product *per se* claims to DNA, would still allow the patenting of the method of testing and the reagent kits used in these methods. Moreover, the types of claims in DNA patents that cause concern in the clinical sector are in many cases the same claims as those needed by the manufacturing sector for market exclusivity in therapeutic pharmaceutical products. Thus, if protection is reduced for DNA sequence patents, there would likely be an adverse impact on investments in therapeutic research. The workshop did not reach a consensus on how best to address problems of access to genetic tests.

Licensing and pricing of genetic tests

While some companies aggressively protect their genetic inventions, not all firms have participated in the "patent land-grab" or filed patents on all of the DNA sequences of as yet unknown function that they identify. Generally, firms will seek to protect genes, sequences or other biological entities if they have specific information on their utility and can hope to develop new or improved diagnostics or therapies. In general, firms see patents on genes as creating an incentive for the multi-million dollar investment they make in the period before testing is complete or marketing approval obtained. Firms justify the high initial price of a test as necessary to recover their investment.

However, companies' licensing practices differ, depending on their business model. Where some companies do not license in order to develop products in house, others chose to license out certain technologies. For therapeutics, licences are often exclusive, granted to one commercial partner, or non-exclusive but "field limited". In both cases, it is recognised that the licensee will need to make a significant additional investment to develop and test the potential product. Research tools are frequently licensed non-exclusively, to multiple potential users. Licensing patents on genetic tests can also be granted non-exclusively, as Genzyme does for its colon cancer diagnostics (for the p53, MSH-2 and APC genes). However, licence exclusivity may be necessary to make a genetic testing service economically viable, depending on the market and the rarity of the disease. According to one speaker, esoteric, highly complex and specialised tests are more likely to be licensed exclusively. Only high volumes and automation allow genetic testing companies to achieve economies of scale and reduce costs for such tests. Given the competition from academic institutions and hospitals as well as other firms, genetic testing companies may have difficulty creating economies of scale. There may be lessons to be learned from legislation in several OECD member countries to encourage innovations in developing orphan drugs.

The price of certain genetic tests, which can run as high as USD 1 000-5 000, is closely linked to the issue of access. Creating economies of scale may help reduce costs in the long term, but speakers mentioned that certain pressures are likely to increase prices. In particular, the need for more and higher-quality epidemiological and genetic population data, increasing regulatory costs, including stricter quality assessment and quality control requirements, laboratory certification costs, increased needs for counselling, and, potentially, liability costs can push up the price of tests. Genetic testing services are at present offered by many organisations, but these pressures may not only increase prices but also lead

to a professionalisation of the testing laboratories that may in the end favour the emergence of larger, commercially oriented laboratories.

Private and public approaches to access

Speakers at the workshop identified some of the tools available to address the social concerns related to patents (*e.g.* access and affordability) without unduly lessening private incentives to innovate. The use of exclusions permitted in the WTO TRIPS Agreement, higher patent standards, opposition procedures and the threat of compulsory licences are perceived as means of limiting patent owners' rights and thus their licensing practices. The private sector stressed, however, that other solutions for improving clinical access might be preferable because they would be less arbitrary, probably less costly for all, and neither discriminatory nor a misuse of patent rights. Such alternatives include: creating pools or clearinghouses to make it easier for laboratories to obtain licences for patented genetic inventions and thus reduce transaction costs; increased pressure on licensors in negotiations by large providers or through public pressure; and anti-trust solutions.

Speakers recognised that the clinical environment is very different from R&D and commercial settings. After identification and publication of gene sequences, many clinical laboratories are quickly able to offer tests, usually months before the patent covering a particular gene is actually granted. In the discussion, several participants' comments suggested adopting a more liberal policy towards patents on genetic tests to increase access. Permitting more clinical use of genetic tests without infringement, for example, may arguably not amount to significant damage to the interests of the patent owner but be of great social benefit. Nevertheless, most participants agreed that it is not desirable to exclude genetic tests entirely from patentability. This would be a harsh solution and one likely to have broad negative consequences for the development of therapeutics. Members of the public and private sectors put forward several alternative suggestions, which involve regulatory, administrative and/or self-regulatory measures:

- ***Compulsory licences.*** Governments can opt to issue, or threaten to issue, compulsory licences for the sale of certain (or all) patented genetic tests as a mechanism to increase access and lower prices. While the use of such "liability rules" is gaining popularity in the academic and popular press, the implementation of compulsory licensing is very complicated and raises thorny problems of valuation and compensation (Epstein, 2001).

- ***Anti-trust laws.*** In some cases, governments may be in a position to enforce anti-trust laws against companies. Companies may, for example, illegally abuse their position by tying licences to patented technologies with unpatented technologies (*i.e.* forcing clients to buy another product or service if they want access to a patented technology) or by asserting broader rights than those granted in their patent claims. However, speakers noted that, in most cases, owners of genetic tests merely exercise their legal rights and do not run afoul of anti-trust regulations.
- ***Clinical use exceptions.*** A more comprehensive, but less arbitrary, policy would be to enact a "clinical use" exception similar to the research exemptions in effect in some countries.[29] The difficulty with such an approach would be to distinguish clinical research use from commercial use. It is unclear at this point what effect a clinical exemption would have on research, commercial investment in test development, quality, cost or access.
- ***Patentability criteria.*** One recommendation was to use administrative rules to limit the scope of protection by "raising the standards" for the granting of gene patents. Patent offices could apply more stringent criteria for inventiveness in judging the patentability of genetic inventions, especially as they apply to product patents claiming utility as diagnostic tests (Nuffield Council on Bioethics, 2002).
- ***Non-patent incentives.*** More radical solutions included alternatives to patents for genetic inventions. Instead of making patent rights available to incite research, the state could sponsor competitions or grant entitlement to compensation for use of a new technology by others. One suggestion was that an orphan-drug type of protection, perhaps of shorter duration than that of patents, be extended to genetic tests for rare diseases.
- ***Public pressure.*** Industry representatives recognised that governmental and public pressure (particularly from patient groups and the medical establishment) have a powerful influence on their licensing strategies. Public reaction against ill-conceived licensing and enforcement practices carries weight in corporate decision making.

If one views the problem of access to genetic tests as a failure in licensing, however, another possible solution would be to encourage the formation of patent clearinghouses. If the failure of clinical testing organisations to obtain licences in order to continue offering patented tests is due to the perceived difficulty or expense of negotiating licences with each patent holder, a simplified mechanism

for obtaining licences could make licences more accessible. Patent clearinghouses might offer a self-regulatory measure for managing problems that arise with gene patents. A patent clearinghouse would be a "one-stop shop" offering clinical laboratories non-exclusive licences to a range of patented genetic tests on reasonable terms. It remains to be seen whether such an organisation could work in practice or who might instigate its establishment. On occasion, large funders of public research or public health providers have acted as central negotiators in order to obtain licences on favourable terms for their constituents (*e.g.* the DuPont Cre-lox case, the WiCell stem-cell case).

Whether or not funders or national health providers would be involved in creating a patent clearinghouse, there was sympathy at the workshop for the view that licensing complications cannot be resolved by public clinical test laboratories alone. They probably need an organisational infrastructure with leverage to address access and pricing concerns. Clearinghouses might be a good market-based alternative to access problems, but their establishment may require government action.

Ethical issues

Over the last two decades, the ethical implications of patents for biological materials and processes have been the subject of heated public debate. Gene patents, as viewed by the general public, present special ethical and social problems that are unlikely to be resolved in the short term. Questions which still generate controversy include: *i)* the distinction between discoveries and inventions; *ii)* the criterion for excluding patentability of genetic inventions for reasons of morality or public order; *iii)* the patentability of living organisms and the human body and the impact on human dignity; and *iv)* the trade-off between patents and the protection of plants and species.

Patent authorities are often the target of public criticism about the ethics of patentability. This is undoubtedly because the patent laws of the European Patent Convention, as well as those of many other countries, contain provisions relating to the morality of certain kinds of invention. As mentioned earlier, however, the morality clauses focus on the morality of the eventual exploitation (use) of an invention. The patent authorities do not presume to judge the morality of the R&D which precedes the patent application. In Europe, case law on how to interpret the morality and public order clauses has begun to develop as a result of formal oppositions to particular patents by special interest groups.

Workshop participants generally agreed that in cases where fundamental ethical decisions are at stake, the debate needs to take place in society at large rather than in patent offices, which have no special authority in moral matters. For example, some commentators claim that gene patents confer "ownership" of part of our natural heritage, disturb ethical balances, improperly restrict research and experimentation and even violate human dignity. If such objections are valid, there would be a case for considering a modification of the present law. But the patent law itself is most probably not a suitable medium for the raising of philosophical objections to the patenting of living organisms and genetic inventions. In such cases, legislative or regulatory action should be envisioned. Although some observers would encourage legislators to adopt a broader vision of patent law as an ethico-legal instrument of public policy, it was generally agreed that IP law is fashioned primarily to promote inventiveness and the disclosure of advances in technology and cannot be easily reformed to include such a vision.

Broad debate about issues like ethics should set the context in which patent law operates and not *vice versa*. However, public policy makers need to look for appropriate instruments within the broader policy context and then ensure that patent law operates within that context.

Chapter 5

CONCLUSIONS

The objectives of the workshop were to assess the impact of patents on genetic inventions on access to the information and technologies covered by DNA patents and to discuss the challenges they pose for scientists, industrialists and medical practitioners.

The discussion set out to identify the access problems that are perceived to exist and to assess the extent to which such perceptions might be justified. It drew on recent studies of the licensing of genetic inventions and on the testimony of experts familiar with the needs of academia, pharmaceutical biotechnology and clinical testing laboratories. The major conclusions of the workshop were that:

- The patentability of genetic inventions is not fundamentally in question among the users of the system, be they from the public or private sectors or from the medical establishment.
- The available evidence does not suggest a systematic breakdown in the licensing of genetic inventions. The few examples used to illustrate theoretical economic and legal concerns related to the potential for the over-fragmentation of patent rights, blocking patents, uncertainty due to dependency and abusive monopoly positions appear anecdotal and are not supported by existing economic studies.
- However, in specific areas there is evidence of problems associated with the numbers and breadth of gene patents now being issued. Many consider the rise of patents with reach-through claims problematic and feel that this may require government attention. Empirical studies have shown problems arising over access to diagnostic genetic tests, although the exact cause of these problems has not been fully elucidated.
- The licensing system is not static but is adaptive. Companies, governments and civil society are reacting rapidly to deal with the increasing complexity of the intellectual property system in this area.

Policy-based solutions to current problems will have to be able to cope with the system's evident adaptability.

- Continued monitoring of patenting and licensing of genetic inventions is necessary. So too is the collection and analysis of robust economic data as a basis for action to ensure that access does not become more problematic. More rigorous, data-intensive studies of licensing practices in particular are critical if policy makers are to embark on significant reform of the present system.

The gap between experts' views and public opinion

Patent protection for genetic inventions remains highly controversial. Participants were conscious of a large gap between the views of experts and public opinion about problems engendered by the patenting of genetic inventions. Experts, in both public and private sectors, want to narrow this gap.

Whereas public opinion may express dissatisfaction with the patent system and in some cases seek to exclude genetic inventions from patentability, a large majority of experts support the patentability of genetic inventions. However, experts hold a variety of opinions regarding the permissible scope of patent claims and whether to carve out more exclusions.

Public concerns include the absence of mechanisms for debate on the ethics of gene patenting as well as the apparent lack of regulatory oversight regarding the behaviour of patent holders. The workshop may have helped policy makers better understand the types of problems that gene patents pose for users and thus put proposed remedies in context. However, the workshop did not directly address concerns relating to ethics or access to health care, which are at the heart of public debate on gene patenting.

It is critical to engage public opinion in order to tease out underlying concerns about gene patenting and to address those concerns, if public trust in the patent system and its application to biotechnology is to be rebuilt.

Consensus on challenges

Though experts at the workshop presented a range of opinions about the challenges to be faced, there were a number of points of consensus on key challenges. The divergence of opinion between academia and industry appears

much less polarised than appeared to have been the case in the 1980s. For some decades, many publicly funded organisations have used and accepted patent rights, for genetic inventions as well as for other technologies, as part of their core missions.

There was a broad consensus on the problems encountered by genetic testing laboratories. These laboratories, many of which have a public research mission, are anxious to make use as early as possible of developments published in the scientific literature that could improve their services to the public. The laboratories are concerned about restrictions on access to such research owing to patents which they become aware of after having incorporated the new developments into the tests they offer. Governments are equally concerned about the costs associated with certain licences for diagnostic tests. While authors of scientific publications on genetic associations with diseases would do well to alert their readers to the potential "patent submarine" problem, DNA patents are legally permissible and certain consequences follow from the rights that they give to their owners. Several approaches to discouraging the extreme licensing practices of a small number of genetic test providers were suggested. These are described below.

Workshop experts also agreed that, despite an absence of accurate statistics on DNA patent numbers, the number of such gene patents is rising rapidly and patent thickets and royalty stacking are consequently real concerns.

However, surveys of public research and industrial opinion undertaken so far indicate that while the numbers of patents that may need initially to be considered when determining freedom to operate is frequently large, the core of patents that actually create obstacles to public use or market entry is often much smaller. In most cases, such patents can be licensed through negotiation. This applies to so-called blocking patents and patent thickets. Public research bodies may adopt a different strategy and act as if they benefited from an "informal research exemption" and infringe (knowingly or not) if their use of the invention does not have direct commercial relevance. In either case, the freedom to operate is not unduly impeded.

The recent rise in the use of reach-through claims in patents, especially for research tools, was also flagged as a topic of concern. Reach-through claims increase financial uncertainties for the development of pharmaceuticals and contribute to royalty stacking, which may mean higher prices for end products.

Some experts predicted that there would be challenges at the interface of biotechnology and information technologies. These technologies will require

companies to use a much larger variety of IP, including patents, database rights and copyright. According to some experts, the problems inherent in the interaction among these various types of IP are likely to be destabilising and may change industry dynamics, raising new access issues.

Remedies

Experts agreed that solutions to these challenges needed to be carefully thought through. Government action would need to involve targeted policy initiatives that focus on remedying problems but involve minimal unintended effects. Policies should not broadly distort incentives to invest in innovation, for example. The difficulty of delivering such targeted action perhaps helps explain why the assembled experts found it difficult to agree on specific policies for facilitating access to genetic inventions. The question of how to react to the specific challenges raised by the licensing of genetic tests and the use of reach-through clauses remains. Participants stressed that policy measures should not discriminate against a particular technology or unduly jeopardise incentives to innovate.

In principle, policies to facilitate access might include a range of legislative, administrative or regulatory measures. Put slightly differently, policies can target the IP regime itself, the way patents are administered or change the behaviour of patent holders once they have obtained their rights. Opinions diverge on which route to adopt.

Scope of patents

Some participants questioned the appropriate breadth or scope of protection for genetic inventions. The more conservative critics suggest that problems of dependency and an overly broad scope of claims can be resolved within existing IP regimes, through reforms of the patent administration or simply through opposition procedures and the courts. Others feel that regulatory and even legislative action by government may eventually prove necessary.

The private sector, on the other hand, is generally content with present patent laws and regulations and would not advocate any lessening of the protection accorded genetic inventions. In particular, the private sector does not widely favour the application of a use restriction for patent claims to isolated or synthetic DNA and other forms of genetic material. Nor does it feel that there is a need for a

tightening of administrative conditions for granting patents on genetic inventions ("raising the bar").

Research exemptions

Similarly, uncertainty remains regarding the scope of research exemptions. In most countries, research exemptions are not well defined. Some believe it is necessary to extend research exemptions to include, for example, clinical use exemptions for diagnostic genetic testing with a research purpose. However, defining the parameters of this broader research exemption has proved very challenging. For this reason, some experts advocate maintaining the present level of uncertainty to avoid creating more confusion. Nevertheless, a study of research exemption use and litigation may prove useful in determining the extent to which the current system might need attention.

Regulatory solutions

Although the workshop concluded that there is no evidence of systematic failure of the licensing system, a few extreme examples of behaviour have elicited public interest and disapproval. A number of regulatory solutions were proposed as a way to mitigate such extreme behaviour.

Licence agreements and the terms and conditions entered into contractually by licensor and licensee are confidential to the parties, but licensing agreements can come under public scrutiny if they are anti-competitive.

It is also possible for countries with such provisions to issue or threaten to issue compulsory licences if there is a public health imperative. While this option is rarely used and difficult to implement because of technical problems regarding instigation, valuation and compensation, it is increasingly discussed in the economic and legal literature. It may be that the threat of compulsory licensing is enough to give governments influence over certain licensing terms for genetic inventions.

Workshop participants agreed that if regulatory action were to be considered, such as higher standards for the patentability criteria for genetic inventions, the expanded use of compulsory licences and an expansion of the exclusions permissible under TRIPs, these would need to be studied further to understand what their impact might be on research and commercial development.

Monitoring

Workshop participants concluded that continued monitoring of licensing practices and their economic and social impacts was important to ascertain that the system continues to function and functions across all countries. Currently, there is a conspicuous absence of rigorous economic studies that explore the impact of present patenting licensing practices on industry and public research. The literature on patenting DNA relies heavily on case studies and on theoretical legal arguments. OECD countries should address this lacuna.

Good licensing practice

Experts suggested that governments consider the development of good practice guidelines or codes of conduct. Good licensing practices are already being developed by public-sector research organisations for internal use (*e.g.* MTAs, policies on research tools and licensing clauses). Guidelines could also be developed in consultation with industry to determine the limits of acceptable licensing practices. Governments, many noted, should not underestimate the potential impact of such approaches.

Self-regulation

Workshop participants were interested in a number of "working solutions" and self-regulatory options for ensuring access to genetic inventions. Research organisations in both the private and public sectors are experimenting with contractual means of maintaining access. Novel solutions, such as patent pools, clearinghouses and collective licensing organisations, should be further explored to understand their potential utility and their real impact on the biopharmaceutical sector.

In summary, participants were wary of advocating legal changes to existing IP regimes. Administrative and regulatory approaches were deemed more acceptable (for example, changes to the patent examination procedure, the creation of codes of conduct or the expanded use of compulsory licences) because they can be better targeted to meet an identified licensing dysfunction. The private sector advocated self-regulation to increase access to genetic inventions when and where necessary. Workshop experts were interested in how such private-sector initiatives might help maintain access. However, all recognised that some government leadership may be necessary to catalyse such initiatives.

Areas for future work

The workshop contributed to the debate on genetic inventions by providing a platform for researchers, industry and governments to discuss both the access problems they have encountered and to begin to debate possible remedies. The high level of scientific, legal, and economic expertise helped focus policy discussions on challenges that need be addressed to ensure that patents on genetic inventions do not unduly impede scientific and technological progress.

Much work is needed to elucidate further the economic impact of the present system of protection, to understand the advantages and disadvantages of various policy solutions and to rebuild public trust. More work at international level might be done in the following areas:

- Data on biotechnology patenting and licensing practices remains sparse but would be an invaluable resource for policy makers. Further monitoring of licensing practices in particular would help to understand, for example, how research delays and transactions costs affect biomedical research. The OECD will conduct a targeted study of the impact of patents and licensing practices for genetic inventions on the availability of genetic testing services in 2002-03.
- A guide for policy makers could be developed on indicators that could be used when performing economic impact studies of patenting and licensing practices for biotechnology inventions.
- Good practice licensing guidelines might be developed, in the first instance, for and by public research organisations involved in biomedical research. Such guidelines could be developed in consultation with industry.
- A comparative review could be undertaken of possible policy measures being developed to enhance legitimate access to information and technologies. What are their advantages, disadvantages, and side effects? How likely are they to be used or effective?
- Rigorous economic studies might be undertaken to explore the actual impact of present patenting licensing practices on industry and public research.
- A study of research exemption use and litigation might help to determine the extent to which the current system might need attention.

NOTES

1. Leroy Walters, DNA Patent Database, Georgetown University and Foundation for Genetic Medicine, cited on the World Survey of Genomics Research Web site: www.stanford.edu/class/siw198q/websites/genomics/.

2. This point was made by Fredrik von Arnold.

3. A point made by Dr. Kaoru Inoue of the Japan Bioindustry Association. See www.jpo.go.jp/infoe/dnas.htm

4. For examples of trilateral co-operation in biotechnology, see their reports: "Trilateral Project B3b Mutual Understanding in Search and Examination: Report on Comparative Study on Biotechnology Patent Practices – Reach Through Claims" and "Trilateral Project B3b Mutual Understanding in Search and Examination: Report on Comparative Study on Biotechnology Patent Practices – Patentability of DNA Fragments". Available at: www.jpo.go.jp/saikine/tws/sr-3-b3b.htm. The Trilateral Commission is presently establishing guidelines for the patentability of protein structure patents.

5. For a good review of some of the objections to gene patents and their validity, see D. Resnick (2001).

6. Gold (2002) makes the argument that DNA sequences have a dual character as patentable molecules and as unpatentable information *per se*.

7. The question of transaction costs due to diffusely held title to inventions is not unique to pharmaceuticals or biotechnology. A similar situation exists in the semiconductor industry, for example.

8. See *Signals Magazine* (1998, 2000). Royalty exposure to net sales means the percentage of net sales on a product that must be paid in royalties to the licensors of technologies used in the development of an end product.

9. According to one source, 436 clinical genetic tests were available as of 2001, and hundreds are in development. Some of the most common tests include those for cystic fibrosis, hereditary haemochromatosis, Huntington's disease, Duchenne muscular dystrophy, Tay-Sachs disease, BRCA1 and BRCA2 hereditary breast cancer.
For a complete list of gene tests, see: www.genetests.org.

10. This option may not appeal to public-sector research bodies and individual researchers for whom open disclosure of research findings through scientific publications is a cardinal principle of scientific progress.

11. All the signatories to the World Trade Organisation must put in place patent systems which offer a minimum patent term of 20 years from date of filing as part of the TRIPs Agreement.

12. According to the Erosion Technology and Concentration (ETC) Group (ETC, 2001), 46% of all biotechnology patents challenged in US courts are overturned. Surprising as this figure may seem, it is roughly equivalent to the total number of patents in all fields invalidated by the courts. In court decisions covering all fields of technology, patents are held valid by lower courts only 54% of the time and by the Federal Circuit 52% of the time (Lemley and Allison, 2000).

13. This list was compiled by Ulrich Schatz of the EPO.

14. According to White (2000/2001), "a claim to a chemical compound *per se* is infringed by any act of making, supplying or using that compound… even when that use is wholly different in character from any use described in the specification".

15. This suggestion comes from Professor Claude Henry of the Econometrics Laboratory, École polytechnique. For another view on the importance of regulation in patent reform, see Judge Paul Michel's Keynote Address, "Patent System Reform", given at UC Berkeley's Boalt Law School Conference on Patent System Reform, University of California at Berkeley, 1-2 March 2002.

16. According to Leroy Walters, DNA Patent Database, Georgetown University and Foundation for Genetic Medicine, as cited on the World Survey of Genomics Research Web site: www.stanford.edu/class/siw198q/websites/genomics/.

17. USPTO, Patent Full Text and Image Database. Available at: www.uspto.gov

18. Thanks are due to Dr. Kaoru Inoue of JBA for his help with this search. The search was of the Industrial Property Digital Library at the JPO Web site (www.jpo.go.jp). The search fields were limited to IPC code C12N15/00-15/90.

19. Relevant parts of the directive are Articles 3(a), 5(2), 5(3), and Recital 23.

20. For examples of such movements, see the Nuffield Council on Bioethics Report (2002), the Ontario Report to Premiers (2002), and Rivers (2002).

21. A point made by Richard Gold of McGill University.

22. For one publication resulting from this last project see Orsenigo *et al*. (2000).

23. For a discussion of the potential use of research exemptions in biomedecine see Mueller (2001).

24. The literature does not identify the level of royalty exposure that would make a product's commercialisation unviable. Pharmaceutical companies appear to try to keep royalties on net sales of a given product below 20-25%. (Signals Magazine, 1998).

25. The Intellectual and Technical Property Components of pro-Vitamin A Rice (GoldenRice TM), International Service for the Acquisition of Agri-Biotech Applications, ISAAA Brief No. 20-2000.

26. For a list of the studies of the Trilateral Commission, see: www.jpo.go.jp/saikine/tws/sr-3.htm

27. For a discussion of how patent pools function see Merges (1998).

28. The companies are: AstraZeneca PLC, Aventis, Bayer AG, Bristol-Myers Squibb Company, F. Hoffmann-LaRoche, Glaxo Wellcome PLC, Novartis, Pfizer Inc., Searle, SmithKline Beecham PLC, Motorola Inc., IBM.

29. The Canadian Biotechnology Advisory Council has recommended an exemption for private or non-commercial study or research on the subject matter of the patent invention. In the United States, two recent bills (2002) have been introduced by Congresswoman Lynn Rivers, the "Genomic Science and Technology Innovation Act of 2002" and the "Genomic Research and Diagnostic Accessibility Act of 2002" which propose research and clinical use exemptions to patents.

Annex 1

GLOSSARY

Art or prior art. A term used in consideration of the problem of patentable novelty encompassing all that is known prior to the filing date of the application in the particular field of the invention, represented by already issued patents and publications. (University of Pennsylvania)

Art, state of the. In the language of patent law this expression is used in a somewhat different sense to that which it has in science and technology. In the European Patent Convention (EPC) the state of the art is defined as: "everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the European patent application". This definition signifies all that is part of public knowledge and experience before the attempt is made to protect an invention. Thus it is another form of reference to the prior art, *i.e.* that which is old and therefore cannot be patented. For the assessment of novelty (though not for inventive step), EPC law also includes within the state of the art the contents of prior filed European patent applications which proceed to publication; these are deemed part of the state of the art from their filing date. (Crespi)

Case law. Many principles of patent law are stated explicitly in written statutes. Others are derived from decisions of courts of law in particular cases and these are referred to collectively as case law. Case law is binding, or at least influential, on subsequent decisions of courts at the same or lower level. From time to time, established case law becomes codified into written statutes when new or amending legislation occurs. As regards biotechnology a considerable body of precedent now exists in the form of case law. (Crespi)

cDNA. Strong, cloned copies of otherwise fragile mRNA – the essential messenger element of the genes in the DNA which help in the coding of proteins. (University of Pennsylvania)

DNA. Deoxyribonucleic acid; the molecule that controls inheritance. (University of Pennsylvania)

European Patent Convention (EPC). This Convention, signed in October 1973, established the European Patent Organisation as a legal entity comprising the European Patent Office and an Administrative Council as its two organs. The Convention came into force in June 1978. It provides for a single patent application to be prosecuted before the European Patent Office (EPO) designating any number of contracting states (up to 24 states). The initial application may be made in any of the regional offices of the EPO (national patent offices) but is in due course examined by the EPO in Munich. Upon grant the European patent does not mature into a single item of property but enters the national phase in each designated state and emerges as a "bundle" of national patents, *e.g.* European patent (United Kingdom), European patent (France), etc., which thereafter become independent objects of property. Under the Community Patent Convention (not yet in operation) a single application filed through the European Patent Office will mature into a single unitary indivisible object of property covering the whole of the European Economic Community. (Crespi)

EPO. European Patent Office.

EST. An expressed sequence tag (EST) is a small part of the active part of a gene which can be used to fish the rest of the gene out of the chromosome. ESTs are isolated from mixed mRNAs and converted back to cDNAs. Because each EST is related to an mRNA it must represent the part of a gene which encodes a protein. Using known techniques, the location of the EST on the genome can be determined. The production of a particular protein associated with a condition may be investigated through an EST. While the EST itself is not "functional" (it does not code for a protein), many researchers are attempting to obtain patents on them. Opponents of gene patenting argue that since the functions of ESTs are not known, they fail the requirements for patentable material. (University of Pennsylvania)

Gene. A sequence of nucleotides coding for a protein (or part of a protein). (University of Pennsylvania)

Gene fragments. Gene fragments are pieces of genes containing only the exons (those parts of the gene which actually encode the protein sequence). They are composed of cDNA. (University of Pennsylvania)

Gene pool. All the genes in a population at a particular time. (University of Pennsylvania)

Genome. The full set of DNA in a cell or organism. (University of Pennsylvania)

Grace period. The all-embracing definition of the state of the art in the Strasbourg and European Patent Conventions has been adopted in national patent laws in European countries as part of the policy of harmonisation with European law. As a result this eliminated from some national laws previous provisions exempting any publication emanating from the applicant. These publications were not prejudicial to the applicant's position provided a patent application was filed within a specific period and this came to be known as a "grace period". At present the United States and Canada both have a grace period of one year. (Crespi)

JPO. Japanese Patent Office.

Licence. A licence is a contract between the owner(s) of the subject matter of the licence and one or more parties that seek the right to make, use, sell or import the subject mater of the licence. Commonly, a licence conveys rights to patented subject matter, but it may also convey rights to tangible subject matter that is not patented. Licences are negotiated agreements that become binding contracts when signed by the parties. Although licences generally address a standard set of legal issues, there is no standard licence or licence term. The terms negotiated into licences by the parties are as varied as the circumstances driving the agreement. (NIH)

Standard issues addressed by negotiated licence terms include: the general use that may be made of the subject matter (research use, commercialisation); whether only one party obtains rights (exclusive), more than one but still only a few (co-exclusive), or potentially many (non-exclusive); the specific type of applications which may be pursued by the party (field of use to develop vaccines, diagnostic products, therapeutic products, human uses, veterinarian uses); royalty rates, or how much the user will pay the owner for the rights conveyed by the licence (fee upon signing, annual fee, percentage of net sales, reimbursement of patent costs, costs of enforcing and defending the patent).

MTA. A material transfer agreement (MTA) is a negotiated contract between the owner of a tangible material and a party seeking the material and the right to use the material for research purposes. The material may be either patented or unpatented. Material transfer agreements tend to be shorter than licence agreements, and they are generally considered to be more informal than licence agreements, although both are enforceable contracts. The purpose of an MTA is to document the transfer and outline the terms of use, including identification of the research project, terms of confidentiality, publication and liability. As for licences,

there are no standard MTAs, although the academic community and NIH developed a model MTA for biological materials called the Uniform Biological Material Transfer Agreement (UBMTA). (NIH)

Non-obvious. In order for a patent to be granted, the claimed invention must be "non-obvious" to one of "ordinary skill in the art". For example, if one obtains a new and unexpected result, the invention is said to be non-obvious. (University of Pennsylvania)

Novelty. A requirement for patentability. If an invention has been used or was known to others it is probably no longer novel and therefore not eligible for patent protection. (University of Pennsylvania)

Nucleotide. The building block of DNA. There are four basic building blocks, which are arranged in units of three called codons. (University of Pennsylvania)

Oligonucleotides. A short polymer of, for example, 20 or so deoxyribonucleotides or ribonucleotides; thus a fragment of DNA or RNA. (University of Pennsylvania)

Patent. A patent is a grant issued in the name of a country. In the United States, for example, a patent under the seal of the Patent and Trademark Office "confers the right to an applicant to exclude others from making, using, or selling an invention in the United States" and its territories for 20 years from the application filing date. (University of Pennsylvania)

Patents are granted according to the laws of individual states and have effect only within the jurisdiction of the relevant state. In the field of patent law, however, there is a strong tradition of over a century of international co-operation by means of international conventions which regulate formal and substantive patent matters between member states. (Crespi)

Patent application. A formal application to a patent-granting authority (industrial property office, patent office) which involves the filing of formal documents prescribed by the appropriate law or official regulations, including an "application form" or "request for grant" and a specification describing the invention. The terms "application" and "specification" are sometimes used synonymously. (Crespi)

Patent claims. The claims of an application or patent are verbal formulae defining the invention or the scope of protection sought or obtained. These are appended to the technical description and together therewith form the specification as a whole.

Claims are expressed in terms of apparatus, device, process, product, method or use, as appropriate.

There are two main types of claims: the product *per se* claim and the product-by-process claim. A *per se* claim is one that extends to the product (*e.g.* substance or micro-organism) as such and is independent of any defined process of preparation or derivation. This is also referred to as absolute product protection. A product-by-process claim, on the other hand, defines the product in terms of some particular method of production. Hence, it is more limited in scope than the *per se* claim and may perhaps be avoided by the choice of a method or route to the procurement of the product different from that defined in the claims. A form of product claim is sometimes met which uses process terminology to indicate how the product may be obtained but does not restrict the claim to the use of such a process; although apparently in product-by-process form, such a claim is in reality a product *per se* claim. (Crespi)

Patent procedure. It is normal practice for an applicant to make a patent application first in his country of residence and to file corresponding applications abroad at a later date. In view of the priority provisions of the Paris Convention the filing of patent applications for corresponding foreign protection may be delayed up to but no more than one year after the first (home) filing if the so-called Convention priority of the latter is to be claimed. Foreign applications may be filed separately in each country under the respective national laws. For those states that are parties to the European Patent Convention, protection may be sought either as separate national applications or in the form of a European application which also may claim Convention priority from the first application. Another option is to file a so-called international application under the provisions of the Patent Co-operation Treaty (this embraces many European and non-European states). An international application also may be filed within one year from the first application and claim its priority date under the Paris Convention. An international application proceeds as a single application for certain preliminary investigations (formalities, novelty search, etc.) but must then move to the national phase in the designated states for substantive examination on its merits. Thus, an international application ultimately results in separate national patents. (Crespi)

Patent specification. The written description of an invention which must be filed when an application for a patent is made. This must include a technical description which can be appreciated by a person of ordinary skill in the art and a statement (one or more “claims”) of the scope of protection sought. The term “patent” is

often used to denote the specification but this usage is only strictly correct after the grant of patent rights. (Crespi)

Patent Co-operation Treaty. This treaty (PCT) was established in 1970 and came into force in June 1978 along with the European Patent Convention. The PCT is of the broadest international scope and is open to adoption and use on a world scale (at present, 115 member states). It is administered by the Geneva-based World Intellectual Property Organisation (WIPO). Patent applications filed under PCT are described as "international" because they are initially processed by an international body (WIPO) before being formally introduced into designated national systems. The international phase is mainly concerned with formal preliminaries, a prior art search and publication of the application. (Crespi)

Patent thickets. The term "patent thicket" has been coined to characterise a technological field where multiple patent rights are owned by multiple actors. The numerous rights that may need to be brought together for work in this field might possibly impede research and development because of the difficulty or cost of assembling the necessary rights.

Protein. A molecule made up of a sequence of amino acids. Proteins are the most common organic molecule found in living organisms. (University of Pennsylvania)

Reach-through claims or rights. Reach-through claims are claims made in a patent or licence to the "ownership" of future inventions based on currently disclosed inventions. These include claims made to candidate compounds that might be identified using basic screening methods and to downstream uses of such candidate compounds. These are rights to potential future inventions made by the user of the patented or licensed research tool. For example, providers of research tools may seek royalties on future product sales, options to acquire exclusive or non-exclusive licences under future patents, or even outright ownership of future inventions as a condition for making the tools available.

Reach-through provisions are common in MTAs which do not usually require financial payments at the time of the transfer. Many MTAs allow the provider to either own, or license exclusively, or obtain payments upon the sale of, developments that the recipient makes with the provider's materials. These are loosely called "reach-through" provisions, and are considered by many providers to be desirable because they allow the provider to obtain rights to subject matter that the provider would not otherwise have rights to through ownership or patent coverage of the material alone. Reach-through provisions are considered

undesirable by many recipients because they burden all the developments created after the use of the material, and because they are seen as providing an unfairly high level of compensation to the provider for use of the material. (NIH)

Research tools. Research tools in their broadest sense embrace the full range of resources that scientists use in the laboratory including cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry libraries, drugs and drug targets, clones and cloning tools, methods, laboratory equipment and machines, databases and computer software. (NIH)

Royalty stacking. In commercialising a product, an entity may find it necessary to take licences under numerous patents. Each of these licences commits the licensee to pay a series of royalty payments to the respective patent holders often amounting to a significant share of the sales of the final product. The accumulation of royalties to be paid for intermediary technologies is termed "royalty stacking".

SNPs. Single nucleotide polymorphisms. SNPs are sites in the genome in which there is variation among the population of one base in the sequence. Many SNPs are in the regulatory regions, in promoters, rather than in coding regions of the genome. If a certain population with a certain condition is found to have the same SNP this may be significant.

USPTO. United States Patent and Trademark Office.

Vector. An agent, often a virus or plasmid, used to carry foreign DNA into a cell. (University of Pennsylvania)

Definition sources:

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Annex 2

AGENDA

GENETIC INVENTIONS, INTELLECTUAL PROPERTY RIGHTS AND LICENSING PRACTICES

Berlin, Germany
24-25 January 2002

THURSDAY, 24 JANUARY 2002

REGISTRATION

WELCOME ADDRESS

Edelgard Bulmahn, Minister, Federal Ministry of Education and Research, Germany

WORKSHOP GOALS

OECD Opening: John Dryden, Deputy Director, Directorate for Science, Technology and Industry, OECD

Workshop Chairman: Joseph Straus, Director, Max Planck Institute for Foreign and International Patent, Copyright and Competition Law, Germany

SESSION 1: THE IPR SYSTEM AND ITS RELEVANCE TO GENETIC INVENTIONS

Chair: Christina Sampogna, Industry Canada, Canada

Ulrich Schatz, Principal Director, EPO, Germany

Alain Gallochat, Ministry of Research, France

SESSION 2: SURVEYS OF PATENTING AND LICENSING PRACTICES FOR GENETIC INVENTIONS

Chair: Mildred Cho, Stanford University, United States

Joseph Straus, Director, Max Planck Institute, Germany

John Walsh, Professor, University of Illinois at Chicago, United States

Fabio Pammolli, Professor, University of Florence, Italy

SESSION 3: THE IMPACTS OF PATENTING AND LICENSING PRACTICES ON RESEARCH

Chair: Waldemar Kütt, European Commission, Belgium

PRO Strategies for Exploitation and Access: Research Tools, Nature-identical Materials, MTAs, Research Exemptions, Grace Periods

Maria Freire, CEO, The Global Alliance for Drug Development, Belgium, United States, and South Africa

Christian Stein, Director, Ascencion GmbH, Germany

Fabirama Niang, Directeur des Relations Industrielles, Université Louis Pasteur and President, Réseau Curie, France

SESSION 4: THE IMPACTS OF PATENTING AND LICENSING PRACTICES ON NEW PRODUCT DEVELOPMENT

Chair: Richard Johnson, Arnold & Porter, United States

How Real Are Patent Thickets, Reach-through Rights, Royalty Stacking, Dependency, and Freedom-to-Operate Restrictions?

Philip Grubb, Intellectual Property Council, Novartis International AG, Switzerland

Jacques Warcoin, Cabinet Regimbeau, France

Erik Tambuyzer, Genzyme Corporation, Belgium

Novel Approaches to IP Management: Consortia, Patent Pools, Collective Rights Organisations

Lawrence Horn, Vice President MPEG LA, LLC, United States

Richard Johnson, Arnold & Porter, United States

FRIDAY, 25 JANUARY 2002

SESSION 5: IMPACTS ON HUMAN HEALTH AND TECHNOLOGY UPTAKE

Chair: Iain Gillespie, OECD

Impacts of Patents on Provision of Clinical Genetic Testing Services

Mildred Cho, Stanford University, United States

Jeffrey Kushan, Powell, Goldstein, Frazer and Murphy, LLP, United States

Possible Policy Responses: Negotiation, Licences and Opposition

Richard Gold, McGill University, Canada

Bioethics, IPR and Human Health

Ludger Honnefelder, University of Bonn, Germany

SESSION 6: POLICY ISSUES AND SUMMARY

Chair: Joseph Straus, Max Planck Institute, Germany

Rapporteur, Review of Key Policy Questions

Stephen Crespi, United Kingdom

Roundtable Reactions and Policy Recommendations

Selection of speakers and chairs from public research, industry, ethics, health care, and the legal system:

Wes Cohen, Carnegie Mellon University, United States

Maria Freire, The Global Alliance for Drug Development, Belgium, United States, and South Africa

Philip Grubb, Novartis International AG, Switzerland

Christian Stein, Director, Ascencion GmbH, Germany

Bénédicte Callan, OECD

Summary of Lessons Learned

Joseph Straus, Director, Max Planck Institute, Germany

STEERING GROUP AND SPEAKERS:
DISCUSSION OF POSSIBLE FUTURE RESEARCH AND ACTIVITIES

Annex 3

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