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EUROPEAN COMMISSION

Patenting DNA sequences (polynucleotides) and scope of protection in the European Union: an evaluation

Background study for the European Commission within the framework of the Expert Group on Biotechnological Inventions

Sven J. R. Bostyn

Directorate-General for Research
2004 Food Quality and Safety EUR 21122

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Foreword

Life sciences and biotechnology are fundamental to our ability to meet societal, environmental and economic challenges, be it the health care needs of a rich but ageing population in Europe, food security and improved health care for the ever growing populations of the developing world, or the need to transform our economies and lifestyles towards more sustainable patterns. The new knowledge offers many opportunities, and competitive challenge obliges us always to seek to use our knowledge and techniques in ever more efficient and effective ways.

In order to derive maximum benefit from recent and continuing progress in the life sciences and biotechnology, Europe needs to invest more in the skill- and knowledge base, make more risk capital available and provide a coherent regulatory framework for the deployment of new innovations. In this respect, a strong, harmonised and affordable intellectual property protection system is of utmost importance.

The European Parliament and Council directive 98/44/EC of 6th July 1998 on the legal protection of biotechnological inventions came into place almost a decade after its first draft had been proposed by the Commission. This piece of legislation was crucial in order to foster the innovation and provide European companies with adequate protection in their domestic market. However, despite a deadline of July 2000, a large number of Member States still have not transposed the directive into national legislation or are proposing new legislation that may even be in conflict with the directive itself. All this is adding legal uncertainty and may hamper the full potentials of biotechnologies to be exploited for the benefit of patients and the competitiveness of our industry.

Article 16c of directive 98/44 requires the Commission to monitor “the impact of patent law on biotechnology and genetic engineering” and provide annual reports (“16c reports”). In order to support the Commission in this process and to provide advice on critical issues that have been associated with directive 98/44 our services have jointly set up an expert group bringing together research, industry, patent experts and representatives of International Organisations such as the European Patent Office.

The first issue discussed by the expert group was related to the scope of protection to be given to patents related to sequences or partial sequences of genes isolated from the human body. The current publication provides the background report delivered by Prof. Sven Bostyn and a summary of a discussion of the expert groups meeting of March 27 2003 on this subject. We would like to thank the expert group for their contribution and in particular Professor Bostyn for his excellent background paper. We fully acknowledge that this work has been prepared without any Commission support.

We hope that the background report and the conclusions of the expert group will help in shaping the European patent system in a way that it supports innovation to the benefit of economy and the society at large.

Philippe Busquin	Frits Bolkestein
Research Commissioner	Internal Market Commissioner

Commission expert group on biotechnological inventions

Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions requires the Commission through its §16c to publish annually a report on the development and implications of patent law on biotechnology and genetic engineering (the "16c report"). The first such report - COM(2002) 545 - was issued by the Commission in October 2002.

Following this first report, the Commissions Directorate Generals' Internal Market and Research have set up a group of experts in December 2002 to advise and assist it in preparing future annual reports. The group's mandate is to analyse important issues surrounding biotechnological inventions. It aims not to touch upon ethical issues, which are the mandate of the European Group on Ethics, but instead focus more on legal and technical aspects and on the mutual impact of the legal framework and the research and innovation area.

The group brings together renowned experts including representatives from the patent profession, patent practitioners (from the private sector, big business and a small biotech company), three legal experts, two scientists and representatives from the European Patent Office and the World Intellectual Property organisation (WIPO). The mixed composition of the group ensures that all relevant aspects are dealt with, taking into account the various related policy areas and the interests of different stakeholders. A list of the expert group members can be found in the annex.

In its 2003 working period, the group has focused on two particularly sensitive fields:

- the scope to be given to patents related to sequences or partial sequences of genes isolated from the human body;
- the potential patenting of Human Stem Cells and cells lines obtained from them.

The current publication consists of an extensive background paper on the first topic prepared by Professor Sven Bostyn, then Maastricht University, for the groups meeting on March 27th 2003. A background report by Ms Geertrui van Overwalle of the University of Leuven in Belgium on "the patentability of human stem cells and cell lines derived from them", which was prepared for the groups meeting on May 27th, will be the subject of a forthcoming publication.

Members of the expert group - 2003

Chairman:

- *Mr Vincenzo Scordamaglia* (Honorary Director-General of the EU Council - Consultant in IPRs IT)

Reporters:

- *Ms Geertrui Van Overwalle*, (Centre for Intellectual Property rights Faculty of Law Leuven BE)
- *Mr Sven Bostyn*, then Assistant Professor of Commercial and Intellectual Property Law (Maastricht University NL), now Legal Counsel, De Clercq, Brants & Partners Patent Attorneys (Belgium), Associate Professor of Intellectual Property Law (Institute for Information Law, Faculty of Law, University of Amsterdam NL)

Members:

- *Ms Anne McLaren* (Wellcome CRC Institute University of Cambridge UK),
- *Ms Siobhan Yeats* (Director Biotechnology Directorate European Patent Office),
- *Mr Jacques Warcoin* (Patent agent Cabinet Regimbeau FR),
- *Mr Daniel Alexander* (Barrister, London, UK),
- *Mr. Bo Hammer Jensen* (Director, Senior Patent Counsel Novozymes A/S DK),
- *Mr Francisco Bernardo Noriega* (Deputy Director, Intellectual Property, PharmaMar S.A. - ES)
- *Mr Joseph Straus* (Professor of law and Managing Director, Max Planck-Institute for Intellectual Property, Competition and Tax Law, Munich DE),
- *Mr Francis Quétier* (Genoscope- Evry, FR),
- *Mr Ingwar Koch* (Director, Patent Law Directorate - European Patent Office),
- *Mr Kjeldgaard* (Senior Counsellor Biotechnology and Genetic Resources, Traditional Knowledge Division World Intellectual Property Organisation).

Secretariat:

Jean-Luc Gal and *Giuseppe Bertoli* DG MARKT, Unit E2 and *Waldemar Kütt,* DG RTD, Unit E1:

Links to the full text of Directive EC 98/44 on the legal protection of biotechnological inventions and of the Commission's 2002 and 2003 reports, including conclusions and recommendations from the expert group on above mentioned issues can be found at:
http://www.europa.eu.int/comm/internal_market/en/indprop/invent/index.htm

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Chapter 1. Introduction*

Biotechnology does not suffer from a lack of interest from the general public nowadays. This has been different in the past. It may not be forgotten that biotechnology in the broad sense, i.e., technology based on the use of biological material, is far from new. It has been successfully applied for years in the agricultural (e.g., plant breeding) and medical area (e.g., antibiotics). What has made the public becoming more interested in and especially more concerned about this technology? This is undoubtedly linked to the rapid evolution in the level of sophistication of the technology, and the fact that research extends to human genetic information, our own blueprint. In general, such a raised awareness is positive. It shows that people are interested and concerned about the level of knowledge of and interference with the human genetic blueprint one is prepared to undergo. But at the same time, it is necessary to emphasize that such an evolution also has its drawbacks. The fact that the public has become more interested, and thus also more susceptible to receive such information, has also made the public more susceptible to so-called 'Frankenstein information'. Some have focused on the potential negative consequences of an increasing interference with human genetic information. Such a critical approach must always be welcomed. But it must also be made clear that there are very few technologies which have had the same fate of being so thoroughly scrutinised and criticised. It can be readily admitted, however, that the consequences for human beings of the use of this technology are far more intruding than any other technology can ever be, both in terms of short and long term effects. Gene technology applied in the medical field has a number of established advantages for society at large. It is indispensable in our search for cures for hereditary and often lethal diseases. It becomes also increasingly important for non-hereditary lethal diseases.

The aim of this background study is to give an overview of the various issues involved in the patentability of DNA sequences (polynucleotides) and the scope of protection of such patents. It does not deal with ethical issues, which were excluded from treatment in this study, as they require a different approach, which was outside the scope of the mission of the author and the Expert Group on Biotechnological Inventions. This study is more a discussion paper than a report containing fixed rules and viewpoints. It has been the basis for discussion in an Expert Group on Biotechnological Inventions and the 16(c) Report which the

* The opinions expressed in this report are those of the author, and do not necessarily represent the views of his firm or its clients. You can contact the author at bostyn@jur.uva.nl.

Commission is committed to produce yearly evaluating the functioning of Dir. 98/44/EC and its contents in the Member States.[1] The Commission must transmit each year to the European Parliament and the Council a report on the development and implications of patent law in the field of biotechnology and genetic engineering.[2] The present study contains a number of arguments which could and have been used in favour or against the patentability of DNA sequence inventions or relating to the scope and manner of protection of such inventions. They do not necessarily reflect the personal opinion of the author, but it was felt necessary to mention them, in order to provide a forum of discussion concerning the various issues discussed in this paper. It is in some cases left to the reader to draw final conclusions, even though this study does contain some viewpoints which are the consequence of careful evaluation of the pros and cons made by the author.

Indeed, EC directive 98/44/EC of the European Parliament and of the Council of July 6 1998 on the legal protection of biotechnological inventions is the central focus of this study. As is probably known by most readers, this directive has faced a birth in turmoil. And even today, it remains a rather controversial piece of legislation. This is evidenced by the fact that the majority of the member states has to date not implemented the directive yet, even though this should have been done by July 30, 2000 at the latest.[3] The European Commission has, after various warnings, decided to take action, and starts proceedings against those countries that have not transposed the directive yet before the European Court of Justice for non-implementation of the directive.[4] In some of these countries, bills have already been introduced in Parliament, but are still awaiting final discussions and votes. And the controversy goes even further. Some of these bills contain provisions which are an incorrect transposition of the directive. The legislative process as it

1 This is an obligation which is laid down in Art. 16(c) of EC directive 98/44/EC of the European Parliament and of the Council of July 6 1998 on the legal protection of biotechnological inventions, OJ L 213/13, 30 July 1998.

2 The last report on the basis of which this report has been drafted and this Expert Group has been composed is, Report from the Commission to the European Parliament and the Council. Development and implications of patent law in the field of biotechnology and genetic engineering, Brussels, 7 October 2002, COM(2002) 545 final.

3 The current situation (October 2004) is the following: Czech Republic, Denmark, Spain, France, Finland, United Kingdom, Greece, Hungary, Ireland, Malta, Portugal, Poland, Sweden and Slovakia have implemented the directive. Austria, Belgium, Cyprus, Germany, Estonia, Italy, Luxemburg, Lithuania, Latvia, the Netherlands and Slovenia have not yet implemented the directive. France, Belgium and Luxemburg have already been convicted by the European Court of Justice.

4 See IP/03/991.

takes place in some member states is the scene for attempts to introduce more fundamental changes in the patent system, which were not or arguably the subject of the directive, such as purpose-bound patent protection, exclusion of product protection for DNA sequences altogether, a new consent requirement for inventions based on biological material taken from the human body etc. Some of these more fundamental changes, the compatibility of which with the directive can be doubted, will be discussed in this study.

The approach followed by the author in this study aims at encouraging an information-based debate concerning the patentability of DNA sequences. Such an information-based debate will demonstrate, on the basis of this study, that things are much more complicated than some might believe on the basis of the traces of information which have seen daylight in the broader media. It will, amongst others, show that the patent system as we know it today in Europe, is a highly sophisticated piece of legislation and a system with a considerable number of checks and balances, which are for the large part capable of tackling a number of objections which might be raised against some features of patenting DNA. The European Patent Office examines patent applications, taking into account these checks and balances laid down in the patent system. A high standard of review should be capable of ensuring that a fair and just conclusion is drawn after examination of the patent application. The extensive review procedures which are available in the European Patent Office (opposition, appeal) also provide a safety net in order to ensure that the decisions taken by the patent office are the result of a correct application of the patent system these same offices are to work with. Perfection is not a worldly virtue, however, and consequently there will always be less fortunate decisions made by patent offices. But it would do injustice to the patent system as a whole to magnify these exceptions and make them the standard case.

This study is drawn up of various parts. To start with, the importance of biotechnology research is re-emphasised. Subsequently, a number of basic features of the patent system are highlighted, in order to place it in perspective, and to provide the reader with an overview of the basic checks and balances present in the system. The economic rationale of the patent system will then be reviewed, in order to give some society perspective to the existence of the system. We will then continue with a discussion of the various issues which are at the core of this study, i.e., the patentability of DNA sequences, and scope of protection. It must be said here from the outset that DNA is considered to be a chemical substance, and consequently, the basic patent law principles applicable to chemical inventions will equally be applicable to DNA inventions. This shows again that one should in

patent law not solely emphasise on the exceptional nature of DNA, but on its existence within the current patent system. Finally, some conclusions and recommendations will be drawn and made.

Chapter 2. Importance of Biotechnology Research

Research in biotechnology can hardly be overestimated in our present-day life. Both in the public and private sector, considerable investments are made in this type of research. It is easy to understand why. Biotechnology is, and will become even more in the future, the 'life and blood' of medical research. Biotechnology is the only solution for most hereditary genetic diseases, and it becomes even crucial for the treatment of bacterial infections. It is thus a most promising area of scientific research, and of the utmost importance for the future of health care, and therefore it deserves our support in the struggle against debilitating and lethal diseases, for which we all desire to find a cure.

Life sciences and biotechnology are widely regarded as one of the most promising frontier technologies for the coming decades. Life sciences and biotechnology are enabling technologies - like information technology, they may be applied for a wide range of purposes for private and public benefits. On the basis of scientific breakthroughs in recent years, the explosion in the knowledge on living systems is set to deliver a continuous stream of new applications. There is a huge need in global health care for novel and innovative approaches to meet the needs of ageing populations and poor countries. There are still no known cures for half of the world's diseases, and even existing cures such as antibiotics are becoming less effective due to resistance to treatments. Biotechnology already enables cheaper, safer and more ethical production of a growing number of traditional as well as new drugs and medical services (e.g. human growth hormone without risk of Creutzfeldt-Jacobs Disease, treatment for haemophiliacs with unlimited sources of coagulation factors free from AIDS and hepatitis *C* virus, human insulin, and vaccines against hepatitis *B* and rabies). Biotechnology is behind the paradigm shift in disease management towards both personalised and preventive medicine based on genetic predisposition, targeted screening, diagnosis, and innovative drug treatments. Pharmacogenomics, which applies information about the human genome to drug design, discovery and development, will further support this radical change. Stem cell research and xenotransplantation offer the prospect of replacement tissues and organs to treat degenerative diseases and injury resulting from stroke, Alzheimer's and Parkinson's diseases, burns and spinal-cord injuries.[5] Another promising example is that human genome analysis into so-called

[5] Communication from the Commission to the Council, the European Parliament, the Economic and Social Committee and the Committee of the Regions. Life sciences and biotechnology – A Strategy for Europe, Brussels, 23 January 2002 COM(2002) 27

"gluten allergy" may ultimately lead to the development of allergen-reduced cereals. A first fully integrated Community project has recently been launched to ensure leadership at the genomes medicine interface where biotechnology is yielding innovative approaches to treatments of human and animal diseases.[6]

For those reasons, biotechnology is also a fast growing sector of science and industry. If we take a look at the figures for industrial products, we can see that in recent years, the worldwide biotechnology-based products market has grown at an annual average rate of 15% to reach a value of about € 30 bn in 2000. Biopharmaceuticals dominate this market (€ 20 bn), with agriculture related products making-up the balance. Biopharmaceuticals account for less than 5% of the total pharmaceuticals market but are growing at 2.5 times its overall growth rate. There is little doubt that biotechnology presents a significant potential for growth and creation of wealth. Eventually, a substantial part of Europe's GDP could be generated by and spent on biotechnology products.[7]

Important to establish is also that biotechnology is one of the most R&D-intensive areas. This is particularly true for R&D in biopharmaceuticals. This high level of R&D brings with it that huge amounts are invested in the development of new products and processes, for which the investor wishes to obtain some return. The patent system is capable of providing at least a forecast of return of investment to the investor/inventor. The patent system thus serves here a double purpose. On the one hand it stimulates innovation and R&D by providing return on investment possibilities for those who take the risk to invest in new products and processes. On the other hand, due to the incentive to pursue R&D, social welfare is created for society, which can benefit from those new products, for example to treat lethal diseases which remained untreated in the past.

The level of R&D investments can be illustrated with the pharmaceutical R&D investment figures. In view of the fact that biotechnology is even more capital

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final, at 5-6. An action plan based on this report has also already been published, Communication from the Commission. Investing in research: an action plan for Europe, Brussels, 30 April 2003 COM(2003) 226 final.

6 Communication from the Commission to the Council, the European Parliament, the Economic and Social Committee and the Committee of the Regions. Life sciences and biotechnology – A Strategy for Europe, Brussels, 23 January 2002 COM(2002) 27 final, at 8.

7 See, CHRISTENSEN, R., DAVIS, J., MUENT, G., OCHOA, P., SCHMIDT, W., Biotechnology: An Overview, EIB Sector Papers, European Investment Bank (EIB), June 2002, at I.

intensive, the figures will be even more impressive for that sector in the future. In 2000, global pharmaceutical R&D spending totalled roughly USD 55 bn. Pharmaceutical corporations spent almost 80% of this with the rest coming from focused biotechnology companies. On average, the pharmaceutical industry spends about 16% of sales on R&D. R&D intensity of industry leaders, Eli Lilly, Roche, Pfizer and GlaxoSmithKline ranges between 16% and 19%. 56% of total R&D expenses are incurred in the US. An increasing part of the R&D budget of large pharmaceutical companies is spent on the clinical evaluation of new drugs ("clinical trials") – and not on drug discovery where knowledge creation is considered to be crucial. The share of R&D expenditure on clinical trials rose from 33% in 1996 to more than 40% in 2000 – and is likely to increase further. At the same time, the share spent on drug discovery has declined from 28% to 24%. Assuming, as mentioned above, that biopharmaceuticals make up 30% of new drugs, corporate R&D spend on biotechnology-based drug discovery can be estimated at roughly USD 4bn annually. This adds to the USD 11bn spent by biotechnology companies themselves.[8]

[8] CHRISTENSEN, R., DAVIS, J., MUENT, G., OCHOA, P., SCHMIDT, W., Biotechnology: An Overview, EIB Sector Papers, European Investment Bank (EIB), June 2002, at 16.

Chapter 3. The Patent System

3.1. Nature of a patent

Patents have become part of our present day life. They are present in all areas of technological development, from the rather trivial and not immediately extremely useful gadget over the highly sophisticated elements of aircraft to the intricate building blocks in drug development. As we will describe in detail further in this study, there is an economic rationale attached to the patent system which makes it a useful and in some cases indispensable tool to recoup investment and further technological progress. This is particularly true for inventions which require huge investments, such as those in the area of biotechnology. There is sufficient evidence that the patent system has an added-value for these research and capital intensive domains of technological development, and that a refusal to grant patents for these inventions would almost certainly have a detrimental effect on this very scientific and technological development. The rate of investments required urge for a system where the providers of the financial resources have a means to recoup their investment.

Discussing the concept of patent protection in general does not cause any specific reaction, but talking about patents in the field of biotechnology has caused considerable arousal. The reasons for this rather remarkable phenomenon are manifold, but are basically to be reduced to two major issues: (1) the connection of life, or bodily parts, with property rights and (2) a rather incomplete understanding of the rather complicated patent system, which as a form of property right, is much more complicated and containing a whole plethora of checks and balances, which are not to be found to the same extent in 'ordinary' property rights such as ownership of consumer goods etc. The first reason mentioned, which addresses emotional reactions of human beings, is actually also based on a misrepresentation of the patent system.

The differences between property in a tangible good and a patent are considerable to the extent that both can hardly be compared. A patent right does not confer ownership on a specific tangible embodiment, which would in the case of biotechnology be a specific DNA sequence or protein. It merely confers a monopoly, a negative exclusionary right to be more precise, in a teaching leading to a process or product. It thus merely excludes others from using the invention claimed without the consent of the patent holder.[9] This is important, because the

[9] See also recital (14) Dir. 98/44/EC.

mere grant of a patent does not necessarily imply that a specific activity is allowed to be performed. There could be legislation in place which prohibits the use of specific technology, while it can be patentable. The grant of a patent is thus not a license to practice the invention. This is often forgotten, also by legislators. Patent law is therefore not the appropriate forum for a discussion on the acceptability of certain technologies, such as e.g. cloning, use of stem cells etc. A legislator regulating the patentability of for example cloning techniques, without regulating the cloning techniques themselves is carrying out a deceptive policy, which will also probably be difficult to maintain. This is because if for example cloning techniques are excluded from patentability because they are assumed to be contrary to ordre public and morality, the mere fact that the technique as such is not prohibited contradicts and annihilates the argument that the invention cannot be patentable because it is assumed to be contrary to ordre public or morality. An activity which is allowed by law can never be contrary to ordre public or morality. This makes a patent provision of the sort mentioned unpractical and thus worthless.

There are also a number of potentially burdensome requirements to be fulfilled in order to obtain that negative exclusionary right. The invention must be novel, involve an inventive step, have an industrial application and it must be disclosed in such a way that the man skilled in the art is capable of carrying out the invention without undue burden or inventive skill. And in Europe, patent acts contain express provisions that inventions are not patentable if their application is contrary to ordre public and/or morality. These checks and balances thus provide a rather complicated evaluation of an invention before society decides to grant an exclusive right to the inventor. This study will make clear that a correct interpretation of these requirements, and of patent law principles in general, applied to inventions in the field of gene technology, leads to a situation where objections as mentioned hereabove can in most cases be excluded. There are, however, far more important and realistic problems arising from the patentability of DNA inventions which deserve our attention here, and these relate, amongst others, to the scope of these patents and their effects on scientific and technological development, and as such to the viability of gene technology in the long run.

3.2. Economic rationale of the patent system[10]

The tension within the patent system lies in the apparent conflicting interests of on the one hand the inventors, who wish to recoup their investments, and therefore ask for some kind of monopoly protection, and on the other hand the other market players, who could be curtailed too much if the normal market place competition is excluded. It is then also said that patent protection provides a monopoly to solve the appropriability problem: if a firm cannot recover the costs of invention because the necessary information is available to all at no cost, it can be expected that the level of innovation will be much lower. Patents prevent others from reaping where they have not sown; in other words it solves the free riding problem.[11] But there is also the other side of the coin. Patent protection leads to what has been called the 'fishing problem'.[12] The prospect of obtaining the patent, i.e., the fish, makes all actors very active in the pool where all the patent-fishes swim. The actors will add to their already current R&D investment rate, in order to be the first to catch the largest fish, which will provide the best opportunities to recoup the investment and to make profit. But there is only one actor who can catch the largest fish, which means that the investment made by the others will be wasted. Competition to catch that fish leads to duplication and overinvestment in R&D. This system thus brings with it that innovation takes place in society at a higher than minimum cost, which creates inefficiencies in economic terms.[13] On the other hand, without a patent system, allowing imitation, the "technological well will run dry".[14]

Patent protection creates positive externalities, i.e., opportunities for third parties to make use of the information disclosed in the patent application. This can make inventors reluctant to disclose information, because they do not want to

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10 Taken from BOSTYN, S.J.R., A European Perspective on the Ideal Scope of Protection and the Disclosure Requirement for Biotechnological Inventions in a Harmonised Patent System; The Quest for the Holy Grail?, 5 Journal of World Intellectual Property, 2002, (1013) 1014.

11 See, DAM, K.W., The Economic Underpinnings of Patent Law, The Journal of Legal Studies, 1994, (247) 247; ARROW, K., Economic Welfare and the Allocation of Resources for Invention, in, Rate and Direction of Inventive Activity, 1962, 609.

12 BARZEL, Y., Optimal Timing of Innovations, 50 Review of Economics and Statistics, 1968, 248-355.

13 BESEN, S.M., RASKIND, L.J., An Introduction to the Law and Economics of Intellectual Property, 5 Journal of Economic Perspectives, 1991, (3) 6.

14 See, SCHERER, F.M., ROSS, D., Industrial Market Structure and Economic Performance, Third edition, Houghton Mifflin Company, Boston, 1990, 624.

provide these externalities to third parties. This can in turn lead to underinvestment in R&D. It has then also been claimed that broad scope could mitigate these effects. Besides the possible negative effects of the externalities created by disclosing the invention, there can also be positive effects. Externalities can also create opportunities for the early innovator, in the sense that he can take advantage of new information developed by competitors. He can thus take advantage of developments made by others, but there is more. If the improvement or further development is made on the basis of the disclosed invention, there is also the opportunity for the original inventor to recoup his investments with licensing fees if there is a dependency situation.[15]

3.3. Invention – discovery

Patents are, at least in Europe, available for inventions that have technical character,[16] are novel, inventive, have industrial application and are sufficiently described in the patent application. One of the major issues in this connection is the distinction between patentable inventions and non-patentable discoveries. Under European patent law, the solution is not that easy to determine, since the statute has not given any definition of either category. This is not that surprising, since those concepts are subject to evolution. The EPO has traditionally held that an invention must be technical in order to be called a patentable invention, irrespective of whether the patentability requirements are being fulfilled. This has for long not been a major issue, but developments in the field of biotechnology and evenly so in the area of computer implemented inventions, have made this position more problematic, especially in view of the fact that it is very difficult to define what technical means. The case law of the EPO has in this respect held that technical means having technical character, or providing a technical contribution,[17] which does not really reveal the exact meaning, since a definition of a term using the term to be defined in the definition cannot be a proper explanation of the term to be explained by that very definition. Under German case law, it has been held that an

[15] JOLY, P.B., Le rôle des externalités dans les systèmes d'innovation. Nouveaux regards sur le dilemme de la propriété intellectuelle, 43 Revue économique, 1992, (785) 787.

[16] See Art. 52 EPC.

[17] See e.g., T 1173/97, "Computer program product/IBM", decision of Technical Board of Appeal 3.5.1. de dato 1 July 1998, OJ EPO, 1999, 609.

invention is actually a teaching to methodical action (Lehre zum planmäßigen Handeln),[18] which distinguishes it from a mere one time discovery.

In the United States, the statute has not given a definition of an invention neither, and what is even more, the statute does not even make a distinction between the word invention and discovery.[19] However, there are a number of judicially created exceptions to patentability. These exceptions were addressed in Diamond v. Diehr, where it was held that "This Court has undoubtedly recognised limits to section 101 and every discovery is not embraced within the statutory terms. Excluded from such patent protection are laws of nature, natural phenomena, and abstract ideas.[20] An idea of itself is not patentable. A principle, in the abstract, is a fundamental truth; an original cause; a motive; these cannot be patented, as no one can claim in either of them an exclusive right."[21] And after referring to the cited cases, the court further held in Gottschalk v. Benson that "Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work. As we stated in Funk Bros. Seed Co. v. Kalo Co., 333 U.S. 127, 130, "He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognises. If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end."".[22] In Parker v. Flook, it was held in this context that "the rule that the discovery of a law of nature cannot be patented rests, not on the notion that natural phenomena are not processes, but rather on the more fundamental understanding that they are not the kind of "discoveries" that the statute was enacted to protect. The obligation to determine what type of discovery is sought to be patented must precede the determination of whether that discovery is, in fact,

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18 BGH Rote Taube, BGH X ZB 15/67, 27 March 1969, 52 BGHZ 74 et seq., GRUR, 1969, 672 et seq.: "[...] als patentierbar eine gewerblich verwertbare neue fortschrittliche und erfinderische Lehre zum planmäßigen Handeln unter Einsatz beherrschbarer Naturkräfte zur Erreichung eines kausal übersehbaren Erfolgs angesehen werden kann."

19 See 35 USC section 101.

20 See Parker v. Flook, 437 U.S. 584 (US Supreme Court 1978); Gottschalk v. Benson, 409 U.S. 63, 67 (US Supreme Court 1972); Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 76 U.S.P.Q. 280 (US Supreme Court 1948).

21 Diamond v. Diehr, 450 U.S. 175, 185 (US Supreme Court 1981).

22 Gottschalk v. Benson, 409 US, at 67.

new or obvious."[23] And there is of course the famous ruling in the Chakrabarty case, where the US Supreme Court held that "everything under the sun made by man is patentable."[24] Under recent US case law, an invention is patentable if it produces a useful, tangible and concrete result.[25] In other words, no mentioning at all of technical character. It is admittedly a broad definition, also including business methods, but it has the advantage of clarity, and it avoids the struggle seen in Europe to try to determine what technical effect means, and in the absence thereof, making assumptions about its meaning.

Having the problem under European patent law that we do not exactly know what an invention is, we could try to find out whether it is easier to define a discovery. It could be said that a discovery is uncovering something which is already existing in nature, but which has not yet been discovered, i.e., it was covered until someone uncovered it. It is distinct from an invention because no inventive activity is required to produce it. A discovery is in other words the mere knowledge about something existing in nature, whereas an invention implies the ability of a human being to use this knowledge in a technical way, the so-called technical teaching, which will be further explained below. The issue could best be illustrated with an example. Suppose someone walks in the woods and finds a fungus. It looks very appealing, and the person having a terrible headache which makes him less prudent, he eats the fungus, and his headache disappears instantaneously. That person has made a discovery, i.e., he has discovered that the fungus is useful as a cure against headache, he has acquired knowledge about that fungus, without being capable of using this knowledge in a technical way. A similar situation is the following. The same hypothetical person walks in the woods, and sees the appealing fungus. He takes the fungus to his private laboratory, analyses it, and is able to extract, i.e., isolate and purify by a technical process, a substance which happens to be useful as a cure against headache. An invention has been made here. More has been done than merely discovering the fungus, a substance has been extracted, isolated and purified, and it has been made possible to reproduce that invention. Following German interpretation, the discovery of the fungus and the eating of it does not present a teaching to

[23] Parker v. Flook, 437 US, at 593.

[24] Diamond v. Chakrabarty, 447 U.S. 303, 309, 65 L. Ed. 2d 144, 100 S. Ct. 2204 (US Supreme Court 1980) (quoting S. Rep. No. 82-1979, at 5 (1952); H.R. Rep.No. 82-1923, at 6 (1952)).

[25] State Street Bank & Trust Co. v. Signature Fin.Group, Inc., 149 F.3d 1368, 1374-75, 47 U.S.P.Q.2D (BNA) 1596, 1602 (CAFC 1998), cert. denied, U.S., 142 L. Ed. 2d 704, 119 S. Ct. 851(1999).

methodical action, while the second example, where the substance is extracted from the fungus in a systematic and reproducible way, is.[26]

The problem described above is also sometimes called the product of nature doctrine. According to that doctrine, products of nature as such are not patentable, but products derived from nature are. This principle has since long been recognised in case law.[27] In a German case decided by the German Federal Patent Court,[28] it was held that "discovery is the finding of something existing but heretofore unknown; it is therefore purely perception. A discoverer turns into an inventor, however, if he provides - based on his perception - instructions for purposeful industrial action."[29] The Court further held that "[naturally occurring micro-organisms] are not eligible for protection, unless the inventor demonstrates a reproducible method whereby naturally occurring micro-organisms may be produced by human means. This Court shares this opinion; it has validity not only in the field of microbiology, but constitutes generally a condition of patentability."[30] In the UK, Lord Wilberforce said *obiter dicta* in the American Cyanamid (Dann's) Patent case before the House of Lords, which dealt with a method for the production of the antibiotic porfyromicin: "The priceless strain, being something living, found in nature, cannot be patented: the prosaic process, as applied to the strain, is capable of protection."[31] In the United States, similar views have been expressed. The US Supreme Court held in Funk Brothers Seed Co. v. Kalo Inoculant Co. that an unknown compound or composition of materials merely discovered from nature is not patentable.[32] Justice Douglas, speaking for the majority of the Court, stated that "patents cannot issue for the discovery of the phenomena of nature. The qualities of these bacteria, like the heat of the sun,

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26 This reasoning is in complete conformity with the landmark German Antamanid case: BPatG 28 July 1977, 16 W(pat) 64/75, "Cyclisches Dekapeptid Antamanid", GRUR, 1978, 238; IIC, 1979, 494.

27 This description is based on BOSTYN, S.J.R., Enabling Biotechnological Inventions in Europe and the United States. A study of the patentability of proteins and DNA sequences with special emphasis on the disclosure requirement, Eposcript Series, nr. 4, EPO (European Patent Office), München, 2001, 69 (hereinafter BOSTYN, EPO, 2001).

28 Cyclisches Dekapeptid Antamanid, BPatG., 16 W(pat) 64/75, 28 July 1977, GRUR, 1978, 238; IIC, 1979, 494.

29 At III. 1 of the reasons.

30 At III. 2 of the reasons.

31 American Cyanamid (Dann's) Patent, House of Lords, RPC [1971] 448 (425).

32 Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 76 U.S.P.Q. 280 (1948).

electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none."[33]

The same principle is also laid down in Art. 3(2) of directive 98/44/EC on the legal protection of biotechnological inventions: "Biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature". We will come back to this distinction when we discuss the patentability of DNA sequences. We suffice to submit here that the EC Directive has made the proper distinction, thus making it impossible to claim discoveries, but only inventions.[34]

In Europe, it has been claimed in the literature, however, that an innovation can only become a patentable invention, and thus really be an 'invention' in the patent law meaning of the word, if a specific industrial application, or function in the case of DNA sequences, is known and made public. In the absence thereof, no 'invention' is present. We will discuss this important issue more in detail further below in this study,[35] but it can be said here that, to the extent that an innovation which does not disclose a specific industrial application or function does not provide a technical or methodical teaching, such a statement can be considered to be a correct interpretation of patent law principles. But to the extent that the disclosure of the specific industrial application or function is not indispensable to have a technical or methodical teaching, it cannot be said that industrial application or function should be a constitutive element of the concept 'invention', but its application should be limited to the patentability requirement it refers to.

3.4. Patentability requirements

Once something can be considered to be an invention in the sense explained above, it must also fulfil the patentability requirements of novelty, inventive step, industrial application and sufficiency of disclosure in order to be patentable. Even though we will discuss these patentability requirements in further detail below when we discuss the patentability of DNA sequences in particular, it is useful to give a general overview of the criteria applied in connection with those requirements. It cannot be sufficiently emphasised that the patentability of DNA related inventions is subject to the same principles, rules and requirements as all

[33] 333 U.S., at 130.

[34] See below sub 4.2.

[35] See below sub 4.2.

other inventions. This is even more so if one takes into account that DNA inventions are considered to be chemical inventions, thus subject to the same principles applicable to this category of inventions.

3.4.1. Novelty

Novelty is an absolute criterion, i.e., something is new if it does not form part of the state of the art.[36] The state of the art consists of all knowledge available, whether in written or oral form. Application of this at first sight rather straightforward requirement is not always evident, as it is not always easy to be aware of knowledge available somewhere in the world. This is particularly true for the new technologies, which develop rapidly, and where the availability of written information is not always at reach. The best example is computer implemented inventions and business methods, where it is generally agreed upon that some of the patents granted consist of knowledge which actually belongs to the state of the art, but which is not easily accessible in databases.

Another controversial issue in the context of novelty is the novelty of chemical substances based on substances occurring in nature. A substance can be novel if it is produced in a purer form than the substance existing in nature. However, this does not necessarily imply that a known substance is necessarily new if it is prepared in a purer form. To establish novelty, it will be necessary to provide evidence that modification of the process parameter result in other products.[37] In other words, novelty can only be acknowledged if the new process for producing the product (in purer form) was not known in the state of the art, and the increased chemical is associated with a technical effect. But if the product is in a different form than the one existing in the prior art, novelty is established. In other words, if a chemical substance in purer form is also a product in a different form or structure, there is novelty. This principle applies mutatis mutandis to DNA. But what then about substances which have an identical structure as the ones found in nature? Can such a substance be considered to be novel? In case law it has been held that such a substance can be considered novel if the already naturally occurring identical substance was not readily available to the public.[38] In the EPO

[36] Art. 54 EPC; 35 USC 102

[37] See e.g., T 0205/83, “Vinyl ester - crotonic acid copolymers/HOECHST”, OJ EPO, 1985, 363.

[38] See e.g. T 0206/83, “Pyridine herbicides/ICI”, OJ EPO, 1987, 5, where it was stated that “a compound defined by its chemical structure can only be regarded as being disclosed in a particular document if it has been made available to the public in the

Guidelines it is said that "[...] to find a substance freely occurring in nature is also mere discovery and therefore unpatentable. However, if a substance found in nature has first to be isolated from its surroundings and a process for obtaining it is developed, that process is patentable. Moreover, if the substance can be properly characterised either by its structure, by the process by which it is obtained or by other parameters and is "new" in the absolute sense of having no previously recognised existence, then the substance *per se* may be patentable."[39] Similar views have been expressed in the US,[40] where it was held that in order for a prior art reference to "anticipate" and therefore negate the novelty of a later claimed invention, the reference must identically describe or disclose the invention in such a manner as to place it in the public domain.[41]

And in the context of DNA sequences, it has been held in EPO case law that the mere fact that a DNA sequence claimed was already existing in a DNA library is not novelty destructive vis-à-vis the sequence claimed,[42] in view of the fact that the sequence, which is present in the DNA library is not readily available to the public: "DNA sequences according to claim 1(b) had not been made available to the public by this publication itself or through this publication from the [Lawn gene] bank. […] The mere existence of a DNA sequence coding for a polypeptide of the IFN-α type, within the multitude of clones of [the] gene bank cannot automatically mean that the chemical compound (polynucleotide) concerned does become part of the state of the art. The latter would only then be the case if the existence of the compound concerned had recognisably been made publicly available."[43] It can be questioned whether this solution would still be valid today, in view of automated processes to retrieve specific sequences in libraries. But even in that event, there is presumably still room for selection inventions[44] in this area.

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sense of art. 54(2) EPC. [...] The requirement is fulfilled if a reproducible method is described in the same document."; Cyclisches Dekapeptid Antamanid, BPatG., 16 W(pat) 64/75, 28 July 1977, GRUR, 1978, 238; IIC, 1979, 494.

39 EPO Guidelines, C IV 2.3.

40 E.g., In re Arkley, 455 F.2d 586, 587 (CCPA 1972); In re Brown, 329 F.2d 1006, 1011 (CCPA 1964); In re LeGrice, 301 F.2d 929, 930 (CCPA 1962)

41 JOHNSTON, S., Patent protection for the protein products of recombinant DNA, 4 High Technology Law Journal, No. 2, 1989,257.

42 T 0301/87, "Alpha-interferons/BIOGEN", OJ EPO, 1990, 335.

43 At 5.8. of the reasons.

44 This concept will be explained further in this study, see sub 4.4.

3.4.2. Inventive step

An invention fulfils the inventive step criterion[45] if the result achieved with the claimed invention is not obvious vis-à-vis the state of the art.[46] In Europe, the EPO traditionally uses the problem-solution approach.[47] First the closest prior art and the technical effect achieved by the closest prior art is established. Subsequently, the claimed invention and the technical effect achieved by the claimed invention is established. These are the two extremes. Then, the objective technical problem to be solved in order to go from the closest prior art to the claimed invention is to be defined. Hindsight is to be avoided in this context. If the solution to this objective technical problem is not obvious, then the inventive step hurdle is passed.[48] The standard is whether an invention is obvious or not, and not whether it is obvious to try, as illustrated in case T 0296/93:[49] "the fact that other persons (or teams) were also working on the same project might suggest that it was 'obvious to try' or that it was 'an interesting area to explore', but it does not necessarily imply that there was 'a reasonable expectation of success'. 'A reasonable expectation of success', which should not be confused with the understandable 'hope to succeed', implies the ability of the skilled person to reasonably predict, on the basis of the existing knowledge before the starting of a research project, a successful conclusion to the said project within acceptable time limits. The more unexplored a technical field of research is, the more difficult is the making of predictions about its successful conclusion and, consequently, the lower the expectation of success."[50,51] Certain indications can be taken into account for the determination of inventive step, such

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45 Art. 56 EPC; 35 USC 103

46 Cf. EPO Guidelines, C IV 9.3: "The term 'obvious' means that which does not go beyond the normal progress of technology but merely follows plainly or logically from the prior art, i.e., something which does not involve the exercise of any skill or ability beyond that to be expected of the person skilled in the art."

47 T 0024/81, "Metal Refining/BASF", decision of Technical Board of Appeal 3.3.1 of 13 October 1982, OJ EPO, 1983, 13.

48 See EPO Guidelines C IV 9.5.

49 T 0296/93, "Hepatitis B virus antigen production/BIOGEN", 28 July 1994, OJ EPO, 1995, 627.

50 T 0296/93, at 7.4.4 of the reasons.

51 See BOSTYN, S.J.R., Enabling Biotechnological Inventions in Europe and the United States. A study of the patentability of proteins and DNA sequences with special emphasis on the disclosure requirement, Eposcript Series, nr. 4, EPO (European Patent Office), München, 2001, 74 (hereinafter BOSTYN, EPO, 2001).

as an unexpected or surprising effect, better or unforeseeable results, or particularly good properties.[52]

In the United States, the basic test for the determination of inventive step or obviousness[53] has been promulgated in the landmark US Supreme Court case of Graham v. John Deere Co. According to the Supreme Court, the obviousness test is the following: "under section 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or the non-obviousness of the subject matter is determined."[54]

3.4.3. Industrial application

The industrial application requirement[55] was until recently not a major issue in patent law. Under European patent law, an invention has industrial application if it can be applied in any field of industry, which is interpreted rather broadly, also including for example agriculture. According to the EPO Guidelines, "'Industry' should be understood in its broad sense as including any physical activity of "technical character" (see IV, 1.2), i.e. an activity which belongs to the useful or practical arts as distinct from the aesthetic arts; it does not necessarily imply the use of a machine or the manufacture of an article and could cover e.g. a process for dispersing fog, or a process for converting energy from one form to another. Thus, Art. 57 excludes from patentability very few "inventions" which are not already excluded by the list in Art. 52(2) (see IV, 2.1). One further class of "invention" which would be excluded, however, would be articles or processes alleged to operate in a manner clearly contrary to well-established physical laws, e.g. a perpetual motion machine. Objection could arise under Art. 57 only in so far as the claim specifies the intended function or purpose of the invention, but if, say, a perpetual motion machine is claimed merely as an article having a particular specified construction then objection should be made under Art. 83 (see II, 4.11)."[56]

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52 See also EPO Guidelines C IV 9.8.

53 35 USC 103.

54 Graham v. John Deere Co. of Kansas City, 148 USPQ 459, at 467 (US Supreme Court 1966).

55 Art. 57 EPC; 35 USC 101

56 See EPO Guidelines C IV 4.1.

It is further said in the EPO Guidelines that "(4.4) Methods of testing generally should be regarded as inventions susceptible of industrial application and therefore patentable if the test is applicable to the improvement or control of a product, apparatus or process which is itself susceptible of industrial application. In particular, the utilisation of test animals for test purposes in industry, e.g. for testing industrial products (for example for ascertaining the absence of pyrogenetic or allergic effects) or phenomena (for example for determining water or air pollution) would be patentable. (4.5) It should be noted that "susceptibility of industrial application" is not a requirement that overrides the restriction of Art. 52(2), e.g. an administrative method of stock control is not patentable, having regard to Art. 52(2)(c), even though it could be applied to the store of spare parts of a factory. On the other hand, although an invention must be "susceptible of industrial application" and the description must indicate where this is not obvious the way in which the invention is so susceptible (see II, 4.12), the claims need not necessarily be restricted to the industrial application(s)."[57] According to EPO document EUROTAB 2/99 as well as the submission from the EPO, as regards the distinction between the criterion of technical character (see the EPO Guidelines, C-IV 1.2 (ii) and 2.2) and the criterion of industrial application, an invention susceptible of industrial application does not necessarily have a technical character. If the claimed subject matter as a whole lacks technical character, an objection to it cannot be raised under Article 57 of the Convention on the Grant of European Patents European Patent Convention (EPC) [industrial application], but should be based on Article 52 EPC [patentable inventions].[58] The EPO Boards of Appeal have held that the requirement for industrial application implies a "commercial exploitation,"[59] with the purpose of achieving "financial gain".[60] On the other hand, it was confirmed in decision T0074/93 that,[61] when a method falls entirely

[57] See EPO Guidelines C IV 4.4 - 4.5.

[58] See, WIPO document SCP/9/5, 2.

[59] E.g., T 0204/93, "System for generating software source code components/AMERICAN TELEPHONE AND TELEGRAPH COMPANY", decision of Technical Board of Appeal 3.5.1. de dato 29 October 1993, not published.

[60] See e.g., T 0144/83, "Du Pont/Appetite suppressant, decision of Technical Board of Appeal 3.3.1. de dato 27 March 1986, OJ EPO, 1986, 301.

[61] T 0074/93, "BRITISH TECHNOLOGY GROUP/Contraceptive method", decision of Technical Board of Appeal 3.3.1 de dato 9 November 1994, OJ EPO, 1995, 712.

within the private or personal sphere of a human being, it cannot be considered to be susceptible of industrial application.[62]

With the advent of the modern technologies, the situation of relative silence surrounding the application of this requirement has changed. In the field of biotechnology, inventions were made for partial DNA sequences without any known function. Only the raw information was known and disclosed. This raised questions as to the interpretation of the industrial application requirement – or utility requirement as it is called under US patent law – to inventions with no specified utility or function. The standard to be tested boils down to the question as to whether it is sufficient to state that the invention can potentially be used for specific purposes, or whether it is required to disclose at least one specific utility. The US has been a trend-setter in this discussion. The USPTO promulgated in 2001 new Utility Guidelines.[63] Still according to these Guidelines "a claimed invention must have a specific and substantial utility. This requirement excludes 'throw-away,' 'insubstantial,' or 'non-specific' utilities […]." According to these new Guidelines, "an invention has a well-established utility (1) if a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (2) the utility is specific, substantial, and credible".

In recent EPO case law, a similar, narrow, interpretation has been given to the industrial application requirement of Art. 57 EPC.[64] Identical, or at least very similar wording was used as those used in the USPTO Utility Guidelines. This new interpretation under EPO case law of the Opposition Division is not based on the text of the statute, and not on Technical Board of Appeal precedent. It is therefore to be seen whether this interpretation will be upheld in the future.

We will dwell further upon the industrial application requirement later in this study when we discuss the important provision of Art. 5(3) Dir. 98/44/EC.[65]

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62 See WIPO SCP/9/5, 3.

63 'USPTO Guidelines for Examination of Applications for Compliance With the Utility Requirement' (2001) 66 Federal Register, 5 January, at 1092 et seq.

64 See, "ICOS/SmithKline Beecham and Duphar International Research", decision of the EPO Opposition Division of 20 June 2001, OJ EPO 2002, at 293 et seq. An appeal has been lodged against this decision, but is not further pursued.

65 See below sub 4.6.

3.5. Scope of protection issues

3.5.1. Introduction

Scope of protection, or strength of the patent, can be influenced by various means, directly or indirectly. It can be influenced indirectly via the application of the patentability requirements of novelty, inventive step and industrial application. If an invention is easily considered to be new and inventive, i.e., if minor incremental improvements are sufficient to pass the inventive step hurdle, it will probably have a rather narrow scope of protection, since a minor improvement will be considered to be another – patentable – invention. Industrial applicability has a similar effect. If patent offices easily accept an industrial application, i.e., that the invention has a credible use, this will stimulate innovators to file patent applications in early stages of development of technology, which could lead to a large amount of narrow patents, or a few broad patents with reach-through claims.[66] It can more directly be influenced by the application of the disclosure requirement, which will be discussed in detail in one of the following sections.[67]

At the level of post-grant, scope of protection becomes an important issue to establish the limitations of the patent and the extent to which others might possibly infringe on such patents. The doctrine of equivalence is of crucial importance here. However important this issue might be, it is not covered in this study. But also the disclosure requirement has its continuing influence, in the context of revocation proceedings in court, be it autonomous, or in the framework of a counter-claim against an infringement claim.

3.5.2. Importance of scope of protection from an economic point of view[68]

That patent breadth is a crucial issue in the whole patent system, is not doubted by most patent lawyers. Also economic scholars today believe it to be a crucial

[66] Reach-through claims are further discussed in this study, see below sub 4.9.

[67] See below sub 3.5.3.

[68] Taken from BOSTYN, S.J.R., A European Perspective on the Ideal Scope of Protection and the Disclosure Requirement for Biotechnological Inventions in a Harmonised Patent System; The Quest for the Holy Grail?, 5 Journal of World Intellectual Property, 2002, (1013) 1015.

issue.[69] The question has for a long time already been: is it desirable to stimulate broad scope or narrow scope, a question still relevant today in the context of for example the disclosure requirement, as further illustrated below. The scope of protection must be broad enough to recompense the cost of invention. If the scope of protection is not broad enough, trivial improvements can be produced by competitors without committing a patent infringement. This situation is harmful to the original patent holder, because he invested a considerable amount of money to come up with this wonderful invention, and finds himself now in a situation that it is easy and relatively cheap for competitors to make a slightly improved version of the patented invention without the patent holder being able to reap anything. On the other hand, if the scope is too broad, the monopoly can have a stifling effect on technological development, i.e., competitors see no use in and have no incentives to make improvements.

Narrow scope has from an economic viewpoint the advantage that it creates more competition after the original innovation. But more competition can also be socially costly, in the sense that it can lead to e.g. duplication of entry costs, inefficient production etc. Due to the fact that the scope is narrow, and that more competitors are thus attracted to enter the market with competing products, there is less profit for the original innovator, because of the limited-value monopoly right. This could lead to a reduced incentive to innovate, or a tendency to keep innovations secret.[70] And secrecy of inventions leads to duplicative R&D investments, because more people are busy 'reinventing the wheel', in the absence of knowledge available to the public.[71]

Broad scope has the advantage that it provides better protection for the original inventor against (trivial) improvements and second-generation innovators. That is why patents must in any event have a certain breadth, because too narrow a patent will not provide the protection mentioned, and will then prove to be of little value. Broad scope allows the patent holder to collect most of the social value. This

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69 "The appropriate margin on which patent policy should operate may not be patent length, but rather patent breadth." See, GILBERT, R., SHAPIRO, C., Optimal Patent Length and Breadth, 21 Rand Journal of Economics, 1990, (106) 106.

70 DENICOLÒ, V., Patent Races and Optimal Patent Breadth and Length, XLIV The Journal of Industrial Economics, 1996, (249) 251 et seq.

71 CHANG, H.F., Patent Scope, Antitrust Policy, and Cumulative Innovation, 26 Rand Journal of Economics, 1995, (34) 52.

creates in turn a situation wherein he is less inclined to keep the invention secret.[72] And since inventors are less inclined to keep their inventions secret, there is a positive effect on the dissemination of information.[73] But broad scope makes it more difficult for newcomers or subsequent innovators. It hinders competition. When the scope of protection is broad, there can be a tendency to disinvest, because the broad scope of protection makes it less interesting for competitors to enter the market, or to invest in improvements and other innovations based on the broad scope protected invention. If that would be the case, it could have a stifling effect on technological development.[74] That is why, according to some, it is better to have a more rivalrous system, which has its inefficiencies of course, as outlined above, because such a system would generate a more rapid technological progress.[75]

3.5.3. The disclosure requirement: definition and rationale[76]

Conceptually speaking, the disclosure requirement in patent law is the principle according to which the invention must be disclosed in such a way in the patent application that the man skilled in the art is capable of carrying out the invention without undue burden or inventive skill. This general principle is common to the patent systems of the industrialised world. In Europe, the requirement is laid down in Art. 83 EPC: "The European patent application must disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art." Also relevant in this context is Art. 84 EPC: "The claims shall define the matter for which protection is sought. They shall be clear and concise and be supported by the description." In the US, the enablement requirement as it is called

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72 SCOTCHMER, S., Standing on the Shoulders of Giants: Cumulative Research and the Patent Law, 5 Journal of Economic Perspectives, 1991, (29) 30.

73 CHANG, H.F., loc.cit., 52. It is important to observe here that CHANG presupposes that there is a sufficient disclosure, otherwise the positive effect on dissemination of knowledge can of course never be achieved. See BOSTYN, EPO, 2001, 48.

74 SCOTCHMER, S., Standing on the Shoulders of Giants: Cumulative Research and the Patent Law, 5 Journal of Economic Perspectives, 1991, (29) 33.

75 MERGES, R.P., NELSON, R.R., On the Complex Economics of Patent Scope, 90 Columbia Law Review, 1990, (839) 908.

76 Taken from BOSTYN, S.J.R., A European Perspective on the Ideal Scope of Protection and the Disclosure Requirement for Biotechnological Inventions in a Harmonised Patent System; The Quest for the Holy Grail?, 5 Journal of World Intellectual Property, 2002, (1013) 1016.

there, is covered by section 112: "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is mostly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

The rationale of the disclosure requirement is the *quid pro quo*, i.e., a monopoly right is granted in exchange for a description of the invention in the patent application, which allows the public and others active in the same field, to make use of the technology disclosed in order to make further technological developments. In other words, technological development is stimulated by disclosure. There is thus some kind of contract between the patent applicant and society, according to which the former is entitled to a patent, under the condition that he makes his invention available to the public and that he describes it in sufficient detail.

The German Federal Patent Court held in 'Typ II-Restriktionsendonuklease':[77] "The question of when an invention characterised through parameters fulfils the requirements of sufficient disclosure can only be answered, in the absence of an express rule of law, with regard to the purpose of this requirement for patentability. The requirement is associated with the grant of a patent which in turn creates a monopoly, providing an incentive for the enrichment of commercially useful technical knowledge. […] The requirement for a sufficient disclosure of the invention is […] fulfilled if the claimed or granted protection can be considered a reasonable compensation for the enrichment of the technical world through the disclosure of the invention."

The Technical Boards of Appeal of the EPO have also emphasised this rationale of the disclosure requirement in their case law. In case T 0169/83, "Wallelement/VEREINIGTE METALLWERKE",[78] it was held that "in construing Article 83 it is important to bear in mind that justification for patent protection is based on the fact that in making his invention generally available through publication an inventor enables the public at large to benefit from it in the sense that knowledge is increased and specialists in the field are stimulated to make further technical advances. The inventor, therefore, helps to enrich technology and

[77] BpatG 18 April 1991, 16 W (pat) 64/88, "Typ II-Restriktionsendonuklease", BpatGe 32, 174.

[78] T 0169/83, "Wallelement/VEREINIGTE METALLWERKE", decision of Technical Board of Appeal 3.2.1 de dato 25 March 1985, OJ EPO, 1985, 193.

his just reward for so doing under patent law takes the form of sole rights to his invention for a limited period. […] Sufficiency of disclosure is therefore of eminent importance for the theory of just reward."

In the US, the rationale of the disclosure requirement was already a point of focus in early days. The US Supreme court held in 1832 in Grant v. Raymond (US S. Ct. 1832):[79] [The enabling disclosure, being the *quid pro quo* of the monopoly grant], "is necessary in order to give the public, after the privilege shall expire, the advantage for which the privilege is allowed, and is the foundation for the power to issue the patent." And in Bonito Boats, Inc. v. Thunder Craft Boats, Inc. (US S. Ct. 1989)[80] that same court said: "The Patent Clause itself reflects a balance between the need to encourage innovation and the avoidance of monopolies which stifle competition without any concomitant advance in the 'Progress of Science and useful Arts.' As we have noted in the past, the Clause contains both a grant of power and certain limitations upon the exercise of that power. Congress may not create patent monopolies of unlimited duration, nor may it 'authorise the issuance of patents whose effects are to remove existent knowledge from the public domain, or to restrict free access to materials already available." The US Supreme Court continued by bringing to our attention the careful balance which has to be struck between competition and monopoly protection: "From their inception, the federal patent laws have embodied a careful balance between the need to promote innovation and the recognition that imitation and refinement through imitation are both necessary to invention itself and the very lifeblood of a competitive economy. […]. The federal patent system thus embodies a carefully crafted bargain for encouraging the creation and disclosure of new, useful, and nonobvious advances in technology and design in return for the exclusive right to practice the invention for a period of years. [The inventor] may keep his invention secret and reap its fruits indefinitely. In consideration of its disclosure and the consequent benefit to the community, the patent is granted. An exclusive enjoyment is guaranteed him for seventeen years, but upon expiration of that period, the knowledge of the invention inures to the people, who are thus enabled without restriction to practice it and profit by its use." Chisum has said in this context: "A primary purpose of the patent system is to provide incentives for the disclosure of valuable inventions that might otherwise be kept secret. The Government offers a bargain: a limited period

[79] Grant v. Raymond, 31 U.S. (6 Pet.) 218 (US Supreme Court 1832).

[80] Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 109 S.Ct. 971, 9 USPQ2d 1847 (US Supreme Court 1989).

of statutory exclusivity for the claimed invention in exchange for full disclosure of the invention."[81]

3.5.4. Disclosure and connection with scope of protection[82]

Scope of protection is traditionally linked to the post grant phase and even more particular in the context of a patent infringement claim and the possible application of the doctrine of equivalence. But the scope of protection of a patent can only be based on the scope of the invention or the inventive concept. Before one is capable of determining the scope of protection of the patent in suit, it is necessary to determine the scope of the inventive concept.[83] Even though the scope of the invention and the scope of protection of the patent have to be distinguished from a systematical point of view, they are in my view two different approaches to the same substance.[84] And in the context of the determination of the scope of the invention, the disclosure requirement comes into play. The degree of strictness in the application of this requirement will have an influence on the scope of the patent based on the scope of the invention. For example, if I claim a genetically manipulated animal in general in my patent application, but I only disclose the invention applied to mice, what is then the scope of my invention, the genetic manipulation of animals or of mice or rodents? A strict application of the disclosure requirement could lead to the conclusion that the scope of the invention is mice. In my view, the scope of protection of such a patent will be identical to the scope of the invention, and thus it can be concluded that scope of invention and scope of protection are different terms used in different phases of the patent grant (and later juridical claims) for the same phenomenon. It is not possible to determine the scope of protection without knowing the scope of the invention, and once the scope of the invention is identified, this will then be the scope of protection.

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81 CHISUM, D.S., Patents. A Treatise on the Law of Patentability, Validity and Infringement, Matthew Bender, Release n° 70, 1999, loos-leaf; § 7.05[1], at 7-200.

82 Taken from BOSTYN, S.J.R., A European Perspective on the Ideal Scope of Protection and the Disclosure Requirement for Biotechnological Inventions in a Harmonised Patent System; The Quest for the Holy Grail?, 5 Journal of World Intellectual Property, 2002, (1013) 1018.

83 BOSTYN, EPO, 2001, 145 et seq.

84 BOSTYN, EPO, 2001, 146 and 287.

In this view, the disclosure requirement plays a crucial role in the patent system, because its level of application will have an influence on the scope of the invention.[85] Suppose that we interpret the disclosure requirement in such a way that everything which has not been disclosed in the patent application, does not fall under the patent. That would mean that the inventor has to disclose all possible applications in the patent if he is to obtain a broad scope patent. Suppose on the other hand that we are very lenient, and that we agree that as soon as the applicant has disclosed an example, we are prepared to grant a broad patent, following the assumed general application of the invention disclosed in the patent application in general, broad terms. These are probably the two extremes between which the disclosure requirement moves. The disclosure requirement can thus be used as an instrument to tackle overbroad claims, supposedly embracing a wide variety of embodiments.[86] Patent granting bodies, appeal bodies and judges have the task to develop a policy in this respect. Adelman et.al. put it this way: "Patent claims may be seen as abstractions based upon a specific bit of working technology; but just how broad and sweeping should the patent system allow a claim to become? The enablement requirement serves to delimit the boundaries of patent protection by ensuring that the scope of a patent claim accords with the extent of the inventor's technical contribution."[87]

Some examples can clarify the various problems that might arise in the determination of sufficient disclosure. If a patent is claimed for an invention relating to protein production, does the patent cover both the protein isolated and purified from nature as well as the recombinant produced protein? If a recombinant protein is claimed, does it cover all generations or only one type of recombinant protein (the one which is expressly described in the patent application)? If a method for the production of a recombinant protein is invented, can the patent cover all methods of production of recombinant proteins? If a DNA sequence is claimed, can the patent cover all possible DNA sequences coding for a specific protein, or is it limited to the DNA sequence disclosed? Related to this question, if a number of DNA analogues have been described in the patent application, does the scope of the patent also extend to analogues which have not been described, and which are unknown at the time of application, but which might admittedly

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85 Also emphasizing the interrelationship between the disclosure requirement and scope of protection, BARTON, J.H., Patent Scope in Biotechnology, 26 IIC, 5/1995, (605) 606.

86 For more details, BOSTYN, EPO, 2001, 145 et seq.

87 ADELMAN, M.J., RADER, R.R., THOMAS, J.R., WEGNER, H.C., Cases and Materials on Patent Law, St.Paul, Minnesota, West Group, 1998, 567.

have a similar therapeutic effect? A claim for a genetically manipulated animal. Does it embrace all animals genetically manipulated in the claimed way, or should protection be confined to the animals described in the application? How broad is a claim defined in functional terms,[88] e.g. "a polypeptide having X antigen specificity"?

US case law provides us with good examples of the issues at stake. In O'Reilly v. Morse,[89] the famous Morse telegraphy patent was to be scrutinised, and more specifically the eighth claim according to which Morse did not "propose to limit myself to the specific machinery, or parts of machinery, described in the foregoing specifications and claims; the essence of my invention being the use of the motive power of the electric or galvanic current, which I call electro-magnetism, however developed for marking or printing intelligible characters, letters or signs, at any distance, being a new application of that power, of which I claim to be the first inventor or discoverer." The US Supreme Court decided that the claim was overly broad: "It is impossible to misunderstand the extent of this claim. He claims the exclusive right to every improvement where the motive power is the electric or galvanic current, and the result is the marking or printing intelligible characters, signs, or letters at a distance. […] Some future inventor, in the onward march of science, may discover a mode of writing or printing at a distance by means of the electric or galvanic current, without using any part of the process or combination set forth in the plaintiff's specification. But yet if it is covered by this patent the inventor could not use it, nor the public have the benefit of it without the permission of this patentee. Nor is this all, while he shuts down the door against inventions of other persons, the patentee would be able to avail himself of new discoveries in the properties and powers of electro- magnetism which scientific men might bring to light. *In fine* he claims an exclusive right to use a manner and process which he has not described and indeed had not invented, and therefore could not describe when he obtained his patent. The Court is of the opinion that the claim is too broad, and not warranted by law."[90]

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88 Functional terminology means that one defines something by what it does or the result it achieves, e.g. "DNA sequence X, when used in a host, is capable of expressing protein Y", or "recombinant protein X sufficiently pure to have a therapeutic effect in the production of…" or "DNA macromolecule X capable of expressing therapeutically effective amounts of protein Y." Functional terminology definitely broadens the scope of protection, by its nature.

89 O'Reilly v. Morse, 56 U.S. 62 (US Supreme Court 1854).

90 Reprinted in, CHISUM, D.S., NARD, C.A., SCHWARTZ, H.F., NEWMAN, P., KIEFF, F.S., Principles of Patent Law, New York, Foundation Press, 1998, 163 et seq.

In National Recovery Technologies Inc., v. Magnetic Separation Systems Inc.,[91] the CAFC took the opportunity to demonstrate the central issues in disclosure analysis: "The enablement requirement ensures that the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims. The scope of the claims must be less than or equal to the scope of the enablement. The scope of enablement, in turn, is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation. The case before us presents a classic example of a claim that is broader than the enablement as taught in the specification. The specification […] first acknowledges the problem. […] The ideal solution to this problem is clear. […] Claim 1 claims this ideal solution. […] However, the specification […] does not describe how to perform this ideal selection step."

3.5.5. Enabling disclosure requirement: which standard to apply?

The importance of a correct application of the enabling disclosure requirement cannot be overestimated. As we have seen, scope of protection decisions will have an important effect for the strength of the patent for the patent holder. And we have also seen that the disclosure requirement is capable of having an important influence in determining this scope. It is therefore most relevant to know how this requirement ought to be applied in the evaluation of patent applications. It is difficult to give a recipe that is applicable to all possible situations, as patentability requirements have to be applied to the specific application and situation at stake. What is clear, however, is that there is some evidence that overbroad protection, and a lenient interpretation of the disclosure requirement is not recommendable, as it bears with it a high social cost.

A policy vis-à-vis the disclosure requirement can basically be reduced to three possible tiers. First, one can decide to use a strict application of the requirement: what is not expressly disclosed is not protected. Such an approach implies in effect that protection is limited to the examples and embodiments mentioned in the patent application. Advantage of such an approach is that it is straightforward, easy to apply, and it provides legal certainty. It could also be said to be fair, because it gives the patent applicant protection for what he has provided to the public, i.e., his

[91] National Recovery Technologies Inc., v. Magnetic Separation Systems Inc., 49 USPQ2d 1671, at 1676 (CAFC 1999).

invention, being the particular piece of knowledge he has added to the state of the art, "to the storehouse of knowledge".[92] This approach becomes more problematic in its application if the invention is a general principle, applicable to an unlimited number of embodiments. Such an invention is per se broader than the examples mentioned in the patent application. It could then also contravene against the "quid pro quo" principle of patent law.[93]

At the other end of the spectrum is a lenient application: according to this approach, the patent applicant is entitled to obtain a broad protection for sharing his invention with the public, even if he confines himself to a very general disclosure,[94] for example because we consider his invention to be very valuable, pioneering. Problem with such an approach is that it is very difficult to draw the line between a general disclosure and too general a disclosure. It is also difficult in this approach to determine how broad then the scope ought to be. A fair application of such an approach becomes also problematic if the invention is not the application of a general principle but relates only to discrete products or methods. Allowing general disclosure makes it more attractive for applicants to frame their claims in general wording, i.e., the application of a general principle, and the more lenient approach will most presumably not sanction this strategy. This approach is surrounded with too many difficulties, disadvantages and imbalances to be defended.

A third possible approach, and in the author's view the most balanced one, is a kind of middle way. It fully takes advantage of the reasoning used by Lord Hoffmann in the Biogen case.[95] He held in that case that "if the invention discloses a principle capable of general application, the claims may be in correspondingly general terms. […]. On the other hand, if the claims include a number of discrete methods or products, the patentee must enable the invention to be performed in respect of each of them. Thus if the patentee has hit upon a new product which has a beneficial effect but cannot demonstrate that there is a common principle by which that effect will be shared by other products of the same class, he will be entitled to a patent for that product but not for that class, even though some may

92 As Justice Douglas said in, Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, at 130, 76 U.S.P.Q. 280 (US Supreme Court 1948).

93 BOSTYN, EPO, 2001, 293.

94 With general disclosure, meant is a disclosure which is not commensurate with the number of embodiments claimed.

95 Biogen Inc. v. Medeva plc, House Of Lords, 31 October 1996, RPC [1997] 1. For a detailed analysis of this case, see BOSTYN, EPO, 2001, 190 et seq.

subsequently turn out to have the same beneficial effect. […]. On the other hand, if he has disclosed a beneficial property which is common for the class, he will be entitled to a patent for all products of that class even though he has not himself made more than one or two of them."[96] After having established the type of invention one is dealing with, which admittedly is not an easy task for the competent authorities to do, sufficiency is determined by applying the following standard: if the invention is a general principle, then disclosure of only one or some embodiments representing the application of the principle suffices. No exhaustive enumeration is required, because one deals with a general principle applicable to an unlimited number of embodiments. If the invention does not relate to a general principle, but only to discrete products or methods, then the disclosure requirement is only fulfilled if all products or methods claimed are also described in the application. Such an approach responds best to the "quid pro quo" principle of patent law, to the principle of fair protection and has no clear disadvantages both from a legal and economic point of view. It is difficult to see any objection against a refusal to grant broad protection to an applicant who has not enriched society with a general principle but has only made some narrowly defined products or methods available to the public. In the same train of reasoning, there is no objection against granting a broad patent if the disclosure is commensurate with the scope claimed.

In effect, a similar line of reasoning is followed in recent EPO case law. The Mycogen case is probably the best example.[97] In that case, the Technical Board of Appeal held the following: "A proper balance must be found between, on the one hand, the **actual** technical contribution to the state of the art by the invention disclosed in said patent application, if any, and, on the other hand, the **manner of claiming** so that, if patent protection is granted, its scope is fair and adequate."[98] […] "In certain cases a description of one way of performing the claimed invention may be sufficient to support broad claims with functionally defined features, for example where the disclosure of a new technique constitutes the essence of the invention and the description of one way of carrying it out enables the skilled person to obtain without undue burden the same effect of the invention in a broad area by use of suitable variants of the component features. In other cases, more technical details and more than one example may be necessary in order to support

96 Biogen Inc. v. Medeva plc, House Of Lords, 31 October 1996, RPC [1997] 1, at 48-49.

97 T 0694/92, "Modifying plant cells/MYCOGEN", decision of Technical Board of Appeal 3.3.4. de dato 8 May 1996, OJ EPO, 1997, 408.

98 T 0694/92, at 3 of the reasons.

claims of a broad scope, for example where the achievement of a given technical effect by known techniques in different areas of application constitutes the essence of the invention and serious doubts exist as to whether the said effect can readily be obtained for the whole range of applications claimed."[99] […] "The experimental evidence and technical details in the description of the patent in suit are not sufficient for the skilled person to reliably achieve without undue burden the technical effect of expression in **any** plant cell of **any** plant structural gene under the control of **any** plant promoter and that, consequently, they do not provide sufficient support for a claim, such as present claim 1, broadly directed to such a method."[100]

The standard of review as it has been applied by Lord Hoffmann provides a fair and balanced test for enablement, a goal of patent law. Overbroad and overnarrow patents must be avoided. Or as Merges put it: "The ever-present tension in the law of enablement [is]: the desire to restrict the patentee's property right to that which she has actually invented, while at the same time guarding against too skimpy a right, which would in fact be no right at all given the ease of inventing around it."[101] Patent law is evidently linked to competition between companies and/or innovators in general for innovation. One of the goals of the patent system is to find the balance between competition and monopoly protection. Lord Hoffmann said in this context: "But care is needed not to stifle further research and healthy competition by allowing the first person who has found a way of achieving an obviously desirable goal to monopolise every other way of doing so."[102]

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99 T 0694/92, at 5 of the reasons. This distinction is very similar to the distinction made by Lord Hoffmann in the Biogen case

100 T 0694/92, at 19 of the reasons.

101 MERGES, R.P., Patent Law and Policy, The Michie Company, Virginia, 1992, 515.

102 See, Biogen Inc. v. Medeva plc, House Of Lords, 31 October 1996, RPC [1997] 1, at 52.

The principles set out above in respect of the disclosure requirement have to be kept in mind in the further literature of this background study, as these principles can prove to be most valuable in the evaluation of the desirability and scope of specific types of patents for specific types of inventions. They are furthermore proof of the fact that patent granting does not necessarily imply the grant of broad patents, as there are sufficient instruments within the patent system to tackle potential undesirable developments, once the various checks and balances are applied in a proper way by patent offices and courts.

Chapter 4. Specific Issues Relating To the Patentability of DNA Sequences

4.1. How are gene patents claimed?

Patent claims may assert rights over DNA in various ways, and one could make an extensive list of possible applications (drafting an exhaustive one would be even more difficult, if possible at all, in view of the rapid evolution in this field of technology). In this background study, the author has taken advantage of the expertise of the authors of two important reports, issued by the Nuffield Council and the OECD. In the view of the author, these enumerations give a good overview of what is currently claimed, and hence there is no reason to draw up a different list.

Patent claims may claim one or more of the following:[103]

(1) the DNA sequence, whether comprising a complete or partial gene
(2) promoters
(3) enhancers
(4) individual exons
(5) expressed sequences as expressed sequence tags (ESTs) or cDNAs
(6) whole transcribed genes as cDNAs
(7) individual mutations known to cause disease
(8) variation between people not associated with disease (polymorphisms)
(9) cloning vectors, formed from bacterial DNA, which are used to replicate DNA sequences
(10) expression vectors, also formed from bacterial DNA, which are used to express proteins in replicated DNA sequences
(11) isolated host cells transformed with expression vectors, which are cells that have been created to express particular proteins
(12) amino acid sequences (proteins)
(13) the use of such proteins as medicines
(14) antibodies, which are used as markers

[103] Taken from Nuffield Council of Bioethics, The Ethics of Patenting DNA, 2002, 25 (hereinafter Nuffield Report 2002).

(15) nucleic acid probes, which are fragments of DNA that are used to locate particular parts of DNA sequences

(16) methods of identifying the existence of a DNA sequence or a mutation or deletion in an individual

(17) testing kits for detecting genetic mutations whole genomes

Examples of Genetic Inventions and their Patent Claims:[104]

For genetic inventions many different types of patent can be found, varying as to the kinds of claim used and how the set of claims is structured. One can distinguish at least three common categories of patent in this field:

(A) DNA coding for industrially useful expression products.

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

A typical form of claim 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).

(B) 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 at all.

[104] Taken from OECD report, "Genetic Inventions, IPRs, and Licensing Practices. Evidence and Policies", Paris, 2002, 25 (hereinafter OECD Report 2002).

Patents directed to such genetic testing will usually have the following claim 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 claim may not all be present in a single patent; official patent regulations in certain countries may require them to be divided out 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.

(C) Genes which control biological pathways

Research continues to identify receptors and genes involved in biological pathways. Thus, having located such a gene, 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 *e.g.* viruses into the cell. Typical claims are:

1. The Receptor peptide or polypeptide (protein) of 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).

4.2. DNA sequences as inventions v. discovery

The central provision of Dir. 98/44/EC relating to the patentability of DNA sequences is Art. 5:

> (1) The human body, at the various stages of its formation and development, and the simple discovery of one of its elements including the sequence or partial sequence of a gene, cannot constitute patentable inventions;
>
> (2) An element isolated from the human body or otherwise produced by means of a technical process including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element;
>
> (3) The industrial application of a sequence or a partial sequence of a human gene must be disclosed in the patent application.

This article will be the central focus of this section, and equally so of this study. The first question which must be asked is whether DNA sequences are inventions, and potentially patentable, or discoveries, and thus non-patentable. The text of the provision gives us some guidance. It starts by stating that the human body and the simple discovery of any of its elements are not patentable inventions. It is important to emphasise this provision, since Dir. 98/44/EC is often claimed to allow property rights in the human body. The text of the directive could not have been clearer in this respect: under no circumstances can the human body as such be subject to patent protection. This is also correct and logical, because we do not deal here with an invention as defined above in this study.[105] In other words, if one discovers the existence in the human body of a specific DNA sequence without more, this is a mere discovery. This is also laid down in recital (16) of Dir. 98/44/EC: "Whereas patent law must be applied so as to respect the fundamental principles safeguarding the dignity and integrity of the person; whereas it is important to assert the principle that the human body, at any stage in its formation or development, including germ cells, and the simple discovery of one of its elements or one of its products, including the sequence or partial sequence of a human gene, cannot be patented; whereas these principles are in line with the criteria of patentability proper to patent law, whereby a mere discovery cannot be patented."

[105] See sub 3.3.

The situation is different when I isolate the DNA sequence from its natural environment, and when I separate the exons from the introns.[106] In that case I have made an invention, since I have isolated via a reproducible technical process the DNA sequence from the human body, and I have made a selection in the sequence, i.e., I have selected those parts of the sequence I am interested in. I will basically also copy that sequence, and then I have made cDNA, which does not occur as such in nature. All these elements make that the DNA sequence I have isolated is not a mere discovery but an invention, which provides a teaching to methodical action. The isolated sequence is not a product of nature, but a product derived from nature. As already pointed out above, also the directive makes this distinction.[107]

The European Court of Justice has also made this point clear in the Netherlands v. Dir. 98/44/EC case: "As regards respect for human dignity, this is guaranteed in principle by Art. 5(1) of the directive which provides that the human body at the various stages of its formation and development cannot constitute a patentable invention. Nor are the elements of the human body patentable in themselves and their discovery cannot be the subject of protection. Only inventions, which combine a natural element with a technical process enabling it to be isolated or produced for an industrial application, can be the subject of an application for a patent. Thus, as is stated in the twentieth and twenty-first recitals of the preamble to the directive, an element of the human body may be part of a product which is patentable but it may not, in its natural environment, be appropriated. That distinction applies to work on the sequence or partial sequence of human genes. The result of such work can give rise to the grant of a patent only if the application is accompanied by both a description of the original method of sequencing which led to the invention and an explanation of the industrial application to which the work is to lead, as required by Art. 5(3) of the directive. In the absence of an application in that form, there would be no invention, but rather the discovery of a DNA sequence, which would not be patentable as such. Thus, the protection envisaged by the Directive covers only the result of inventive, scientific or technical work, and extends to biological data existing in their natural state in

[106] Introns are the parts of the DNA sequence which do not code for a protein. They can be found amidst the exons, which are the parts of the DNA sequence which code for a protein.

[107] See Art. 3(2) Dir. 98/44/EC.

human beings only where necessary for the achievement and exploitation of a particular industrial application."[108]

All this should make it clear that DNA sequences isolated from the human body are inventions. Another issue is whether patents will be granted for those sequences, since that will depend on the fulfilment of the patentability criteria, which will be further discussed later in this study.

Even though Dir. 98/44/EC has taken a correct view in allowing patents for isolated DNA sequences, and should as such not be the subject of further doubt, there is, however, a recital in the directive which gives more reasons for discussion. In recital (23) of Dir. 98/44/EC it is said that "whereas a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention." In the view of this author, this interpretation deviates from the basic principles of patent law applicable to chemical inventions. Isolating the substance via a reproducible technical process is sufficient to fulfil the requirement of being an invention under traditional chemical patent law. It is of course another question whether such a substance can be patentable in view of the patentability requirements of especially inventive step and industrial application.[109] It is not a general principle of patent law that the product produced or prepared must contain technical information. It is sufficient that the substance is provided by a reproducible technical process. But what is more disturbing, and which has also an influence on the first argument, is the choice of wording, which is unclear as the text refers to DNA sequences not containing any technical information. What does this exactly mean? What is the technical information contained in a chemical substance? It performs a specific function, that is true, but is that to be called technical information? And reference to the function is more an issue to be analysed in the context of the industrial application requirement than it is a constitutive part of the concept of 'invention'.[110]

Apparently, the directive has laid down a new rule for the patentability of DNA sequences. For this type of inventions, the function is an inseparable part of the technical teaching. A DNA sequence claim which does not provide a/the function can according to the directive not be considered to be an invention, and thus is no

[108] Judgement of the ECJ of 9 October 2001, Kingdom of the Netherlands/Council and European Parliament, C-377/98 [2001] ECR I-7079, at point 71-75.

[109] For a detailed discussion of these requirements applied to DNA sequences, see below 4.5. and 4.6.

[110] There are different views on this, however.

teaching to methodical action.[111] Some authors have indeed also defended the position that industrial application cannot be separated from the concept of invention or technical teaching, and as such it is required to provide an industrial application to fall within the category of the concept of 'invention'.[112] According to this line of reasoning, the distinction between a discovery and an invention lies in the goal to be achieved. An invention aims at a specific technical application of the teaching. That makes the industrial application as an integral part of the 'invention' concept.[113]

Under traditional chemical patent law principles, the preparation of a substance without known function would be a teaching to methodical action, being the technical process to prepare those sequences. But it is indeed not a patentable invention because some of the patentability requirements are not fulfilled (basically inventive step and industrial application). It is then also surprising that the Directive deviates from this principle in the case of patentability of DNA sequences. This is even more so because recital (22) confirms that DNA sequence claims are to be subject to the same principles and requirements as applicable in other fields of technology. But recital (8) clears the way for the EC to deviate from this principle with a view to take into account the specific nature of DNA inventions: "Whereas legal protection of biotechnological inventions does not necessitate the creation of a separate body of law in place of the rules of national patent law; whereas the rules of national patent law remain the essential basis for the legal protection of biotechnological inventions given that they must be adapted or added to in certain specific respects in order to take adequate account of technological developments involving biological material which also fulfil the requirements for patentability."

There is thus some confusion as to the exact ambit of the concept of invention in terms of technical character and function of DNA sequences. It is then also very important that this unclarity be resolved for the future. However, this may take a while, since the directive is addressed to the member states that have to transpose it, and there is no guarantee that a uniform interpretation will see daylight in the near future. A single European patent system and a single European patent court

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111 See, STRAUS, J., Produktpatente auf DNA-Sequenzen – Eine aktuelle Herausforderung des Patentrechts, GRUR, 2001, (1016) 1018.

112 In this sense e.g. OSER, A., Patentierung von(Teil-)Gensequenzen unter besonderer Berücksichtigung der EST-Problematik, GRUR Int., 1998, 649 et seq.

113 See e.g., SELLNICK, H.-J., Erfindung, Entdeckung und die Auseinandersetzung um die Umsetzung der Biopatentrichtlinie der EU, GRUR, 2002, (121) 123.

could provide a welcome answer to resolve this issue. It is also interesting to observe that, even though the EPO has taken over the provisions of Art. 5 Dir. 98/44/EC in Rules 23(b)-(e) EPC, the abovedescribed interpretation of these provisions does not seem to correspond with the current position of the EPO vis-à-vis the concept of an invention and its distinction with the patentability requirement of industrial applicability or any other patentability requirement.

4.3. DNA sequences and novelty

Novelty does not present many specific issues to be dealt with in the area of DNA sequence patent applications. To the extent that DNA sequences are claimed which have not been prepared before, the invention fulfils the novelty requirement. In the analysis of novelty, one has to take into account what has been said above in respect of the distinction between invention and discovery. Sometimes, the objection is raised that DNA sequences are not new, because they are already existing in nature. We have seen above that this is not a correct application of patent law. What is claimed is not the DNA sequence as it occurs in nature in the human body. What is claimed is the isolated sequence, performed by a technical process. And what is even more, what is claimed are those parts of the DNA sequence or gene which code for a protein, i.e., the exons. In other words, what is in effect claimed is not identical to what is already existing, and as such it is new from the point of view of patent law.

The directive uses in Art. 5(2) the wording “even if the structure of that element is identical to that of a natural element”. This choice of wording could cause some confusion for the following reason. If the sequence isolated from the human body is identical in structure to the one occurring in the human body, one could argue that the sequence is not novel. If one compares the situation to classical chemistry: is a chemical substance new if it is identical in structure to the substance occurring in nature? The only new element here is the fact that it has been isolated. Makes the mere isolation of a substance existing in identical form in nature the substance new? In the already mentioned German Antamanid case, it was held by the Bundespatentgericht that the substance as isolated and its function were unknown to the man skilled in the art at the time of application, and he was neither capable of using the substance prior to the application date. That alone makes the substance as claimed a new substance. In other words, a substance which already existed in nature before application date, but whose existence and function were unknown, cannot destroy novelty of the later isolated substance, which can have an identical structure. But the Directive refers to some qualifying features in recital (21) which could let us believe that indeed the mere fact that a substance is found, which is

identical to a substance occurring in nature, does not necessarily make it a new substance: "Whereas such an element isolated from the human body or otherwise produced is not excluded from patentability since it is, for example, the result of technical processes used to identify, purify and classify it and to reproduce it outside the human body, techniques which human beings alone are capable of putting into practice and which nature is incapable of accomplishing by itself." The wording 'identical structure' is thus to be qualified such that it means that the substance is prepared in a purer form and/or contains coding sequences. These coding elements are also part of the structure of the naturally occurring DNA, and to that extent the structure could be identical, but the invention is nevertheless novel since the selected elements are as such not yet existing.

The substance becomes definitely new and fulfils the novelty requirement if it is not merely isolated but is also prepared in a purer form, at least to the extent that the chemical structure is not identical to that already belonging to the state of the art.[114] In some cases, this will be the situation at hand. This means consequently that such a substance fulfils the novelty requirement. If we come back now to DNA sequences: in the light of the Antamanid case, it could be argued that the DNA is new, since it was unknown to the man skilled in the art at application date, and neither was its function known.

However, the situation described above is rather hypothetical, since the DNA sequence will in most cases be claimed as a cDNA sequence, which does not occur in nature, and is thus for that reason alone new. It is also new if the sequence claimed contains only the coding parts, because the sequence as it occurs in nature also contains non-coding parts.

But even if one would accept the reasoning, for the sake of argument, that a product can never be novel if it already existed in nature before, there is still the fact that the process for producing the product which is as such known in nature, can be patented. And according to a general principle of patent law, protection for a patented process extends to the product immediately produced by the patented process (Art. 64(2) EPC). That means that protection can extend to products which are as such not new.[115] In other words, and applying this principle to DNA

[114] This point has been described in more detail earlier in this study, see sub 3.4.1.

[115] T 0150/82, "Claim categories/IFF", decision of Technical Board of Appeal 3.3.1 of 7 February 1984, OJ EPO, 1984, 309; T119/82, "Gelation/Exxon" decision of Technical Board of Appeal 3.3.1 of 12 December 1983, OJ EPO, 1984, 217; Kirin Amgen Inc., Ortho Biotech Inc, Ortho Biotech Products, Lp V. Hoechst Marion Roussel Limited, Hoechst Marion Roussel Inc., Transkaryotic Therapies Inc., UK Court of Appeal, 31 July 2002, [RPC] 2003, 1.

inventions, if one starts from the hypothesis that an invention claiming a DNA sequence already existing in nature and having an identical structure as the sequence already existing in nature, cannot be claimed in the form of a product claim due to lack of novelty, it is still possible to obtain patent protection for that DNA sequence indirectly, in view of the extent of protection of the assumed patented process (to produce the DNA sequences) to the product immediately produced by that patented process, i.e., the DNA. But even under this hypothesis, it will never be possible to obtain patent protection for products or elements in their natural environment. The Community legislator has included some safeguards against claiming products of nature in their natural environment. If the substance produced by a patented process is identical to a substance already existing in nature, the patent cannot extend to that already existing substance in its natural environment. This is laid down in recital (20) of the directive: "Whereas, therefore, it should be made clear that an invention based on an element isolated from the human body or otherwise produced by means of a technical process, which is susceptible of industrial application, is not excluded from patentability, even where the structure of that element is identical to that of a natural element, given that the rights conferred by the patent do not extend to the human body and its elements in their natural environment." DNA sequences in the human body thus remain excluded from patentability, and cannot even be covered indirectly by a process patent under Art. 64(2) EPC.

Worth mentioning in the context of novelty is also that the mere fact that a DNA sequence claimed was already existing in a DNA library is not novelty destructive vis-à-vis the sequence claimed,[116] in view of the fact that the sequence, which is present in the DNA library is not readily available to the public. Thus, the presence of DNA sequences in identical form in a DNA library is not as such novelty destructive vis-à-vis an identical DNA sequence claimed in a patent application. It is to be seen to what extent this case law is still applicable today, in view of the automated processes of DNA sequencing, and the enhanced performance of computer programmes to retrieve sequences. What can be said, however, is that patentability of specific DNA sequences within a library will remain possible from the point of view of European patent law, if an unexpected effect can be demonstrated which these specific DNA sequences might have, thus fulfilling the inventive step criterion. The automated processes do not necessarily take away potential unexpected effects of specific sequences. It will then be considered to be a selection invention.

[116] T 0301/87, "Alpha-interferons/BIOGEN", OJ EPO, 1990, 335.

4.4. Overlapping sequences

One of the concerns which might become more explicit in the future is related to the situation that various partial DNA sequences are 'in competition' with each other, in the sense that they partly overlap. The concern relates to the question as to what extent a patent on a partial DNA sequence can have an effect on later claimed or disclosed sequences, with which the first patented sequence overlaps in part. The effect can be that, having regard to the scope of the patent for the partial DNA sequence and the overlap, later disclosed sequences could be considered to fall under the scope of the earlier patent, and for that matter also the full length gene. Any use of those other sequences could then be considered to constitute a patent infringement. Such a situation could have a negative effect on the incentives to disclose later partial DNA sequences or the full-length gene, and to patent and use those.

The Directive has laid down the principle that overlapping sequences do not necessarily jeopardise the patent value of later claimed sequences: "Whereas, for the purposes of interpreting rights conferred by a patent, when sequences overlap only in parts which are not essential to the invention, each sequence will be considered as an independent sequence in patent law terms."[117] It must be made clear, however, that recital 25 does not talk about the patentability requirements vis-à-vis the full-length gene or more generally later claimed sequences. It refers to the rights conferred by a patent. According to this recital, the rights conferred to a (or more) patent(s) for partial DNA sequences are limited so that the scope cannot extend to other DNA sequences with which the patent(s) overlap(s), or with the full length gene for that matter, provided that the overlap takes place in parts which are not essential to the invention. The recital does presuppose the existence of an earlier patent for a partial DNA sequence. In effect, this recital refers to the post-grant issue of determining the scope of the patent. Since the rights conferred to a patent for a partial DNA sequence do not extend to other sequences which only overlap with this patented sequence in non-essential parts, no patent infringement will take place if a later patent is being granted for other sequences which partly overlap in the said manner, or if sequences as referred to are being used for more than pure research purposes.

Problems could thus arise if the DNA sequences overlap in "parts which are essential to the invention". But it is exactly that crucial part of the sentence which

[117] Recital (25) Dir. 98/44/EC.

is also the cause of unclarity. What is exactly meant with these words? Does one mean here that if the overlap is situated in a part of the sequence which performs a function, e.g., coding for a protein, being a linker, adaptor, primer, promotor sequence etc., this is presumed to be an essential function and is thus presumed to be essential to the invention? Or is the interpretation limited to a key function of the sequence, which could then be the coding for a protein? And how does one link this to the criterion that the sequences(s) has/have to be essential to the invention, in particular when the invention claims a number of functions, such as e.g. coding for a protein and use in diagnosis or drug discovery? The issue is even more important in the context of so-called spliced genes, which have many functions, and can even code for more than one protein. The wording of the directive does not give much guidance, thus making a uniform interpretation a welcome alternative.

This recital, however, does not provide a rule relating to the patentability of the various partial DNA sequences. As far as their patentability is concerned, the well established general principles of novelty, inventive step and industrial application will apply. A patent application for a partial DNA sequence could still be patentable, it will probably be considered to be a selection invention, a concept already well known in the chemical field of patent law, if all patentability requirements are being fulfilled. As far as selection inventions in general are concerned, it could be said that the concept of a selection patent is that it is a patent granted for making an invention in a field which is, in general terms, already known.[118] Formally, selections involve the recognition of a defined sub-group, sub-range or sub-area as novel embodiments within a generally disclosed broader group, range or area of entities or of processes already known in the prior art, without adding any new feature to the definition.[119] The invention can then only be the selection of a particular compound or relatively small group of compounds from the larger group previously disclosed in broad terms.[120] Actually, selection patents could be described as special cases of improvement patents. There is abundant case law making selection patents possible in the chemical field,[121] and

[118] JEFFS, J., Selection patents, EIPR [1988] 10, 291.

[119] SZABO, G.S.A., Problems concerning novelty in the domain of selection inventions; 20 IIC, 1989, 295.

[120] GRUBB, P.W., Patents in chemistry and biotechnology, Clarendon Press, Oxford, 1986, 131.

[121] E.g., T 0198/84, "Trichloroformates/HOECHST", OJ EPO, 1985, 209 ; T 0007/86, "Xanthines/DRACO", OJ EPO, 1988, 381 ; T 0188/83, "Vinyl acetate/FERNHOLZ", OJ EPO, 1984, 555 ; T 0182/82, "Spiro compounds/CIBA-GEIGY", OJ EPO, 1984, 401.

these principles apply mutatis mutandis to DNA. These selection patents will be dependent patents, however.

But what about the patentability of the full-length gene which will evidently overlap with one or more partial DNA sequences already claimed and patented earlier? This is an important issue in the sense that automated processes are able to produce rather quickly partial DNA sequences, possibly ESTs.[122] There is a justified fear that if these partial gene sequences could destroy the patentability of the full-length genes, research could be jeopardised in this area. The full-length gene could still be considered novel, since not disclosed earlier, and in view of its function(s), it could also be inventive, if unexpected effects can be demonstrated. It will be a dependent patent, however. But to the extent that the overlap with earlier patented partial sequences is in parts essential to the invention, it can be doubted whether such a patent will be granted, probably due to lack of inventive step. In this context it is also worth observing that the mere disclosure of partial DNA sequences without any known function, in other words just raw data, will probably not have a deleterious effect on the patentability of the full length gene, in view of the fact that the function demonstrated with the full length gene might be considered to be inventive vis-à-vis the earlier disclosed partial DNA sequences without function. It is impossible at this point, however, to give a definite answer to these questions, as this will depend on the specific cases at hand. But, as it has already been demonstrated in the chemical field, the patent system is sufficiently flexible to provide patent protection for inventions which fulfil all patentability requirements, be it that in some cases these patents will be dependent ones.

4.5. DNA sequences and inventive step

Fulfilment of the inventive step criterion for DNA inventions is in the light of present day technologies a more difficult hurdle to take than it was some years ago. Inventive step could in principle be found in the difficulties accompanied with providing or preparing a specific substance, in our case DNA. But in view of present day automated techniques, where computers do the whole sequencing process (in silico analysis), it will be rather difficult to prove that the mere preparation of the DNA sequence is sufficient to make the invention non-obvious

[122] An EST is part of a sequence from a cDNA clone that corresponds to an mRNA. An EST can therefore be used as a sequence-tagged marker to locate that gene on physical map of the genome.

or inventive.[123] This is similar to the chemical field, where the mere preparation of a chemical compound is basically not inventive, except in the event that it would be a new structure.

It will thus be necessary to demonstrate other unexpected effects in order to fulfil the inventive step requirement. In this context, one could think of unexpected effects in the area of the substances prepared, which specific protein can be produced with the DNA sequence, and what the specific function of that protein might be. Inventive step might also be evidenced if for example a gene involved in breast cancer, is later found to be also useful for prostate cancer, and the latter use would be an unexpected new effect. To the extent that such a new use can be considered to be a reasonable logical new step, it is less plausible that such a new patent claim will be able to pass the inventive step hurdle. For the specific example mentioned, it could thus also be concluded by the patent office that it is a predictable result to find that the gene in question can also be used for other cancers than the one it has been originally patented for. A claim for an oligonucleotide could also fulfil the inventive step requirement if evidence can be provided that it can be used as a marker associated with diagnosis or disease. Inventive step could also be found in the use of the DNA sequence as a diagnostic tool, or in the use of DNA sequences to control biological pathways, such as for example a specific DNA sequence binding to a specific receptor involved in disease, in which case the DNA is used as a target for diagnosis and drug discovery.

This more stringent interpretation of the inventive step requirement is of importance for the analysis of partial DNA sequences such as ESTs and SNPs.[124] For ESTs, which are partial sequences, and where it is not known whether and for which protein they could code, it will be difficult to pass the inventive step hurdle, since the only feature which is demonstrated is the preparation of the sequence, and a potential use as a probe to find the full gene. But such an application cannot be considered to be surprising or unexpected. If, however, the EST could be used as a

[123] In this sense also, SCHRELL, A., Funktionsgebundener Stoffschutz für biotechnologische Erfindungen?, GRUR 2001, (782) 786: "Nicht mehr derjenige ist innovativ tätig, der routinemäßig DNA-Sequenzen und rekombinante Proteine bereitstellt, sondern vielmehr der, der eine gewerblich anwendbare Funktion aufzeigt."

[124] SNPs are sites in the genome where there is single-base variation among the population of one particular base in the sequence. They occur about once every 1,000 bases along the three billion bases of the human gene. SNPs may be responsible for variations between individuals, including variations which predispose an individual to disease or cause it.

marker (which will be rarely the case), then it could pass the inventive step hurdle. For SNPs, since they are often associated with disease and/or diagnosis, it will be easier to fulfil the inventive step requirement if these features are indeed unexpected or surprising.

The situation is different in the US, where, following the teaching of In re Deuel,[125] a claim for a DNA sequence is prima facie non-obvious if there is no structural similarity to what is known in the state of the art.[126] And since a new DNA sequence claimed is by definition different in structure from other DNA sequences known in the state of the art, prima facie non-obviousness is easy to accomplish. Such an approach does indeed not take into account the processes for preparing and producing these sequences, which, as we have seen above, are automated. The approach of the EPO is therefore in the view of the author the better one.

4.6. DNA sequences and industrial application

4.6.1. The resurrection of the industrial application requirement for biotechnological inventions

The industrial application requirement has gained dramatically in importance since the advent of gene technology. Whereas in the past, this requirement had a rather dormant existence, it has now become a crucial feature in the battle pro and contra patenting DNA. The 1995 NIH patent applications for ESTs without any known function were the cause of this turmoil.[127] Patent offices and governments felt a need to do something against such practices, in view of the potential negative effects on scientific research. This feeling was shared both by publicly funded research institutions and the business community. The idea that patents would be granted for more or less raw data without any known practical utility and no known function was difficult to accept. All over the world, the patent community started thinking about strategies to avoid this type of patent applications in the future. How was this to be tackled in the most efficient way, taking into account basic principles of patent law? The utility or industrial application requirement appeared to be ‘useful’ in this respect.

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125 In re Deuel, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (CAFC 1995).

126 See BOSTYN, EPO, 2001, 118 et seq.

127 For more details, see BOSTYN, EPO, 2001, 134 et seq., with further references.

The industrial application or utility requirement was thus bombarded to become one of the most important criteria in the evaluation of biotechnological patent applications. Problem was, and still is, that due to the fact that this particular requirement has had a rather dormant existence in the past, an exact interpretation was not easy to give. It took the USPTO for example until January 2001 to promulgate new Guidelines for the application of the utility requirement to patent applications. According to these Guidelines, which are also applicable to DNA related inventions, "a claimed invention must have a specific and substantial utility. […] An invention has a well-established utility (1) if a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (2) the utility is specific, substantial, and credible". The EPO has in a recent Opposition Division case also interpreted the industrial application requirement in a manner which shows striking similarity to the wording used in the USPTO Guidelines, even though the requirements in both systems are not identical, i.e., utility in the USA and industrial application within the EPC system.[128] It was held at that occasion that "the potential uses disclosed in the application are speculative, i.e. are not specific, substantial and credible and as such are not considered industrial applications." Question remains with this case whether this interpretation is also supported by the text of the EPC and its traditional interpretation. There is no precedent in case law of the Technical Board of Appeal or the Enlarged Board of Appeal which gives a similar interpretation to Art. 57 EPC. Problem with the use of the wording 'credible' is also that it is not exactly clear what is meant here: what is exactly credible; is a theoretical possibility sufficient for an invention to have a credible use?[129]

Dir. 98/44/EC has already recognised in 1998 the importance of the industrial application requirement in the framework of DNA inventions. It has laid down an express provision in Art. 5(3) saying that the industrial application of a DNA sequence or partial sequence must be disclosed in the patent application. As such, this is a clear rule, but at the same time it leaves open some questions. It must be admitted, this provision of the directive has turned out not to be the most fortunate one of the directive, in view of the divergent interpretations to which its wording might give rise. These variations will be discussed here. It could generally be said that this provision has been inspired by the NIH patent applications, where patent

[128] See, "ICOS/SmithKline Beecham and Duphar International Research", decision of the EPO Opposition Division of 20 June 2001, OJ EPO, 2002, at 293 et seq.

[129] In this sense also Nuffield Report 2002, 31.

applications were filed for partial DNA sequences without any known function. It tributes justice to the framers of the directive to keep that in mind.

4.6.2. Art. 5(3) Dir. 98/44/EC, mere clarification, or more?

But some will argue that such an explanation alone, i.e., that Art. 5(3) merely articulates the industrial application requirement as already existing under Art. 57 EPC, will not be sufficient. There are a number of consequences which could be drawn from this provision. Accepting that it was a mere clarification of the industrial application requirement as it already exists under European patent law is not per se a straightforward assumption. If one considers that the legislator is economical with words, it can be questioned why it has been mentioned, since it does not add anything to current patent law. And that is what makes the provision rather unfortunate. If, as has been said hereabove, the framers of the directive had the NIH applications in mind, and if they thus wanted to avoid that patent applications for DNA sequences without any function might be successful, there was no need to add this provision in the text of the directive, as this was already a well established principle under EPO practice, and in most member states. Hence, it would have been better not to have this provision added to the text of the directive.

The fact that it is in the text of the directive has given ideas for interpretation to people keen on exegesis of the text of the directive. And after performing this exegesis, some might be tempted to assume that the scope of this provision must be broader than a mere clarification. It is definitely a clarification of the industrial application requirement, which is also made clear in recital (24): "Whereas, in order to comply with the industrial application criterion it is necessary in cases where a sequence or partial sequence of a gene is used to produce a protein or part of a protein, to specify which protein or part of a protein is produced or what function it performs." But that still does not explain why this provision was included in the articles of the Directive. An interpretation which might be given, after exegesis, is that it was the intention of the framers of the directive to limit the scope of protection of the patent to the function mentioned in the patent application. They are also helped by the fact that the text refers to the wording '<u>the</u> function'. It would have been clearer if the text would have sounded '<u>a</u> function', in which case the only conclusion which could have been drawn would have been that it is a mere, be it redundant, restatement of the industrial application requirement as it has been applied consistently by for example the EPO.

And this brings us also to recital (23), which makes things more complicated: "Whereas a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention." This could lead one to the conclusion that mentioning the function is a constitutive element of the concept 'invention', so that one cannot assume that an invention in the sense of a teaching to methodical action has been achieved if no function has been disclosed.[130] And if mentioning the function of the DNA sequence is a constitutive element of an 'invention', one could draw from such an assertion that this function must be mentioned in the claims of the patent application. And if the function is to be mentioned in the patent claims, then by definition, the scope of the patent will be limited to the function mentioned.[131]

In other words, the combination of Art. 5(3) and recital (23) could lead someone to the conclusion that the European legislator had purpose-bound patent protection in mind. Worth observing in this context, and further evidencing the confusion surrounding Art. 5(3) Dir. 98/44/EC, is that the European Court of Justice held in its ruling concerning the claim against Dir. 98/44/EC that "the protection envisaged by the Directive covers only the result of inventive, scientific or technical work, and extends to biological data existing in their natural state in human beings only where necessary for the achievement and exploitation of a particular industrial application."[132] The Court refers to 'a particular industrial application', which could also be an argument to be used by proponents of the purpose-bound variant. Such a solution would be a deviation from the traditional patent law principles known in chemical patents, where disclosing the chemical compound does in general provide an absolute product protection for the substance, i.e., not limited to a specific function or use of that substance. Besides the question whether the Community legislator has intended to limit the scope of DNA patents to the specific function disclosed in the patent application, there is of course also the independent question as to whether limiting patent protection for DNA sequences to the function disclosed would be a solution which would benefit scientific research without narrowing down the scope of DNA patents to a level that investment in this area becomes an uninteresting option. Since the type of

130 This has already been discussed in detail earlier in this study, see sub 4.2.

131 In this sense also, SELLNICK, H.-J., loc.cit., (121) 124.

132 Judgement of the ECJ of 9 October 2001, Kingdom of the Netherlands/Council and European Parliament, C-377/98 [2001] ECR I-7079, at point 75.

protection for DNA inventions will be discussed further in this report, the latter question will be dealt with later in this background study.[133]

In the EPO Guidelines, Art. 5(3) Dir. 98/44/EC, which has been implemented in Rule 23e(3) EPC, is explained as follows: "In general it is required that the description of a European patent application should, where this is not self-evident, indicate the way in which the invention is capable of exploitation in industry. In relation to sequences and partial sequences of genes this general requirement is given specific form in that the industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application. A mere nucleic acid sequence without indication of a function is not a patentable invention (EU Dir. 98/44/EC, recital 23). In cases where a sequence or partial sequence of a gene is used to produce a protein or a part of a protein, it is necessary to specify which protein or part of protein is produced and what function this protein or part of protein performs. Alternatively, when a nucleotide sequence is not used to produce a protein or part of a protein, the function to be indicated could e.g. be that the sequence exhibits a certain transcription promotor activity."[134] Such an interpretation makes sense, but must be placed in the framework of and vis-à-vis the considerations given hereabove.

It would again be welcome to have a uniform interpretation of this crucial provision of the Directive. This is even more so because this very provision has obtained a prominent role in some proposals for transposition of the directive in a number of countries. In the view of the author, it could be said that the framers of the directive did not have a purpose-bound product protection in mind when they drafted this provision, but were merely concerned with the possibility that patents would be granted for DNA sequences without any known function. The unclear wording of the directive, however, together with the fact that for transposing the directive, in principle only the text of the directive and its recitals are relevant, might lead to other interpretations. It would in any event have been much better if the wording 'a function' would have been used, which would have avoided much confusion. But probably, it will be up to the European Court of Justice to rule on this matter in the future.

133 See further below sub 4.7.

134 See EPO Guidelines C.IV. 4.6.

4.7. What form of protection for DNA sequences; Purpose-bound product protection?

4.7.1. Types of patents and effects on scope

Basically, there are only two possible types of claims which can be used, i.e., product and process claims. Other types of claims are all variants of these two basic claim types. One variant which is also of interest for this study is the so-called purpose-bound product claim, which is a product claim which is confined to the specific purpose or function mentioned in the claim. The use of these claim types and the potential restriction on the use of some of these claim types imposed upon by the legislator, has been the subject of a heated debate over time, especially in the field of chemical inventions. This debate has been 're-heated' with the advent of biotechnology. The discussion is particularly intense when it comes to DNA sequences. It is partly a consequence of the opposition that has been expressed against the patentability of this type of inventions. While this opposition was at the very beginning aimed at a prohibition of the patentability of DNA sequences, it soon became clear that at least some people were more concerned about the scope of this type of patents and the possible consequences for scientific research than they were fundamentally opposed against any form of patentability of DNA inventions. This is particularly true for university researchers, where a considerable number of scientists are not opposed to the patent system as such, but are opposed to patenting DNA sequences because of the broad scope which might be attached to these patents and the detrimental effect these patents might have on their scientific research.[135] This opposition is also caused by a lack of knowledge of the existing checks and balances already present in the patent system, which are partly also the focus of this report, and the existence, at least in Europe, of a statutory research exemption.

With scope is meant here, the extent to which the patent granted has an effect on activities of third parties, be it at the level of hindrance to produce a specific product, or at the level of (not) being able to carry out specific scientific research. In other words, it refers to some extent to the strength of the patent. This brought the discussion to the level of the best form of protection for DNA sequences, so as

[135] In a recent report of the Netherlands Royal Academy of Arts and Sciences, this was also acknowledged. See, De gevolgen van het octrooieren van humane genen voor het wetenschappelijk onderzoek in Nederland: Advies van de Commissie Genoctrooien, Amsterdam, KNAW, 2003, at 25 et seq.

to indeed avoid that scientific research would be needlessly hampered, without neglecting, however, the advantages of allowing patents on DNA inventions for the advancement of science and drug discovery. Indeed, the discussion is thus linked to scope of patents. Economic research has shown that overbroad patents might have a negative effect on scientific research in general, both in public and private sector, as much at it has shown that patents are indispensable in research and investment intensive areas of science and technological development.[136]

The scope or strength of a patent can be influenced by various means, directly or indirectly. As already made clear earlier in this study,[137] the patentability requirements of novelty, inventive step, utility and sufficient disclosure have an indirect effect on patent strength. For novelty and inventive step the influence lies in the fact that if the threshold becomes higher, small, incremental, and by definition narrow patents will be less easy to obtain, which will have an effect on issues such as patent and royalty stacking, to be discussed later in this study.[138] Drawback of emphasising on these parameters is that the influence on scope could be deceiving, in the sense that more than incremental innovations, with potentially broader scope, are not touched. Industrial application has an obvious influence in the sense that raw data are not patentable since they do not divulge any specific function. Interpreting the industrial application requirement in a specific way prevents to some extent upstream patents in very early stages of technological development.

The type of claim one allows (product, process, use, purpose-bound claim) also has a major effect on the scope of the patent, a product claim having the broadest potential scope, in view of the specific feature of absolute protection attached thereto. If a patent holder has a patent for a product, protection extends in principle to every manner of producing and to all uses of that product. That is potentially a broad protection, definitely if one knows that the product claimed might have various functions (uses), which the patent holder has not entirely described in his patent application. It must be clear from the outset, however, that product protection does not by definition allow to claim future inventions. Future uses can be the subject of new patent applications. Those patents will be dependent, however. And it must also be emphasised that the disclosure requirement, the

136 See earlier in this study, when the economic rationale of the patent system was discussed, sub 3.2.

137 See sub 3.5.1.

138 See sub 8, and passim.

principles of which we have already discussed earlier,[139] should also prevent patent applicants from claiming future uses which they have not disclosed in some way in the patent application.[140]

4.7.2. Full product protection for DNA

What does full product protection for DNA sequences exactly mean? One of the core features of full product protection is, as already said before, that the protection is absolute, i.e., that the patent covers the product for any use of the patented product and for all processes to make it. This is a general rule of patent law which is also applicable in traditional chemistry cases.[141] Worth observing in this context is that this feature is not based on any specific statutory provision, but is based on established case law. In the case of the EPO, there is relevant case law at the highest level, i.e., the Enlarged Board of Appeal. In case G 0002/88, it was held that "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)."[142] Applied to DNA sequence inventions, this would mean that once the invention as claimed in the patent application is capable of passing the novelty, inventive step, industrial application and sufficient disclosure requirement, it covers all uses of the DNA sequences, present and future, and all processes to produce the patented DNA sequences. In view of the fact that DNA can have various functions, not only in the sense that it codes for one or more different proteins (spliced genes),[143] but also that it can be used for different purposes, such as in diagnosis and drug targeting,

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139 See sub 3.5.3. – 3.5.5.

140 This does not take away the fact that an invention can be the application of a general principle, in which case not all uses must be disclosed expressis verbis in the application.

141 E.g., BGH 'Imidazoline', BGHZ 58, 280; GRUR, 1972, 541.

142 G 0002/88, "Friction reducing additive/MOBIL OIL", OJ EPO, 1990, 93, at 5. of the reasons.

143 With the phenomenon of spliced genes is meant the technology where the RNAs made from the genes are spliced, being reflected in the cDNAs prepared from these in the laboratory. In other words, alternative splicing takes place at the level of of genomic DNA – RNA. To date, the most frequent application of alternative splicing results in several slightly different variants of the same protein, all with the same function. It is possible, however, that one finds completely different protein.

scope of protection can be potentially broad. Absolute protection could potentially give the patent holder of the DNA product patent the rights to control these other uses. It deserves special attention that such a statement without more is actually not a correct view of the patent system, in view of the checks and balances within the system, which will be clarified hereunder.

The effects of full product protection in the area of DNA could thus theoretically be substantial. It could also act as an encouragement for researchers/inventors to apply for a DNA patent at an early stage, in view of the positive effects of control over later uses. This might have negative consequences for scientific research and the advancement of technology, for reason that the full product protection and the control potentially exercised might deter others from entering into the same field of research. It has also an increasing effect on transaction costs for new inventions, based on the DNA patent, for which a license has to be obtained before use. This could lead to royalty-stacking.[144] In the worst case scenario, it could have a stifling effect on scientific research. The fact that scientific research has demonstrated that a large number of our genes are so-called spliced genes, i.e., genes that code for more than one protein, and thus multi-functional, has made the problem even more complicated. It must be emphasised, however, that most of these effects have not been evidenced in practice yet. Hitherto, there is no substantial quantifiable effect to be measured. This does not mean that these potential effects can be neglected, and it is important that there is a debate about these phenomena.

4.7.3. The specific nature of DNA

In view of the potential negative effects described above, some have called to evaluate whether the traditional full product protection known from classical chemistry is still apt to be applied to the specific case of DNA inventions.[145] DNA is special and in that sense different from classical chemical substances in that the value of DNA lies more in the informational nature of the substance than in its chemical composition. It is also special in the sense that there will always be a substantial degree of dependency between downstream DNA patents and upstream DNA patents.[146] There is no alternative if for example a subsequent downstream

144 This will be discussed further below sub 8.

145 See e.g. Nuffield Report 2002, 64-66; OECD Report 2002, 43.

146 In this sense also, DÖRRIES, H.U., Patentansprüche auf DNA-Sequenzen: ein Hinderneis für die Forschung? Anmerkungen zum Regierungsentwurf für ein Gesetz zur Umsetzung der Richtlinie 98/44/EG, Mitt., 2001, (15) 20.

inventor has developed a new medical application for a specific disease caused by a defective gene, which has been the subject of an upstream patent. The downstream inventor is obliged to use the DNA patent. This is not necessarily the case in classical chemistry, where there might be different ways to cure a specific non-genetic condition (for example, headache can be treated with various drugs, based on different chemical compounds). In this context, it is also sometimes said that it is impossible to invent around a gene patent. Such a statement reflects that there is indeed a high degree of dependency possible, but is presumably not completely accurate. The connection of genes with disease is often more complex than one might think at first glance. That makes that the patent for a gene involved in a disease is not necessarily covering the whole picture, as the gene in question might only account for a small percentage of a disease.[147]

On the other hand, there are also considerable similarities between DNA and traditional chemistry. As already said earlier in this study, genes are multifunctional. But this is also true for pharmaceutically active chemical compounds. Examples which are well known in the public are Viagra and aspirin, both having various different functions and applications. And the dependency phenomenon is also well known in traditional chemistry, but has not led to the reactions we see in the field of DNA.

4.7.4. Mitigating factors in respect of full product protection

It cannot be sufficiently emphasised, however, that the situation described above and its potential negative consequences have to be mitigated to a certain extent, in the light of the various patentability requirements, which have in this report been called the checks and balances of the patent system. A full product patent still makes it possible to obtain a patent for a new use which the original patent holder could not have foreseen when he applied for a patent, but that will be a use patent, and not a product patent. Such a patent will be dependent on the product patent of the first patent holder. It is also possible to obtain patent protection for a first medical indication,[148] provided that the original patent holder has not already claimed a first medical indication. But in many cases, the patent holder of the DNA product patent will have already claimed a medical indication,

[147] According to, CRESPI, R.S., Gene and Compound Claims – Another View, 5 Bio-Science Law Review [2001/2002] 1, 3-8.

[148] In accordance with Art. 54(5) EPC. This is a purpose-bound product claim limited to the specific use claimed in the application.

in view of the nature of DNA, implying that a first medical indication claim is not feasible anymore. In the event that such a first medical indication claim is still possible, for example a gene therapy claim, then a first medical indication purpose-bound product claim can be used, in conformity with Art. 54(5) EPC. For a second and subsequent medical indication, a manufacturing process claim is to be used, in conformity with the so-called 'Swiss claim' formula.[149] It is, under certain conditions, also possible to obtain a patent for a new process of preparation of the substance in question. But here, reference is made to what has been said earlier in this report in the context of novelty, i.e., that the mere new process of preparation of a chemical substance does not necessarily make the invention novel under patent law. More is required.[150] Summarising, as a consequence of granting a full product patent for the first inventor who prepared the DNA sequence, all future patents will be dependent on that first patent, but it cannot be said that new developments are therefore per se excluded from patentability, as shown here.

Mitigation also in the light of the enabling disclosure and clarity requirement.[151] The scope of the patent is also determined by the disclosure. That will be particularly relevant for those cases where new uses or indications, or new functions, such as coding for a different protein, are invented. These do not necessarily fall within the scope of the patent of the original patent holder for the DNA product. What cannot be avoided, however, is that these new innovations, if patentable, will remain dependent upon the DNA product patent, as these inventions will use that DNA product. This effect is not fundamentally different from traditional chemistry, however, where the abovedescribed situation could also lead to dependency. But it cannot be said as a rule that full product protection, granted for a DNA sequence, automatically leads to a broad patent, since that will also depend on the level of disclosure made in the patent application.

The potential negative consequences in terms of jeopardising scientific research have also to be put in perspective in another context. One may not forget that most countries in Europe have a research exemption in their patent acts. The research exemption allows third parties to use the patented invention without consent of the patent holder for purely scientific research, without committing an infringement. The extent of that research exemption will have an influence on the level of

149 See G 0005/83, "Second medical indication/EISAI", OJ EPO, 1985, 64.

150 See earlier in this study, sub 3.4.1.

151 Art. 83 and 84 EPC.

scientific research which can be freely pursued without being preoccupied with infringement issues.[152]

In some cases, and this is still another mitigating factor, a compulsory license could be granted in order to force access to the patented material. The requirements for granting compulsory licenses are not entirely harmonised, however, so it is to be seen to what extent this system is capable of influencing potential negative effects of DNA patents on scientific research. It is secondly also to be examined as to whether compulsory licensing is a proper means to influence the said effects, taken that it can have some influence.[153]

4.7.5. Purpose-bound patent protection for DNA?

In view of the potential negative effects of full product patent protection for DNA sequences, and leaving aside whether the evidence for these negative effects is established or not, alternative solutions have been developed. One of these alternatives is to limit patent protection to the specific function described, i.e., the inventor who produces for the first time the DNA sequence will only obtain patent protection for the specific function he is able to demonstrate.[154,155] Subsequent inventors are then also in the position to obtain a purpose-bound product patent for new functions they have discovered. At first sight, this could avoid the dependency problems which are present in an absolute product protection scenario, as described above. This is not necessarily true, however, in the sense that when the new patent

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152 We will discuss the research exemption further below, sub 5.

153 On compulsory licensing, see further below, sub 6.

154 Such e.g., VON RENESSE, M., TANNER, K., VON RENESSE, D., Das Biopatent – eine Herausforderung an die rechtsethische Reflexion, Mitt., 2001, 1-4; NIEDER, M., Die gewerbliche Anwendbarkeit der Sequenz oder Teilsequenz eisnes Gens – Teil der Beschreibung oder notwendiges Anspruchsmerkmal von EST-Patenten, Mitt. 2001, 97-99; VAN RADEN, L., VON RENESSE, D., "Überbelohnung" – Anmerkungen zum Stoffschutz für biotechnologische Erfindungen, GRUR 2002, 393-399; More in nuance, WHITE, A.W., Gene and Compound Per Se Claims: An Appropriate Reward?, 5 Bio-Science Law Review [2001/2002], 239-248.

155 Proponents of absolute product protection, e.g., HANSEN, B., Hände weg vom absoluten Stoffschutz – auch bei DNA-Sequenzen, Mitt., 2001, 477-493; KRAUβ, J., Die richtlinienkonforme Auslegung der Begriffe 'Verwendung' und 'Funktion' bei Sequenzpatenten und deren Effekte auf die Praxis, Mit., 2001, 396-400; CRESPI, R.S., Gene and Compound Claims – Another View, 5 Bio-Science Law Review [2001/2002] 1, 3-8.

for the new function also requires the use of the function of the first or prior patent, in some cases automatically and unavoidably, dependency is still present.[156] The multi-functionality of genes and the complex regulatory mechanisms are, amongst others, responsible for this situation. Consequently, the search for legal certainty which was aimed at with a purpose-bound patent protection, i.e., to avoid an avalanche of dependencies, is not necessarily achieved with a purpose-bound product claim.

There are other arguments which could be put forward against limiting patent protection to the specific purpose disclosed in the patent application. As said hereabove, in theory, the advantage of purpose-bound product protection should be that the determination of the scope of protection is much clearer and straightforward than under full product protection, more or less according to the principle 'what you see is what you get'. But it is an illusionary certainty, however. If for example the patent application refers to the use in the treatment of cancer as the purpose envisaged, is protection then limited to the type of cancer which was clear at the time of application, e.g., breast cancer, or does the patent cover the broader purpose, i.e., cancer? In other words, purpose-bound product claims could give the illusion that protection will be narrowly confined to a very specific, narrow and well defined purpose, but that is not a principle under current patent law, where, as it is recalled here, purpose-bound product protection already exists for the first medical indication of a substance already known in the state of the art. In other words, a new purpose could turn out to fall within the scope of the earlier patent. In other words, the so much looked for certainty and clear cut division, appears to be less real than one might be tempted to believe at first glance.

And this brings us to an affiliated issue, the infringement issue in the post-grant stage. The doctrine of equivalence, which exists in most European countries,[157] be it in a varying form and extent, could also bring with it that someone who applies a substance for a new purpose, relying on the fact that an already existing purpose-bound patent for a specific use will be narrowly construed, could end up in committing a patent infringement. A court might come to the conclusion that the new purpose is sufficiently similar so that it can be considered to be an equivalent

[156] KÖSTER, U., Absoluter oder auf die Funktion eingeschränkter Stoffschutz im Rahmen von 'Biotech'- Erfindungen, insbesondere bei Gen-Patenten, GRUR 2002, (833) 841.

[157] This is a doctrine relating to infringement proceedings, consequently in the post-grant stage, and purely based on national law and judicial interpretation. It could be said, generalizing to a major extent that a product or process is equivalent if the accused item performs substantially the same function in substantially the same way to obtain substantially the same result.

use, thus making it fall under the doctrine of equivalence, and thus leading to a patent infringement. These issues are clearly related to claim interpretation, which is governed by Art. 69 EPC and the Protocol.[158]

Another problem which could arise by broadly applying the purpose-bound product principle relates to the economic consequences. If the so-called new purpose turns out to be a trivial, non-inventive new development, there will be no patent protection possible for this new development. This could in economic terms discourage industry to invest in this new purpose in view of the lack of protection. In the long run and on a macro-scale, this can lead to less technological development and less treatments available. The risks attached to developing these new purposes without being able to obtain patent protection could very well deter industry to invest in that particular field in the first place.

Other solutions have also been proposed. One of these, which is tested in the German proposal to transpose Dir. 98/4/EC, makes a distinction between the nature of the invention and the type of patent protection attached to the different types of inventions relating to DNA sequences. If the provision or making available without more, i.e., detecting, determining, isolating etc., of the gene sequence is trivial in view of prevailing scientific and technological development, absolute product protection could be said to be inadequate and over-rewarding. In such a case, a type of patent protection with a narrower scope is preferable. If the making available of the gene sequence per se is inventive, then absolute patent protection is recommended in order to give a sufficient reward to the inventor. If the inventive element consists of finding a function (use) of a gene sequence alone, purpose-

[158] Art. 69(1) EPC reads: "(1) The extent of the protection conferred by a European patent or a European patent application shall be determined by the terms of the claims. Nevertheless, the description and drawings shall be used to interpret the claims. The Protocol to Art. 69 reads: "Article 69 should not be interpreted in the sense that the extent of the protection conferred by a European patent is to be understood as that defined by the strict, literal meaning of the wording used in the claims, the description and drawings being employed only for the purpose of resolving an ambiguity found in the claims. Neither should it be interpreted in the sense that the claims serve only as a guideline and that the actual protection conferred may extend to what, from a consideration of the description and drawings by a person skilled in the art, the patentee has contemplated. On the contrary, it is to be interpreted as defining a position between these extremes which combines a fair protection for the patentee with a reasonable degree of certainty for third parties."

bound patent protection is a sufficient reward.[159] Such a solution has obvious advantages and disadvantages. The advantage is without doubt that it takes into account the fact that in some cases, the inventor makes an important contribution to the state of the art with his invention, for which he deserves absolute patent protection. There is an element of justice here, since the inventor who only provides a modest contribution, will not receive the strong protection which is attached to absolute product protection, but will only receive purpose-bound patent protection, as this function or use is the contribution he made to the state of the art. Major drawback of this solution is that it is difficult to apply, and it creates a more or less new patent regime with two tiers for the same subject-matter. It will probably cause legal uncertainty, and the proponents of this solution should therefore consider whether they should pursue it.

The question must also be put on the table why such a special regime should be conceived for DNA, and not for other scientific domains. And even more, why only in the case of human DNA, and not for non-human DNA, where there is hardly any debate about this issue? It is in any event clear that under current EPO practice, such a solution cannot be put in practice, as it would require an amendment of the EPC. In other words, a mere decision at the level of the European Union would not have any effect on the granting practice of the EPO, as they are bound by the EPC. One of the arguments to give DNA a special treatment could be the special nature of it, i.e., that its value lies more in the information than in the chemical composition, and that it is very difficult to 'invent around', at least more difficult than in traditional chemistry. In the view of the author, an evaluation must be made of the pros and cons in order to take a final decision in this matter. But it is in any event clear that creating a special regime for DNA alone needs very good argumentation. The fact that there is dependency, and that inventing around becomes more difficult or in some cases non-existing is not necessarily convincing as an argument in view of the fact that these phenomena might also occur under traditional chemistry, where such a special regime does not exist. And the legal certainty which it is aimed to achieve, could also turn out to be illusionary, as demonstrated above.

[159] STRAUS sees such a solution as conceivable. See, STRAUS, J., Produktpatente auf DNA-Sequenzen – Eine aktuelle Herausforderung des Patentrechts, GRUR, 2001, (1016) 1020.

4.7.6. Confusion and additional problems

The situation is also rather confusing at this moment. Industry claims that if we would decide to limit patent protection for DNA to the specific purpose disclosed, that would amount to an insufficient level of protection.[160] But that stands at odds with the argument that a purpose-bound protection does not necessarily lead to a much narrower protection, as described above. It seems that there is thus some inconsistency in this reasoning, which influences the value of the argument negatively.

There is also another problem that could show up, and that is conformity of the special regime for DNA sequences with Art. 27(1) TRIPS, according to which "subject to the provisions of paragraphs 2 and 3, patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application. Subject to paragraph 4 of Article 65, paragraph 8 of Article 70 and paragraph 3 of this Article, patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced." Question is whether this provision allows to construe a regime which deviates, in the type of protection it provides, from other types of inventions. There is no uniform interpretation of Art. 27(1) TRIPS. It could be argued that TRIPS does not allow discrimination as to the field of technology for which patent protection must be available. But the provision does not say that patent protection must be of the same type for all technologies mentioned. It simply refers to the requirement that patent protection must be available for all fields of technology, whether process or product patents. A member state can thus not exclude subject matter from patentability, besides the exceptions under Art. 27(2) + (3) TRIPS, but member states can determine the type of protection they provide. It does not necessarily have to be product protection exclusively, otherwise, one could object second medical indication claims under European patent law, which are manufacturing process claims.

Summarising, limiting patent protection for DNA inventions to the specific purpose disclosed in the patent application remains a rather controversial issue. There are clear advantages and disadvantages to such a solution, even though it has to be taken into account that some advantages, such as more legal certainty and a clear-cut scope of the patents concerned, can in some cases turn out to be merely illusionary. Regard must also be taken to the effects of such a solution in terms of

[160] See e.g., HANSEN, B., Hände weg vom absoluten Stoffschutz – auch bei DNA-Sequenzen, Mitt., 2001, 477-493.

investment rate in technological development and effective patent protection. The rather contradictory statements by proponents of full protection, i.e., purpose-bound patent protection is not effective since it is illusionary to limit the scope of the patent, and the observation on the other hand that purpose-bound patent protection would provide insufficient protection, make the debate more complicated. This debate will continue for a while, and it will remain important to maintain lucidity and try to achieve consistency in the reasoning.

4.8. Research tool patents

Patents for DNA as research tools have also aroused the scientific community,[161] even though it is not always clear on which grounds this type of patents should be objectionable. Some of the concerns which have been raised are probably due to a lack of understanding of the possibilities which the research exemption provides. There are a number of difficulties, however, that arise when research tool patents are discussed. A first problematic issue is the definition of a 'research tool'. This can be defined very broadly or in a more narrow sense. Following the definition used in the NIH Working Group on Research Tools Report (1998), it could be said that "we use the term 'research tool' in its broadest sense to embrace the full range of resources that scientists use in the laboratory, while recognising that from other perspectives the same resources may be viewed as 'end products'."[162] DNA sequences can thus also fall under this definition.[163] ESTs and SNPs will in most cases be research tools, but also full-length genes, and genes with our without known function could also fall under the definition of research tools. In general it could be said that those DNA inventions fall within this category which are used in research but have no immediate therapeutic or diagnostic value. They could be used as an element to make a commercial product, but they are no commercial products in itself.[164]

This classification is of course somewhat theoretical, and is not crucial to analyse patentability issues. As for all inventions, the patentability requirements have to be fulfilled also for this type of inventions. From a patent law point of view, there is first of all no reason to exclude them 'as such' from patentability. All requirements, and the question whether they are an invention in the first place,

[161] See amongst others in the Nuffield Council Report 2002.

[162] See also Nuffield Report 2002, 47.

[163] E.g., as markers, assays, receptors, etc.

[164] Nuffield Report 2002, 56.

have to be analysed in accordance with the rules set out above in this study. And as it has become clear, it is not easy to obtain patent protection for raw material. In the worst case, and depending upon the interpretation taken, they could not be considered to be an invention,. i.e., a teaching to methodical action, if no function can be demonstrated. If that hurdle can be passed, these innovations still have to pass the patentability requirements. Novelty is not that much of a problem. Inventive step will be more difficult since, as explained above, the mere preparation of the sequences will not be sufficient, more specific effects must be demonstrated. The same is true for utility or industrial application, where according to recent standards of review, the utility must be specific, credible and substantial. Speculative and theoretical uses will thus not be sufficient.[165]

Also important as a possible hurdle for this type of inventions is the disclosure requirement. In some cases, patent applicants claim a broad scope with a number of applications and uses. To the extent that the applicant is not capable of demonstrating that he actually knows how to carry out the invention for these applications, it could be said that the invention is not sufficiently disclosed, as it claims applications which have not been described in the application. This is even more problematic if no general underlying principle is disclosed which could then be applied to the various applications or embodiments claimed. One could, besides disclosure, also reject the application on the basis that the claim is not supported by the description if the latter does not describe the applications.

It is observed in this context that the Nuffield Council also referred to this problem, but then in the context of utility.[166] It is submitted here that it is probably more accurate and a more proper application of patent law principles to solve insufficient disclosure and speculative applications with the aid of the disclosure requirement, instead of the utility or industrial application requirement. For the latter requirement, it is sufficient to demonstrate a specific utility to satisfy the said requirement, while the disclosure requirement assumes a full disclosure of the invention over the whole range of applications claimed.

Summarising, it could be said that the potential disadvantages caused by research tool patents can be tackled with a proper application of the checks and balances built in the existing patent system. Raw material will not pass the stage of being an ‘invention’, and if it does, will most probably fail on the level of inventive step

[165] For further comments on the fulfilment of the patentability requirements, reference is made to the discussion made earlier in this study, which is equally applicable to this type of innovations.

[166] Nuffield Report 2002, 57.

and/or utility. Research tool inventions with more practical applications will be checked for overbroad claiming (and in that respect they fall under the category of reach-through claims, discussed further in this study) in terms of possible applications falling under the scope of the patent with the aid of the disclosure requirement. If there is no overbroad claiming to be detected, there is no justified reason to exclude research tool patents from patentability.

What is more relevant, is to analyse the consequences of their patentability, as far as e.g. transaction costs, patent and royalty stacking, blocking effects etc. is concerned. Research tool patents will have an effect on later innovations which also use the patented research tool. In such a situation, one ends up in a dependency situation. And this dependency situation could lead to patent and royalty stacking, and possibly also have a blocking effect. The potential negative effects of these phenomena will be examined later in this study.[167] Worth analysing in the future is thus the actual effect of patenting research tools on technological development, in terms of patent and royalty stacking, and blocking effects. It should also be a subject of further study to analyse to what extent purpose-bound patent protection for DNA inventions could mitigate those negative effects, given that they are present. In other words, assuming for the sake of the argument that granting upstream patents for research tools indeed leads to patent and royalty stacking and blocking, and given that such a situation has a negative influence on scientific research and technological development, it should be further examined whether a limitation of DNA patents to the specific purpose disclosed in the patent application is capable of mitigating that effect, without forgetting the potential negative effects of limiting DNA patents to a specific purpose for technological development, which should equally be a subject for further study.

However, one must always keep in mind that the use of a patented research tool is possible without patent infringement in the framework of the research exemption. This takes away possible objections from the university scientific community that research tool patents are detrimental to fundamental scientific research. Situations where the patented research tool is used for predictive diagnostic testing, or for drug screening, are not straightforward to answer, because that will depend upon the interpretation of the research exemption.[168] Also here, a uniform rule and interpretation with the European Union would be warmly welcomed.

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167 See further below sub 8.

168 Which is explained further below sub 5.

Allowing patents for research tool inventions, which are building blocks for further practical applications, will indeed create, at least to some extent, stacking at the downstream level. But this must of course be placed in the perspective of the extent to which patents will be granted, in view of a correct application of the patentability requirements, as described above. Stacking as such cannot be avoided in a field of science and technology that is built on incremental innovations, small steps at a time. Stacking is in general a problem in patent law, and it is to be examined carefully how to address this problem. But the solution is not to be found in denying patent protection for inventions which are perfectly patentable. The solution is to be found in a strict application of the patentability requirements, so as to make sure that it becomes less easy to obtain a research tool patent that would not fulfil all patentability requirements interpreted in a strict but correct manner, which implies less stacking. Secondly, the effects of stacking might probably also be mitigated by applying a somewhat more lenient research exemption policy, especially in terms of screening and testing.[169] A third way to tackle stacking is patent pools, which could lead to lower licensing fees.[170] Finally, the effects of stacking can also be mitigated by a broader application of the compulsory licensing scheme, which has in se a number of deficiencies, however, which make it far from certain that it is a practical instrument to achieve the goal of less stacking. But this will be explained further in this study.[171]

4.9. Reach-through claims

The issue of reach-through claims is closely connected to the research tools issue described above. Reach-through claims cover products 'identified by' the patented tool or method.[172] Reach-through patents might have consequences for scientific research, in the sense that they could in principle provide overbroad protection to the research tool patent holder, which is not in conformity with the ambit of the invention made. Reach-through claims can also lead to further royalty-stacking and have a blocking effect: the patent holder will not only be able to license the research tool, but will also license the product identified by the tool. And royalty stacking can have a negative effect on scientific research, as it raises transaction costs. There are a number of cases both in Europe and the US where

169 See further below sub 4.10 and 5.

170 See further below sub 9.

171 See below sub 6.

172 OECD Report 2002, 15.

reach-through patents have been granted, e.g., (1) European Patent 724 637 B1, which claims CRF2 antagonist and its use for the manufacture of a medicament; (2) 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; (3) 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.[173] But it must be said, at least in Europe these must be considered to be exceptional cases, since most reach-through claims are rejected by the EPO during the examination procedure, predominantly for lack of sufficient disclosure and clarity.

However, once again the potential negative effects of this type of claims must be placed in perspective. It is admitted that the grant of such patents can be a cause of concern, but that is not due to the patent system as such, but is the responsibility of the granting policy of patent offices. A proper application of patent law principles and requirements as discussed in detail above is capable of tackling most of the problems connected with reach-through patents. The major instrument which can be used in this context is the enabling disclosure requirement, and lack of clarity and support by the description. As described above, according to the disclosure requirement the invention must be sufficiently disclosed, so as to allow the man skilled in the art to carry out the invention without undue burden or inventive skill. That implies that claiming subject matter which is not supported in any way by the disclosure must lead to a rejection. If the patent applicant is not capable of demonstrating that he actually possesses the product(s) identified by the research tool, the disclosure requirement is not fulfilled, the claim for the product merely being speculation. The man skilled in the art will not be capable of carrying out the invention, i.e., to produce the product identified by the tool, if the patent application gives no guidance. A claim covering the product identified by the tool will also face difficulties in being granted if there are no features mentioned in the application which shed some light on the product (substance), in terms of for example structure, or process of production.

Summarising, reach-through claims should lead (and this is also what generally happens) in most cases to a rejection of the claim due to lack of clarity, lack of support by the description, or insufficient disclosure. It is thus in particular the

[173] These examples were provided by GRUBB, P., "How Real are Patent Thickets, Reach Through Rights, Royalty Stacking, and Dependency." Presentation at the OECD's January 24-25, Berlin Workshop on Genetic Inventions, Intellectual Property Rights and Licensing Practices.

mission of patent offices to apply the existing patent law principles strictly, so that the large majority of this type of patent applications will be rejected. In the Trilateral Project concerning the patentability of reach-through claims, it has become clear that the policy of the European Patent Office is to be very reluctant to grant patents for such claims, and it can be said that scrutiny by the EPO is accurately thorough, thus leading in practice to a very limited number of patents for reach-through claims, only in cases where all patentability criteria can be considered to be fulfilled, which will be rarely the case.[174] It could then also be said that the potential negative consequences of overbroad claiming with reach-through claims in Europe, if existing, would be rather limited, due to the strict policy of the EPO in this respect.

But to the extent that the disclosure in fact identifies and described the product(s) identified by the patented tool, there is no reason to refuse the patent. A correct application of patentability requirements may prevent that patents are granted which should not have been granted, but once the patent application fulfils all requirements, a patent should be granted, which still leaves us with the stacking problem. This learns us once again that the checks and balances within the patent system are not capable of doing away with all forms of patent and royalty stacking, which is an inherent feature of the patent system. Important is to understand the long term effects of patent and royalty stacking in biotechnological research and technological development before appropriate measures can be taken, if that turns out to be necessary.

4.10. DNA and diagnostic testing patents

4.10.1. Introduction

As we have seen above, gene sequences can also be used as the basic material for a genetic disease diagnostic test, be it at the stage of pure diagnosis, or predictive diagnosis. Patents can be and have been claimed both for DNA sequences used in such tests, and for diagnostic testing methods.[175,176] Generalising

[174] See Trilateral Project B3b, Mutual Understanding in search and examination. Report on Comparative study on biotechnology patent practices (EPO, JPO, USPTO). Theme: Comparative study on “reach-through claims”, San Fransisco, 5-9 November 2001.

[175] The most famous examples are the BRCA1 and 2 patents. There are various patents granted both in the US and Europe relating to the breastcancer genes. Some of the more notorious ones are EP 699754, granted 10 January 2001, and EP 705903, granted 23 May 2001. As an example, claims 1-12 of patent EP 699754 (containing 29 claims). Claim 1: “A method for diagnosing a predisposition for breast and ovarian cancer in a

the various forms in which these inventions might be claimed, it could be said that the identification of genetic mutations which are responsible for a number of

human subject which comprises determining whether there is a germline alteration in the sequence of the BRCA1 gene coding for a BRCA1 polypeptide having the amino acid sequence set forth in SEQ.ID.NO:2 or a sequence with at least 95% identity to that sequence, said alteration being indicative of a predisposition to said cancer." Claim 2: "A method for diagnosing a lesion of a human subject for neoplasia associated with the BRCA1 gene locus which comprises determining in a sample from said lesion whether there is an alteration in the sequence of the BRCA1 gene coding for a BRCA1 polypeptide having the amino acid sequence set forth in SEQ.ID.NO:2 or a sequence with at least 95% identity to that sequence, said alteration being indicative of neoplasia." Claim 3: "A method as claimed in claim 2 wherein said lesion is a breast or ovarian lesion." Claim 4: "A method as claimed in any one of claims 1 to 3 wherein the sequence of the BRCA1 gene in said sample is compared with the sequence of one or more wild-type BRCA1 gene sequences selected from the sequence set forth in SEQ.ID. No. 1 from nucleotide 120 to nucleotide 5708 and wild-type allelic variants thereof." Claim 5: "A method as claimed in any one of claims 1 to 3 wherein the level and/or sequence of an expression product of the BRCA1 gene in said sample is investigated." Claim 6: "A method as claimed in claim 5 wherein said expression product is mRNA." Claim 7: "A method as claimed in claim 6 wherein mRNA of said sample is contacted with a BRCA1 gene probe under conditions suitable for hybridization of said probe to an RNA corresponding to said BRCA1 gene and hybridization of said probe is determined." Claim 8: "A method as claimed in any one of claims 1 to 4 wherein a BRCA1 gene probe is contacted with genomic DNA isolated from said sample under conditions suitable for hybridization of said probe to said gene and hybridization of said probe is determined." Claim 9: "A method as claimed in claim 7 or claim 8 wherein said probe is a mutant, allele specific probe." Claim 10: "A method as claimed in claim 5 wherein said expression product is the polypeptide encoded by the BRCA1 gene in said sample." Claim 11: "A method as claimed in claim 10 wherein said polypeptide is detected by immunoblotting or immunocytochemistry." Claim 12: "A method as claimed in claim 10 wherein binding interaction is assayed between the BRCA1 gene protein isolated from said sample and a binding partner capable of specifically binding the polypeptide expression product of a mutant BRCA1 allele and/or a binding partner for the BRCA1 polypeptide having the amino acid sequence set forth in SEQ.ID NO:2." Patent EP 705903 contains another 18 claims relating to different methods of using the BRCA 1 gene for diagnosis and determining predisposition.

[176] For a discussion of this type of patents, see BOSTYN, S.J.R., A Test too Far? A Critical Analysis of the (Non)-Patentability of Diagnostic Methods and Consequences for BRCA1 Gene Type Patents in Europe, 5 Bio-Science Law Review, [2001/2002] 4, 111-121.

genetic diseases, has increased the possibilities to use this knowledge as a basis for clinical diagnosis. One of the methods used is with the aid of SNPs. The quality of these tests in terms of predictive value and in relation to the complexity of some genetic diseases varies. The tests are generally limited to a number of mutations, thus not being capable of selecting all mutations which could demonstrate susceptibility for a genetic disease. Added thereto is also the fact that some (presumably the majority of) genetic diseases involve more than one gene, i.e., they are polygenic. The development of most diseases is affected by a combination of factors, which is first of all a combination of genetic factors, and also environmental factors.[177] It is also not evident to find out the relative importance of a specific gene in a polygenic disease, which also influences the predictive value of developed tests.

The DNA sequences claimed in this connection can be of variable forms. In some cases, only a partial sequence is claimed, with no known biological function in terms of protein synthesis, but with the function of being used as a marker: the sequence is used as a basis for detecting and characterising the gene in the patient with a view to find mutations. In other cases, a full-length gene is already known. In the case of SNPs, only nucleotides of a few bases are used, preferably of key locations in the gene.

The grant of a number of patents in this field of technology has caused considerable arousal,[178] and some of these patents are at this very moment still subject to a debate, besides being subject to opposition or appeal proceedings. In Europe, an opposition has been lodged against some of these patents, such as e.g., the BRCA1 gene patents.[179] It is therefore useful to analyse some of the issues that are raised and which deserve an evaluation. There are different issues which are to be dealt with in this context. First, it must be analysed whether this type of inventions fulfils the patentability requirements. A second problem is the scope of

177 Nuffield Report 2002, 48.

178 Examples could be found in, Report from the Commission to the European Parliament and the Council. Development and implications of patent law in the field of biotechnology and genetic engineering, 7 November 2002, COM(2002) 545 final, at 21.

179 Patent EP 699754 has been revoked on 18 May 2004 for technical reasons. The invention was considered to lack inventive step, due to the fact that a gene sequence which was made available earlier, contained some errors in the listing, and the later corrected sequence was considered to be obvious over the previous listing, which was considered prior art.

such patents, in other words, the question as to whether the patents granted for this type of inventions are not overbroad, and if so, how to tackle this problem. A third problem relates to the question whether patents ought to be granted for diagnostic test methods. A fourth question is then whether clinical use of this type of patents should be exempted form patent infringement.

4.10.2. Predictive DNA diagnostic testing methods and patentability requirements

Before we look at the patentability requirements, we should first determine whether this type of innovation is an 'invention' in the technical patent law meaning of the word, i.e., a teaching to methodical action. Following the same principles as for all DNA sequence inventions, it could be said that these sequences, including the SNPs, are an invention. However, taking into account the interpretation that an invention must have a utility in order to be called an 'invention' in the patent law meaning of the word, the situation requires some clarification. The sequences claimed in the context of diagnostic testing do not necessarily have a known biological function, thus from that perspective, there is no utility. However, they are used as a marker or basis for (predictive) diagnosis, which is sufficient a utility to fulfil the requirement. And there are of course also the methods claimed with the aid of the sequences, which have a specific utility, thus definitely fulfilling the requirement of being an 'invention'.

In terms of patentability requirements, novelty will basically present very little problems, as emphasised earlier in this study. Inventive step could, as repeatedly said before, be more problematic. The mere preparation of these sequences to be used in diagnosis is an automated process, and as such not sufficient to fulfil the inventive step requirement. The use of these sequences in the process of predictive diagnosis, where the DNA is used as the basis for detecting genetic information in the patient, and establishing whether there are mutations, is arguably also not inventive to the extent that this is also largely an automated process. But even though this process as such is not inventive, it could be considered inventive to come up with this test, and the development as such could be considered as an unexpected effect of the DNA. It might have been obvious to try to develop such a test, but that does not necessarily make it obvious.[180] It must be added thereto, however, that progress in scientific development and automating processes will

[180] As we have seen earlier in this study, obvious to try is not the standard used for evaluating inventive step.

have a determining effect on the future of the patentability of this type of tests. It could be assumed that in the light of scientific development it would become obvious to demonstrate the use of DNA sequences for diagnosis for genetic diseases. A different situation in terms of unexpected effects could exist in cases where the aim of the test is to diagnose acquired instead of inherited diseases, in view of their complexity.[181] Fulfilling the utility requirement will, as already said, not be major hurdle in this context, if the utility demonstrated is substantial, specific and credible. Using a partial gene sequence as a basis for genetic testing is a specific utility.

Another, more controversial issue is the question as to whether some of the patents granted for (predictive) diagnostic testing are not overbroad. The problem is that in some cases, as has been done in the context of the BRCA1 gene patents, broad claims are submitted, thus not only claiming the gene sequences as such, but also a plethora of applications, i.e., a variety of (predictive) diagnostic tests, and in some cases also including gene therapy claims. Such a practice seems to fall under the category of reach-through claims, and as such they could present the problems addressed earlier in this study.

It can also be questioned whether all the tests claimed can be carried out without undue burden. If carrying out these tests is merely the application of a single principle, which could then be applied to all the tests, in view of automated processes, there is no reason to deny patent protection for this type of patents, even though questions could then be raised in respect of inventive step, however. But to the extent that some of the tests claimed are not described, and where some doubt might exist as to whether they can be carried out with the aid of the description in the patent application and the knowledge present in the state of the art, they could fail on the basis of insufficient disclosure. As we have seen earlier, the invention must be described in such detail in the patent application so that it is sufficient to cover the whole area claimed. It is not necessary to disclose all conceivable embodiments of the invention in the patent application if the invention as claimed is the application of a general principle applicable to an unlimited number of embodiments. However, applications must be subject to thorough scrutiny in order to determine whether the invention claimed is indeed the application of a general principle, applicable to an unlimited number of embodiments which can then be produced without inventive skill. Inserting speculative applications will not fulfil

[181] For example, determining the genetic changes underlying particular cancers, examining the patterns of gene expression in various diseased tissues. See Nuffield Report 2002, 52.

this standard. The further applications which are claimed, such as for example gene therapy etc. could also present problems relating to sufficiency of disclosure, provided again that the patent application does not give sufficient detail. Merely claiming that the invention can be useful in gene therapy, without describing in detail the gene therapy could be considered to be speculative.

4.10.3. Excluding predictive DNA diagnostic testing methods from patent protection?

Another question which is worth addressing, is whether one should exclude this type of testing methods from patentability. Under the EPC, methods for diagnosis on the human body are excluded from patentability.[182] This has been done because it was considered that medical and diagnostic methods should be available to the medical society without the additional burden of a patent holder and the consequent necessity to acquire a use license. In other words, it could be said that health care concerns and accessibility to health care related methods have led to this position. In the US, no similar exception exists in the patent act, but a similar result is achieved by providing for a system where, under specific conditions, use of a patented medical treatment method without consent of the patent holder will not be subject to damages.[183] However, in Europe, the exception for diagnostic

[182] See Art. 52(4) EPC.

[183] See 35 USC 287(c)(1)-(4). According to this provision, the term 'medical activity' means the performance of a medical or surgical procedure on a body, but shall not include (i) the use of a patented machine, manufacture, or composition of matter in violation of such patent, (ii) the practice of a patented use of a composition of matter in violation of such patent, or (iii) the practice of a process in violation of a biotechnology patent. The term 'medical practitioner' means any natural person who is licensed by a State to provide the medical activity described in subsection (c)(1) or who is acting under the direction of such person in the performance of the medical activity. The term 'related health care entity' shall mean an entity with which a medical practitioner has a professional affiliation under which the medical practitioner performs the medical activity, including but not limited to a nursing home, hospital, university, medical school, health maintenance organization, group medical practice, or a medical clinic. The term 'professional affiliation' shall mean staff privileges, medical staff membership, employment or contractual relationship, partnership or ownership interest, academic appointment, or other affiliation under which a medical practitioner provides the medical activity on behalf of, or in association with, the health care entity.

methods is limited to methods performed on the human body, i.e., in vivo. Recent case law has made the interpretation of what this exclusion might embrace stricter, so as to allow a broader exclusion of patentability. While in the past, only those methods were excluded which had an immediate effect on the diagnosis to be made,[184] recent case law has held that any method which is of value for purposes of diagnosis, is excluded from patentability: "the Board is of the opinion that Article 52(4) EPC is meant to exclude from patent protection all methods practised on the human or animal body which relate to diagnosis or which are of value for the purposes of diagnosis."[185] Thus also intermediary steps, which have some value in the final diagnosis, are excluded from patentability, provided they are carried out on the human body. The President of the European Patent Office has recently referred a number of questions to the Enlarged Board of Appeal on the basis of Art. 112(1) EPC, since it was considered that case T 0385/86 and T 0964/99 are two divergent decisions.[186]

Predictive genetic testing methods, however, are not carried out on the human body. Body samples are taken, and the testing is done outside the human body, i.e., ex vivo. As the law stands today, these methods do not fall under the exception of Art. 52(4) EPC. Voices have raised the viewpoint that it is time to exclude also ex vivo diagnostic methods. The reasoning behind this is that also ex vivo diagnostic methods are diagnostic methods, and there is no reason to follow a different strategy for ex vivo and in vivo methods, as the rationale for the exclusion of in vivo methods is partly also concern for the accessibility of health care related methods. In this line of reasoning, a similar health care concern should govern ex vivo diagnostic methods. An argument added in this connection is that broad patents granted in this area could have a stifling effect in terms of investments made to develop new tests. Stifling in the sense that broad patents, covering almost all plausible tests conceivable, do not give any further incentive to innovators to

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184 See e.g. T 0385/86, "Non invasive measurement/Bruker", decision of Technical Board of Appeal 3.4.1 of 25 September 1987, OJ EPO, 1998, at 308. Headnote 1 reads: "The only diagnostic methods to be excluded from patent protection are those whose results immediately make it possible to decide on a particular course of medical treatment. Methods providing only interim results are thus not diagnostic methods in the meaning of Article 52(4), first sentence EPC, even if they can be utilised in making a diagnosis."

185 T 0964/99, "Device and method for sampling of substances using alternating polarity/CIGNUS", decision of Technical Board of Appeal 3.4.1 of 29 June 2001, OJ EPO, 2002, 4, at 4.4 of the reasons.

186 Referral dates from 29 December 2003. The case is pending under reference G 1/04.

develop eventually improved tests. But it must be clear; any change as discussed here requires an amendment of the EPC.

An argument against excluding ex vivo diagnostic methods is the consequences which such a broad exclusion might have on research and development in this important area of scientific research, in terms of health care improvement. Ex vivo diagnostics is an important business today, which is capable of providing diagnostic solutions for a large number of diseases. And it must be remembered that diagnosis is evidently a first step in the whole treatment process. A broad exclusion might deter investors or researchers to develop specific tests in the first place. And in view of the importance of developing such tests for the future of health care, it could be said that it deserves attention that investments are attracted instead of being discouraged. Indeed, reference is made to the entire diagnostics business, as there is no good reason to exclude only DNA related ex vivo diagnostic methods, and not other ex vivo diagnostic methods.

In view of the potential negative effects resulting from excluding ex vivo diagnostic methods, there are other means, however, to tackle some of the objections against DNA predictive testing patents in particular. A careful and strict application of the patentability requirements (as we have discussed earlier), especially in respect of inventive step and the disclosure requirement should in most cases be capable of providing comfort to those who have serious concerns about the effects of broad DNA predictive diagnostic testing patents.

4.10.4. Predictive DNA diagnostic testing methods and the research exemption

A fourth issue is the question whether (predictive) diagnostic genetic testing methods should fall under the research exemption when they are applied for clinical use. We will discuss this issue in detail when we discuss the research exemption.[187] Allowing the use of these testing methods for clinical purposes, and letting them fall under the research exemption, would allow clinical practice to continue using these tests without the burden of, in the worst case, exorbitant licensing fees, or the necessity to submit body material to the patent holder for analysis, as is now the case under the BRCA1 gene patent.

[187] See below sub 5.

The arousal which these patents have caused is basically to be reduced to the possibilities of research institutes to carry out this type of tests in their research laboratories and the rather elevated licensing fees charged for the use of these tests by the patent holder.[188] A number of observations must be made in this context, however. The fact that the DNA sequence is patented will in any event lead to a dependency situation for later new tests to be developed by others, which will require the DNA sequence. But it does thus not imply that any new test developed, such as e.g. tests which search for other mutations in other locations, not covered by the tests covered by the patent,[189] will be considered to be a patent infringement, provided a license is asked for the use of the DNA sequence. If the research and development is pursued in a pure research environment, the research exemption could even provide free use of the DNA sequence. But such a solution will also partly depend on the interpretation of the concept of 'research exemption', i.e., whether it includes activities which do not fall under the classical pure research, which could be the case with predictive diagnostic tests methods, being more a clinical use issue. We will dwell further upon this important issue later in this study.[190]

4.10.5. Effects on health care costs

An issue which arises in the context of patenting inventions with immediate impact on health care, such as diagnostic test methods and therapies, is the effects of such patents on the cost of health care. One of the arguments presented in this context is that this type of patents can have a detrimental effect on the cost of health care, due to the higher prices charged. It is inevitably true that the existence of patent rights will influence the price level of the product or process provided. However, acting against this type of patents predominantly for reason of potential price consequences might not be the appropriate strategy. Patent law is not a price regulating instrument. There are more effective strategies to influence the price of a product so that it remains accessible for most people. The mere fact that a patent

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188 For a recent first impression survey concerning the effects on research in university institutions in the US, see CHO, M.K., ILLANGASEKARE, S., WEAVER, M.A., LEONARD., D.G.B., MERZ, J.F., Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services, 5 Journal of Molecular Diagnostics, February 2003, 3-8.

189 It must be admitted, however, that the solution will also depend on the application of for example the doctrine of equivalence in an infringement claim.

190 See further below sub 5.2.

would not be granted, would not by definition lead to lower and more affordable prices, even though it will in some cases admittedly do so. However, it is to be reminded that in the absence of patent protection, part of the know-how might be kept secret, which could have an effect on research costs for those who wish to develop such tests. An effective instrument to affect the price of health care products or services is government intervention, as we know it in many European countries in the area of medicament price control. If the only problem attached to predictive diagnostic test methods is price, government price control is the preferred strategy. But, as it has been demonstrated above, there are more serious concerns in the context of patenting this type of methods which require thorough scrutiny, such as scope of protection issues, patent and royalty stacking, research and clinical use exemption etc.

Worth mentioning is that in the US, a bill has been introduced to exclude the use of genetic diagnostic testing methods from patent infringement.[191] This initiative is in line with a similar provision which is already in force relating to the use of medical treatment methods. To achieve that effect, the term 'medical activity' is amended by including "performance of a genetic diagnostic, prognostic, or predictive test or a medical or surgical procedure."[192] Further, the bill added some definitions: "The term 'genetic diagnostic, prognostic, or predictive test' means any test, designed to detect disease, to predict the potential for a medical disorder, or to predict the effectiveness of therapeutics, which uses either an ordered listing of nucleotides comprising a portion of a human pathogen genetic code or the proteins encoded by such nucleotides."[193] At this moment, it is unclear what the fate of this initiative will be, as the bill is now in the Intellectual Property Subcommittee of the House of Representatives under discussion. The said bill has opted for a very specific exclusion, limited to genetic diagnostic, prognostic and predictive testing. This has, as already said hereabove, drawbacks in itself, as it is not clear beyond doubt why an exception should be limited to this type of methods only.

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191 H.R. 3967, March 14, 2002, 'Genomic Research and Diagnostic Accessibility Act of 2002'.

192 Amending 35 USC 287(c)(2)(a).

193 Adding 35 USC 287(c)(2)(f).

Chapter 5. Research (And Clinical Use?) Exemption

5.1. Scope of the research exemption unclear

An important but often forgotten feature of the patent system is the existence of the experimental use or research exemption in patent law, according to which acts done for experimental and research purposes are exempted from patent infringement. It is an important feature because it puts in perspective the hypothetical stifling effects of patent protection on fundamental scientific research. Some of the objections expressed against patenting DNA inventions have focused on the idea that scientific research would be jeopardised since expensive licenses would have to be acquired before such material could be used, which would be unaffordable for public research institutions. Reality is different, however. The research exemption allows use of patented material without consent of the patent holder, i.e., without a license, for experimental and research purposes. However, to the extent that such research requires the use of patented material which has to be acquired from the patent holder or his licensee, in other words, that the material cannot be produced in the laboratory, the risk of high licensing fees remains, as the obtaining of the material embraces payment of a licensing fee.

Even though the research exemption is a fundamental principle of European patent law, contrary to US patent law where no general statutory research exemption provision exists,[194] it is not uniformly conceived and applied in the European Union. Most countries have some form of research exemption, but its exact ambit varies between countries. And what is even more, countries with similar statutory exemptions, have developed in case law a different interpretation. A well known example is the issue of clinical trials and the question whether they fall under the research exemption. More in particular, the documented cases dealt with clinical trials in the context of generic drugs. According to the Netherlands Supreme Court, clinical trials in the framework of market approval for generic drugs do not fall under the research exemption, and thus there is no reason for setting aside the requirement to obtain a license from the patent holder. The reasoning behind this position is that clinical trials have as their main goal to make sure that all conditions for registration as a medicament can be fulfilled. In that respect, clinical trials are not merely confined to research, but are the last step before actual full commercialisation. The research exemption is to be interpreted

[194] And in recent case law, the case law based research exemption was even narrowly interpreted. See, John M.J. Madey v Duke University, 307 F.3d 1351, 64 USPQ 2d 1737 (CAFC 3 October 2002).

restrictively and must be confined to activities with the patented invention with a view to improve or further develop technology. This is not the case with clinical trials, which are aimed at the registration of the medicament, and hence only embrace those research activities pursued with a view to achieve registration, thereby excluding all possible obstacles such as e.g. negative side-effects etc.[195]

In Germany, however, the situation is a different one. According to Federal Court of Justice (Bundesgerichtshof) case law,[196] clinical trials could fall under the research exemption, if these trials are aimed at the search for further medical applications, or aimed at obtaining more information about the effects and the tolerability of the drug which incorporates the patented substance. The Federal Court held that trials in relation to the patented subject matter are free. This includes all types of trial activities, irrespective of their nature, even if there is a commercial motivation to perform them. What is required under the law is that through the trials, new insights are developed in respect of the patented subject matter, therein included insights in respect of the application of the patented subject matter. These insights must then be used to solve possible uncertainties. These requirements are fulfilled if a pharmaceutical compound, which contains the patented substance, is tested on its effect and tolerability with the assistance of clinical trials. The statute does not make a distinction between commercial and non-commercial trials. It would be unreasonable not to allow trials which do further scientific research and development, for the simple reason that, besides those effects, they also have a commercial goal. The rationale underlying the research exemption allows the use of clinical trials without committing a patent infringement if they provide more information about the effect and tolerability of a drug on human beings in which the patented invention (=substance) is incorporated, even if they have as a supplementary goal to collect data to be used for the registration process in the framework of official drug approval by the competent authorities. But this does not automatically imply that all trials are allowed. If the trials are not connected to the technical teaching of the invention, or if their scope is overbroad, then they do not fall under the research exemption.[197]

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[195] See decision of the Netherlands Supreme Court (Hoge Raad (HR)) of 18 December 1992, Nederlandse Jurisprudentie, 1993, at 735, at 3.3.3 of the reasons. Confirmed in a later case, HR 23 June 1995, Nederlandse Jurisprudentie, 1996, at 463.

[196] Bundesgerichtshof X ZR 68/94, "Klinische Versuche II", 17 April 1997, OJ EPO, 1997, at 589. Indirectly confirmed by the decision of the Bundesverfassungsgericht, 1 BvR 1864/95, 10 May 2000, GRUR 2001, 43-45.

[197] Taken from, BOSTYN S.J.R., The Prodigal Son: The Relationship Between Patent Law and Health Care, 11 Medical Law Review, 2003, (67) 110-111.

Interesting to observe in this connection, even though not immediately relevant for the European situation, is that also in the US, even though recent case law has given a very narrow interpretation of the research exemption, the judiciary has still not solved for itself the exact scope of the research exemption. Judge Newman wrote in her dissenting opinion in the Integra v. Merck case that "the panel majority states that because the Scripps/Merck research had the goal of curing cancer and commercializing the cure, this purpose moved the research outside of any common law exemption. However, an ultimate goal or hope of profit from successful research should not eliminate the exemption. The better rule is to recognize the exemption for research conducted in order to understand or improve upon or modify the patented subject matter, whatever the ultimate goal. That is how the patent system had always worked: the patent is infringed by and bars activity associated with development and commercialization of infringing subject matter, but the research itself is not prohibited, nor is comparison of the patented subject matter with improved technology or with designs whose purpose is to avoid the patent."[198]

The abovedescribed case law illustrates that there is no uniform interpretation of the research exemption in patent law. This is to be deplored, in view of the importance of this exemption in the context of both the patent system and scientific research. The rationale of the research exemption is to allow third parties to use the patented invention to pursue research or perform experiments, without the burden of having to acquire the consent of the patent holder first, and consequently also without the burden of licensing fees. Such a policy is capable of stimulating scientific research and furthering technological development. In other words, providing for this exemption is said to have positive effects on scientific research and development. One may not forget that in some sectors, and biotechnology is one of them, fundamental scientific research is of vital importance for the development of products and processes which bring us closer to cures for (non-) hereditary diseases.

But the full effect of this exemption can only be guaranteed if its scope is clearly defined. One of the key issues in this connection is evidently to be able to make the distinction between use for research or experimental purposes and other uses. Unfortunately, it is not always easy to make this distinction, and third parties will in some cases try to test the elasticity of the concept. The case law described

[198] Integra Lifesciences I, Ltd. and The Burnham Institute, and Telios Pharmaceuticals, Inc., v. Merck KGaA, and The Scripps Research Institute and Dr. David Cheresh, Appeal 02-1052, 1065, 2003 U.S. App. (CAFC 2003).

above concerning clinical trials is a good example. While it could be argued that clinical trials are not mere experimental or pure research activities, and should as such not fall within the ambit of the research exemption, it could also be argued that clinical trials also aim at testing side effects or other effects, and as such they can be considered to be experimental or research activities, since there is no immediate commercial activity pursued. This creates a tension between patent holders, who have an immediate interest in keeping the scope of the research exemption as narrow as possible, and third parties involved in activities with the patented material, who evidently prefer to pursue these activities without acquiring the consent of the patent holder first, and are thus in a more comfortable position if the scope of the exemption is broad.

And this tension is also reflected in economic analysis. Defining the research exemption narrowly would have the disadvantage that it would reduce the value of the exemption, and its potential positive effects on scientific research. If the number of activities which is allowed to be performed without the consent of the patent holder is very limited, one can question the use of having such an exemption in the first place. That would then imply that scientific research, which we need for further technological development, could be hampered or in any event be made more burdensome. And if more financial resources have to be directed towards avoiding patent infringement, there are evidently less of these resources left for those activities the resources were made available for in the first place, i.e., fundamental scientific research. On the other hand, extending the number of activities that fall under the research exemption could potentially have negative effects on the investment rate for new technologies, since the broad catalogue of exempted activities reduces the possibilities for the patent holder to obtain a return on investment. And if there is doubt about return on investment, there are fewer incentives to make the investment in the first place. And if there is less investment in technological development, this might in the long run have a stifling effect on technological progress at large. The difficult exercise is thus to find an interpretation of the research exemption which takes into account on the one hand the needs of the research community to be able to pursue scientific research without being burdened by patents, and on the other hand to provide the expectation to investors and patent holders that they still have the potential of obtaining a sufficient return on investment.

As we have seen, a uniform interpretation in Europe is crucial. But this supposes the fulfilment of two prerequisites. The first one is the existence of a Community patent, with a single uniform rule governing the research exemption,

such as e.g. Art. 9 of the Proposed Community Patent Regulation[199]: "The rights conferred by the Community patent shall not extend to: (a) acts done privately and for non-commercial purposes; (b) acts done for experimental purposes relating to the subject-matter of the patented invention." The second prerequisite is the existence of a Community Patent Court, capable of providing a uniform interpretation and clarifying the extent of the research exemption.[200] This would, as pointed out above, not only be desirable in the context of the patent system, but also in the framework of European scientific research policy. For that reason also the fact that an agreement has been reached on the Community Patent is a very positive evolution.

5.2. Clinical use exemption?

One of the questions, which arise in the context of the exact ambit and interpretation of the research exemption, is the issue of whether clinical use should also be included as falling within the scope of that exemption. The question has arisen in the aftermath of the BRCA1 gene patent grant, which we have discussed earlier in this study. This patent covers predictive genetic tests, which will predominantly be carried out by research institutions in a clinical phase. This type of testing, which is not a diagnostic test per se, is by its nature bound to be predominantly used in a clinical environment. A first question which we have to find an answer to is whether society at large would benefit from considering clinical use to be an exempted activity.[201] There is the obvious advantage that

[199] Proposed Community Patent Regulation COM(2000) 412 final; for the revised text, dated 8 March 2004, see, Council Document 7119/04 PI 28 (all texts quoted refer to this version).

[200] See also Proposal for a Council Decision conferring jurisdiction on the Court of Justice in disputes relating to the Community patent, COM(2003) 827 final, 2003/0326 (CNS), and Proposal for a Council Decision establishing the Community Patent Court and concerning appeals before the Court of First Instance, COM(2003) 828 final 2003/0324 (CNS).

[201] The author realises that the use of the wording clinical use could give rise to interpretation problems, as its exact ambit is not clear. Clinical use embraces various activities, which are in most countries called clinical phase I, II, III and IV. Phase I is aimed at testing safety of the drug or vaccine. In phase II, the effect and side effects are tested. Phase III embraces testing safety and effects in a larger (patient) population, and is often aimed at registration. Phase IV is a post-registration and post-marketing study aimed at collecting data relating to risks, advantages and optimal use and dosage. See, De gevolgen van het octrooieren van humane genen voor het wetenschappelijk

taking this option would make tests such as the BRCA1 gene tests, or any other clinical use, more affordable, in the absence of licensing fees to be paid. And making these tests more affordable is an obvious social benefit.

A potential negative effect is based on the fact that extending exempted activities to clinical use will cut into the income sources of the patent holder, especially in the case of inventions which are predominantly used in the clinical phase. For this type of inventions, if clinical use were to be exempted, the return on investment forecast would be rather clouded. And this could become a social cost, in terms of reduced incentives to make new technological development, and potential stifling effects. It should be a subject of further study to examine the trade-off between the social benefits and the social costs in order to evaluate which solution turns out to be the better one. In a Workshop held in Berlin in 2002 organised by the OECD, it was said that "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."[202]

Extending the research exemption to clinical use, and assuming that this can be achieved by interpretation of the existing provisions or by including clinical use as a new activity falling within the scope of the research exemption, would broaden the scope of the research exemption, and would thus bring the exempted activities closer to commercial use. That would make it even more difficult to distinguish clinical use from commercial use than it is now to distinguish experimental use from commercial use. Introduction of a new type of exemption (by broadening an existing exemption provision) could create legal uncertainty, and it is to be seen what the effects might be of creating such an exemption for the level of investment in this vital sector of medical science. It must also be borne in mind that the discussion surrounding clinical use has actually only seen daylight after the BRCA1 gene patent grant. In general it can be said that overhauling and amending patent systems in response to a single patent where a patent owner has decided to pursue a strict and aggressive licensing policy is definitely to be avoided. If there is no substantial evidence that a there is a certain policy being developed in respect of

onderzoek in Nederland: Advies van de Commissie Genoctrooien, Amsterdam, KNAW, 2003, at 26.

202 OECD Report 2002, 72.

such a type of patents, it is recommendable to try to solve isolated cases on the basis of the checks and balances already present in the patent system.

Chapter 6. Compulsory Licensing

6.1. Compulsory licensing and when and how to apply the system

Another means to guarantee that patents which are considered crucial and in the public interest can be used on a large scale and under reasonable terms is to grant compulsory licenses. Compulsory licensing is the practice whereby the government or court authorise third parties, or the government itself, to use the patented invention without the authorisation of the patent holder, for reason of public policy. In other words, the patentee is forced to tolerate, against his will, the exploitation of his invention by a third person or by the government itself. In these cases, the public interest in broader access to the patented invention is considered more important than the private interest of the right holder to fully exploit his exclusive rights.[203]

The compulsory licensing system has been developed for a number of reasons. It has first of all been developed as an instrument to ensure that inventions are exploited. One of the first applications of compulsory licensing was the grant of such licenses for non-working. If a patent holder does not exploit his invention during a certain period of time, and he refuses to grant a license, a compulsory license can be granted so as to make sure that the technology embedded in the patent is used for the benefit of technological development and society at large. In the 1883 version of Art. 5A of the Paris Convention,[204] the remedy for non-

[203] See, REICHMAN, J.H., HASENZAHL, C., Non-Voluntary Licensing of Patented Inventions : Historical Perspective, Legal Framework under TRIPS, and an Overview of the Practice in Canada and the United States of America, UNCTAD/ICTDS, September 2002, at 4.

[204] Art. 5A of the Paris Convention is the first international treaty covering patents where a compulsory licensing provision was established (Paris Convention for the Protection of Industrial Property of March 20, 1883, as revised at Brussels on December 14, 1900, at Washington on June 2, 1911, at The Hague on November 6, 1925, at London on June 2, 1934, at Lisbon on October 31, 1958, and at Stockholm on July 14, 1967, and as amended on September 28, 1979). The current text of Art. 5A reads: "(1) Importation by the patentee into the country where the patent has been granted of articles manufactured in any of the countries of the Union shall not entail forfeiture of the patent. (2) Each country of the Union shall have the right to take legislative measures providing for the grant of compulsory licenses to prevent the abuses which might result from the exercise of the exclusive rights conferred by the patent, for example, failure to work. (3) Forfeiture of the patent shall not be provided for except in cases where the grant of compulsory licenses would not have been sufficient to prevent the said abuses.

working was still forfeiture. But because a system of forfeiture had distinct disadvantages, more and more states adopted a system of compulsory licensing instead to tackle non-working.[205] This practice was confirmed in the 1925 version of Art. 5A of the Paris Convention, and further developed until the current version. Non-working has from the very beginning been considered to be a case of abuse of the patent right. Forfeiture, and thus later compulsory licensing was then also the remedy for abuse in general. The refusal to grant a license under reasonable terms is another important example of potential abuse.

Once the practice of granting compulsory licensing was in the process of becoming more established in the various states for reason of abuse, other applications of the system saw daylight. Some countries developed a compulsory licensing system for situations which could be subsumed under the term 'public interest'. In their interpretation, patents covering products such as medicinal and food products fell within this category of 'public interest' and were thus subject to compulsory licensing.[206] An example is the United Kingdom, where section 41 of the UK Patents Act 1949 "distinguished foods, medicines, and surgical devices from other patent-protected products by articulating a rebuttable presumption in favour of compulsory licensing to ensure that the products are 'available to the public at the lowest prices consistent with the patentees' deriving a reasonable advantage from their patent rights'."[207] These provisions were later withdrawn in the 1977 Patents Act. Also Canada had strong compulsory licensing provisions, which went even further than those in many other countries. Since 1923, there were provisions which allowed the grant of compulsory licenses to manufacture within Canada drugs and food products protected by patents. In view of the fact

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No proceedings for the forfeiture or revocation of a patent may be instituted before the expiration of two years from the grant of the first compulsory license. (4) A compulsory license may not be applied for on the ground of failure to work or insufficient working before the expiration of a period of four years from the date of filing of the patent application or three years from the date of the grant of the patent, whichever period expires last; it shall be refused if the patentee justifies his inaction by legitimate reasons. Such a compulsory license shall be non-exclusive and shall not be transferable, even in the form of the grant of a sub-license, except with that part of the enterprise or goodwill which exploits such license. (5) The foregoing provisions shall be applicable, mutatis mutandis, to utility models."

205 REICHMAN, J.H., HASENZAHL, C., op. cit., at 5.

206 REICHMAN, J.H., HASENZAHL, C., op. cit., at 6.

207 SCHERER, F.M., WATAL., J., Post-TRIPS Options for Access to Patented Medicines in Developing Nations, 5 Journal of International Economic Law, 2002, (913) 918.

that there was little production in Canada of drugs, due to the small size of the market and the burdensome procedure, the provisions were very infrequently applied. In 1969, an amendment was made to the law in order to provide also compulsory licenses for import. Importation of bulk ingredients, and especially the compulsory licenses granted for those imports, would be beneficial to consumers, as they would make available drugs to consumers at the lowest possible prices.[208] The system was thus in effect used to build up a generic drugs industry. In the light of world trade negotiations, the law was first weakened in 1987 and the provisions were finally repealed in 1992.[209]

Interesting to observe is that grounds of public interest for the grant of compulsory licensing are not covered by Art. 5A of the Paris Convention, due to lack of consensus during the negotiations process of the 1958 and 1967 text. Nevertheless, all countries in the European Union have provisions in their patent acts which provide compulsory licensing for reasons of public interest. And the European Commission has, in the framework of harmonising these provisions within the European Union, provided a similar public interest exception in the Proposed Community Patent Regulation.[210]

Compulsory licensing can also be used in the context of antitrust cases. This is widely used in the United States. Also in Europe, this is a possible application of the compulsory licensing system.

The compulsory licensing scheme as it can be found in most patent acts is a burdensome procedure, however, subject to a number of requirements which have to be fulfilled. It is also a matter of national authorities and courts, covered by national patent acts, which makes it even more difficult to apply such a system to a problematic patent. Since most patents of interest cover more than one country, the problem of insufficient access to the patented invention under reasonable terms and

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208 SCHERER, F.M., WATAL., J., loc.cit., 918

209 Ibidem, 919.

210 Art. 21(1) Prop. Comm. Pat. Reg.: "The Community Patent Court may grant a compulsory licence for lack or insufficiency of exploitation of a Community patent to any person filing an application four years or later after the patent application was filed and three years or later after the patent was granted if the patent proprietor has not exploited the patent in the Community on reasonable terms or has not made effective and serious preparations to do so, unless he provides legitimate reasons to justify his inaction. In determining the lack or insufficiency of exploitation of the patent, no distinction shall be made between products originating within the Community and imported products."

compulsory licensing will also affect various countries. And as a consequence of this, the procedure becomes even more burdensome and uncertain, as the result will be dependent on the application and interpretation of national rules by national authorities and courts. A uniform European system, applied and interpreted uniformly, would at least have the advantage of uniformity, and in the long run also clarity after courts have had the opportunity to clarify the scope and meaning of those provisions. The proposed Community Patent Regulation should be welcomed in this respect. It must be emphasised, however, that TRIPs also covers compulsory licensing, even though the implementation of the conditions and situations under which such licenses can be granted is left to the member states of the WTO.

The question arises as to whether invoking the compulsory licensing scheme to tackle patent and royalty stacking and potential stifling effects on scientific research, as highlighted earlier in this study, is the appropriate solution. It is most probably not, as the system in its origins has not been designed to cover these situations.[211]

Especially the situation where the patent holder refuses to grant a license under 'reasonable terms' presents a number of problems. First of all, it has to be established what 'refusal to grant a license under reasonable terms' means. Indeed, a compulsory license can in the general public interest in principle only be granted after potential licensees have tried, without result, to obtain a voluntary license from the patent holder under reasonable terms. That also implies that as soon as a patent holder is prepared to give a license to a licensee under reasonable terms, even if it is an exclusive license, no compulsory license will have a chance of being granted. This is important, because the compulsory licensing argument has been used in the context of the BRCA1 gene patent. Myriad Genetics, the patent holder, has granted a number of licenses, be it exclusive ones, hence a strategy calling for compulsory licenses has almost no chances of success, unless one can prove that they would have been granted under unreasonable terms. Thus, in cases where the patent holder is prepared to give an exclusive license, no compulsory license can be granted. Except of course if the patent holder would refuse to grant the license under reasonable terms, whatever that may mean. It will require an evaluation of the terms of the license and the invention, in terms of its importance for society, its value for technological development, the question whether it is a complementary or a supplementary invention, whether it is a basic standard in the field, inevitably to

[211] The potential negative effects of a more expansive use of the compulsory licensing system are explained in more detail further in this study, see sub 6.3.

be used by all other players in the market, whether and to what extent it is possible to use other alternatives, the licensing fee charged originally, the profit margin under the original fee, the marginal production costs, the profit margin to be obtained by the licensee etc. Should the financial position of the state or of its citizens, for example in case of drugs, also be taken into account to evaluate the word 'reasonable'? The criteria enumerated, which are not even exhaustively done so, make clear that such an evaluation can turn out to be extremely difficult and cumbersome, and will without doubt consume a lot of time, which is as such a social cost in economic terms.

Second problem in this standard situation is also that there is basically a time period which has to lapse first before the scheme can be put in action.[212] This requirement can be set aside for exceptional circumstances, further explained below. And it can of course also be set aside if there is a refusal to grant a license to anyone, since that could be considered to be an abuse of monopoly position. This period of time is again one factor which makes the system rather unfit for the purposes it has recently been invoked for, i.e., easy access to patented material to carry out for example predictive diagnostic tests.

The compulsory licensing scheme has originally been conceived as a last resort remedy to stimulate technological development and avoid abuse of monopoly rights. That makes it cumbersome and difficult to apply. And that in turn makes it unfit for a general application, which is probably also a good solution, in view of its exceptional nature.

6.2. Exceptional circumstances make compulsory licensing procedure easier

There are exceptions, however, to the rather strict procedures to be followed in order to obtain a compulsory license. The most important one is the grant of a compulsory license to tackle problems in times of crisis or in other situations of emergency. [213] Under these circumstances, the abovementioned procedure is not to

[212] E.g. s. 48 UK Patents Act 1977, 3 years after grant; s. 24 German Patent Act, a reasonable period; Art. L. 613-11 Code de la Propriété Intellectuelle, 3 years after grant; Art. 57 Dutch Patent Act 1995, 3 years after grant; Art. 31(b) TRIPs, a reasonable period; Art. 21(1) Prop.Comm.Pat.Reg., 3 years after grant.

[213] See Art. 21(3)(a) Prop. Comm. Pat. Reg.: "In times of crisis or in other situations of extreme urgency, including those relating to a public interest of extreme importance, the the Community Patent Court may authorise at the request of a Member State the exploitation of a Community patent."

be followed, i.e., the prerequisite that a voluntary license must first be asked for and was refused under reasonable terms.[214] It is not exactly clear what these exceptional circumstances might embrace, as those provisions have hardly ever been applied in practice. It is generally accepted that public health threats could be such a situation. But that brings us to another criterion to interpret, and that is what is exactly meant by 'public health threats'. Is it required that public health is threatened by an epidemic, or is it sufficient if the threat affects a number of people? Is the nature of the disease, irrespective of the number of victims it affects, the determining factor? Does the threat have to relate to a disease which has already manifested itself, or can it also embrace threats at the level of prediction and potential break-outs? Again, there is no clear interpretation of these concepts for the simple reason that there is insufficient experience with the system.

Art. 31(b) TRIPs also refers to public non-commercial use as an exception to applying the strict procedure. [215,216] Again, this causes problems of interpretation,

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214 Art. 21(5) Prop. Comm. Pat. Reg. reads: "A licence or exploitation set out in paragraphs 1 and 2 may be granted only if the proposed user has made efforts to obtain authorisation from the patent holder on reasonable commercial terms and conditions, and if such efforts have not been successful within a reasonable period of time. However, the authority granting the license may derogate from this condition in the situations set out in paragraph 3a. In these situations, the right holder shall be informed as soon as reasonably possible."

215 See Art. 31(b) TRIPs: "[Where the law of a Member allows for other use of the subject matter of a patent without the authorization of the right holder, including use by the government or third parties authorized by the government, the following provisions shall be respected:] (b) such use may only be permitted if, prior to such use, the proposed user has made efforts to obtain authorization from the right holder on reasonable commercial terms and conditions and that such efforts have not been successful within a reasonable period of time. This requirement may be waived by a Member in the case of a national emergency or other circumstances of extreme urgency or in cases of public noncommercial use. In situations of national emergency or other circumstances of extreme urgency, the right holder shall, nevertheless, be notified as soon as reasonably practicable. In the case of public non-commercial use, where the government or contractor, without making a patent search, knows or has demonstrable grounds to know that a valid patent is or will be used by or for the government, the right holder shall be informed promptly."

216 Interestingly, the Proposed Comm. Pat. Reg. does not refer to public non-commercial use as an exceptional ground for the normal procedure of asking for a voluntary license first. However, in Art. 9a it is stated that: "Any provision in the law of a Member State allowing use of national patents by or for the government may be applied to Community patents, but only to the extent that the use is necessary for essential defence

as it is not clear what public non-commercial use is. An example could be the use by the government of drugs for distribution to the population at no cost, or at production cost. In this case, there is a clear public use, and there are no commercial goals attached. We have seen earlier in this report that clinical use will probably, in some or most countries at least, not fall under the research exemption, because it cannot be considered to be pure research. If it is not falling under the research exemption, can it then still be considered to be public non-commercial use? And if it can be considered to be public non-commercial use, why would it then not fall under the research exemption? It is clear, this type of circular reasoning does not lead us to the solution of the problem, and it illustrates once again that applying the compulsory licensing system on a large scale could be extremely problematic. It would have the advantage that we would at least develop an interpretation of some of the concepts touched upon above, but the question must be raised at what cost, and whether society is prepared to pay that cost, also taking into account potential negative effects on investments in R&D and uncertainty with the public. Worth examining is in any event whether test methods such as the ones claimed in the BRCA1 gene patent could fall under public non-commercial use.

The criterion of public interest is at first sight an efficient argument to apply the compulsory licensing system for circumstances described earlier. But even if one would apply the exceptional circumstances to be relieved from the burden of asking for a voluntary license first, it is re-emphasised that a compulsory license can only be granted if the patent holder refuses to grant a voluntary license under reasonable terms. The reasonableness criterion always pops around the corner. Hence, if a patent holder is willing to grant a voluntary license under reasonable terms, third parties cannot invoke the exceptional circumstances to obtain a compulsory license. An example clarifies the issue: if the patent holder of a drug which is capable of curing a widespread disease in a country, is prepared to grant a license for the drug under reasonable terms, that country or companies within that country cannot simply decide that this drug is to be produced by a third party under a compulsory license. And this brings us back to the interpretation of the wording ‘under reasonable terms’. The French solution illustrates that clearly. According to Art. L. 613-16 “where the interests of public health demand, patents granted for medicines or for processes for obtaining medicines, for products necessary in

or national security. The patentee should be informed as soon as reasonably possible about the act and be compensated in respect of the act by the government concerned. Any dispute as to whether a patent was used or over the amount of compensation shall be decided by the national courts of the Member State concerned.”

obtaining such medicines or for processes for manufacturing such products may be subject to ex officio licenses in accordance with Article L. 613-17 in the event of such medicines being made available to the public in insufficient quantity or quality or at abnormally high prices, by order of the Minister responsible for industrial property, at the request of the Minister responsible for health." The criterion is here 'abnormally high prices', which presents identical problems as the term 'reasonable'. And it is also to be seen whether availability of some testing methods for example, is that much in the interest of public health, knowing that the provision was without doubt drafted with availability of medicaments in mind.

6.3. Why compulsory licensing is not suitable as a remedy in many patent cases

Besides the fact that following a compulsory licensing strategy would be cumbersome and inefficient, and the outcome unpredictable in view of the problems of interpreting the terms and conditions under which compulsory licenses can be granted, there is also an additional drawback attached to the use of that system. Using compulsory licensing on a regular basis in one area of technology and not in another can be difficult to explain and maintain, and the arguments used to defend its use could soon be invoked in other sectors, causing a 'domino-effect', thus leading to a situation where return on investment is made uncertain. That could have a negative effect on investments made in that specific area of technology, and as a consequence it could have a stifling effect on technological progress. One can question whether this and the earlier mentioned negative effect will be outweighed by the beneficial effects of using compulsory licensing schemes for society. The advantage for society at large is that, if we confine ourselves to health care related products and processes, cures will be available to all at reasonable prices. But if of course R&D is negatively influenced by this system, due to insufficient financial resources, the beneficial effect could soon turn out to become a negative effect.

If the aim is to provide cures at reasonable prices, it can be questioned whether compulsory licenses should be the preferred instrument. It has been said in the Nuffield Council Report that "if the monopoly inherent in the patent system as it relates to diagnostic tests based on DNA sequences is having a deleterious effect on society overall, then any remedy, to be effective, must necessarily involve a weakening of the monopoly awarded in this area."[217] One could agree with the

[217] Nuffield Report 2002, 55

argument that if a patent monopoly leads to a deleterious effect on society at large, action is recommendable. But taking action also implies searching for a means to mitigate the negative effect, that means being not only productive but also efficient from an economic point of view. It is submitted that under the present state of the law, and the present problems of interpretation, compulsory licensing is presumably not a system which fulfils those basic efficiency standards, in terms of certainty and guarantee of low prices, without long court proceedings which turn over decisions taken to grant compulsory licenses, which are an additional burden to society, and without having potential negative effects on R&D and technological development. Government interference at the level of price control is probably a more productive strategy, which takes into account on the one hand the financial needs of the industry and return on investment to re-invest in R&D, and the needs of society to have cures at reasonable prices at its disposal.

It must also be observed that the compulsory licensing strategy has become a popular argument since the BRCA1 gene patent. That alone is a bad argument to introduce such a system on a large scale, also in view of the fact that this particular patent is not necessarily representative for all patents granted in the area of gene technology. It could also be said that granting compulsory licensing for these, probably exceptional cases, is not even necessary, in view of the fact that in the end the commercial interests of the patent holder are not sufficient to pursue a strong and aggressive licensing strategy, and that the market will regulate itself.

If policy makers decide,[218] however, that compulsory licensing ought to be used on a more regular basis to tackle practices as described hereabove, and this seems to be the case for some governments, they must be aware first of all of the attraction it might have to other industries. They must also be aware of the fact that a broader application would at least require some amendment of the current compulsory licensing system, since the reasons for which the system is put into practice, such as exceptional circumstances, health threats, crisis or emergency, can generally considered not to be fulfilled in the case of e.g. BRCA1 type tests. In order to take advantage of the exceptional measures in case of compulsory licensing, the only solution is that an amendment should be designed such that health matters in general are considered to be exceptional circumstances. Such a

[218] Such a suggestion was recently made in a report drafted by the UK Royal Society: "We recommend that governments further facilitate compulsory licensing and application of competition law in situations where single or multiple patents do, on balance, unreasonably affect use and development of inventions." UK Royal Society, Keeping Science open: the effects of intellectual property policy on the conduct of science, April 2003, at 10.

broad exception could have serious consequences, as a considerable number of applications are capable of falling under such an exception. Limiting the exception to DNA testing methods seems difficult to justify, as there is no clear reason to consider DNA diagnostic methods as being exceptional circumstances, but not other diagnostic methods. To the extent that governments and courts wish to merely exercise their right to apply antitrust rules, there is evidently no measure which should be taken, as there is already a full antitrust rules system in place. But in this context it must again be observed that it is not completely clear how one could claim that a patent holder abuses his monopoly position if that same patent holder is prepared to grant licenses, be it exclusive ones.

It has already been repeatedly stated in this study that the compulsory licensing system has been developed as one applicable to exceptional circumstances only. Broadening the application of the system to situations for which it has not been originally designed might have negative consequences. It is already clear from the historical development of the system that it appeared to be rather difficult to control. Once the concept was agreed upon, sudden new applications were developed. By expanding the number of applications, the system becomes even less controllable. The effects on the intellectual property rights system can be substantial. In the absence of some certainty, innovators and investors will start doubting about the chances of recouping the investment. And this might in turn have negative effects on technological development. Also if we look at the problem from a purely economic point of view, where the patent system is also considered to be a system to create markets, it might have negative consequences. A broad application of the compulsory licensing system and the correlating uncertainty will also create doubts in the minds of innovators and investors in terms of the potential which remains available to create these markets. Compulsory licenses are by definition an intrusion on this potential.

Another, rather surprising consequence of an expansion of the use of the compulsory licensing system is that it leads to less global trade. Surprising, because it is exactly one of the aims of e.g. the WTO to stimulate global trade. A compulsory licensing system, which by definition is applied nationally, and implies national sovereign decision taking, grants a growing level of discretion relating to the functioning of an intellectual property rights regime to the national governments and courts. This in turns leads to less control, more uncertainty, and less globalisation. Extrapolating this to e.g. the European Union, where the grant of compulsory is still a matter of national governments and courts (and will remain so for some time at least), a lenient application of the system leads to a division of markets, differing standards, less harmonisation, more uncertainty.

These are all very good arguments to stimulate legislators to act prudently when it comes to the application of the compulsory licensing system. It is a positive factor that the system exists, but it would be equally positive if its application could be confined to really exceptional situations. The dramatic situation in some developing countries could be such an exceptional situation. But the mere fact that drugs in our developed world are becoming more expensive due to a patent for an ingredient or element, should not be a cause to apply the system easily. This is even more so if there are other means to tackle such a problem. Compulsory licensing is a last resort, and it should remain that way.

6.4. Non-exclusive licensing an option?

Another option which could be taken is not the compulsory licensing scheme, but a mere exclusion of exclusive licenses in the specific areas. Indeed, one of the phenomena which might occur, and which has actually occurred with the BRCA1 gene patent, is that the patent holder decides to use an exclusive licensing strategy in order to market the invention. An exclusive licensing strategy is advantageous for the patent holder in the sense that he retains some level of control over the licensees, as they are limited, more than this would be the case if a non-exclusive licensing strategy was being used. An exclusive licensing strategy will in many cases also lead to a higher price, even though this is not necessarily the case, since it remains the patent holder who fixes the price of the license to the technology, also under a non-exclusive license. One has to take into account that in the areas we deal with here, the licensees will often be users of the patented technologies, e.g., in order to perform screening or tests protected by the patent. In most cases they will not be manufacturers who have received a license to the technology in order to produce those products which are the subject of the patent. It is thus a different situation from the one where for example a licensee has obtained a license to produce the products which are the subject of the patent. In most cases in the areas dealt with in this study, the licensed technology will be used in further processing to make other products, or will be 'consumed', for example in the case of predictive diagnostic testing methods. And this has its influence on the determination of the price. According to European competition law rules, the

licensor is not allowed to determine the price for the licensed products,[219] but that is of course only true for those situations where the licensee produces patented products under a license. In that case, the licensee must be free to determine the price level himself. In other situations, e.g., if a license is being granted to perform specific predictive tests, the price level is determined by the patent holder – licensor.

Fact remains that a system of exclusive licenses is somewhat more apt to control over all features of the license, and there is limited access for users, since there are only a few licensees on the market. In general it could be said that the patent holder is free to choose the licensing scheme he wishes to apply. One of the characteristics of the patent monopoly is exactly that the patent holder can exercise his monopoly as he sees fit, as long as it is not anti-competitive. And it is a long standing rule in competition law that exclusive licenses are generally considered not to be anti-competitive.[220] Excluding the grant of exclusive licenses as a possible means for the patent holder to exercise his monopoly raises questions as to feasibility, and could also be considered to intrude on the right of the monopoly holder to exercise his monopoly. Under Regulation 240/96/EC, there is a situation in which the grant of an exclusive license is prohibited, however. This is in the framework of a so-called grant-back clause, i.e., the grant of a license to the licensor for improvements made by the licensee on the technology of the licensor.[221] An exclusive license is prohibited if the improvements are severable. This is a logical solution, since otherwise the licensee would be prevented of reaping the fruits of his own independent improvements.

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219 See Art. 3(1) Commission Regulation 240/96/EC of 31 January 1996 on the application of Article 81(3) [former 85(3)] of the Treaty to certain categories of technology transfer agreements, OJ, 1996, L31/2. This regulation has been replaced by Commission Regulation (EC) 772/2004 of 27 April 2004 on the application of Article 81(3) of the Treaty to categories of technology transfer agreements, OJ 27/04/2004, L 123/11. Under this new Block Exemption Regulation, this various black and white lists of allowable and non-allowable clauses will no longer be maintained. This does not take away the validity of the argument, however, as each and every clause in a licensing agreement, also under the new Regulation, needs to be scrutinized.

220 This was expressly recognized in Commission Regulation 240/96/EC, and is still recognized under Regulation 772/2004.

221 See Art. 2(1)(4) Reg. 240/96/EC.

It is more difficult to see a justification for such an exception in the area dealt with in this study. Making such an exception only for DNA would in the view of the author be very difficult to justify. If there would be a health care rationale behind it, then there is no reason to limit such an exception only to DNA. It should then be broadened to all health related technologies, and this might have serious consequences in terms of the extent to which patent holders in this area would still be able to exercise their monopoly. It would definitely be a considerable discrimination vis-à-vis other technologies, and patent and competition law are as a matter of principle non-discriminatory as to the subject matter they govern. Secondly, if such an exception would be created with the goal of keeping prices at an affordable level, it must be said that such a solution will fail, for the simple reason that the patent holder determines the price level, and it does not make any difference whether the license is exclusive or not. If the argument to introduce such an exception would be that particular methods or technologies have to be available in sufficient quantity, it is difficult to see how a non-exclusive licensing system would perform better than an exclusive system, both systems not having any influence on the quantity supplied.

Concluding, if one would decide that a non-exclusive licensing system should be developed for DNA inventions, such an initiative would require considerable convincing power to be successful. There are many arguments against such a policy. And again, it must be emphasised that it is not a sound practice to overhaul not only the patent system but also the competition law system, for reason that some patents have been granted, which turn out to have some unfortunate effects, also in terms of the licensing strategy applied by the patent holder. But whatever may be decided, it will definitely require express statutory provisions, as, in the view of the author, the current state of European competition law does not provide for such a solution.

Chapter 7. Scope of Protection Issues

7.1. Broad or narrow patents

It has been repeatedly mentioned in this study that scope of protection can influence the viability of a specific line of research. But what is even more important, critics of the patentability of DNA inventions in the scientific community have predominantly developed this negative view influenced by scope of protection issues, and in particular by attempts to patent broadly, whether these broad claims were justified or not. Their attitude confirms a tendency to use worst case scenarios as the standard measure for evaluating the desirability of a specific aspect in society. One can regret such a tendency, but it gains in importance. The majority of patents in this area do not have the scope to influence or hamper dramatically scientific research, and most patent holders, whether they have a broad patent or not, are prepared to license their inventions to users at reasonable prices. The few examples which make it in the press are not necessarily representative for the complete research situation in a specific field of scientific research and development, and do not sufficiently take into account the positive effects of the patent system for technological progress, production of new drugs and treatment for debilitating diseases, etc.

It could be submitted that there would be far less resistance if it were made clear to opponents that overbroad scope is indeed not optimal, neither from an economic point of view, nor for society at large, but that the patent system is not necessarily equal to overbroad scope and 'greedy' patent holders. It is thus the responsibility of patent offices and courts to avail themselves of all the checks and balances which are available in the patent system, be it in terms of the patentability requirements of novelty, inventive step and industrial application, or in terms of the disclosure requirement with its effects on scope of protection, or the doctrine of equivalence.

Taking into consideration the above, it can be said that it is impossible to say that narrow patents are always positive, and broad patents are always bad. Patent law is unfortunately a rather complicated area of the law, with major effects on economy and society at large. The quest for the ideal scope of protection is a burdensome journey with many obstacles, and we have not yet arrived at our destination. We can say without any hesitation that overbroad patents are negative for scientific research and society at large. But that is not an answer to the question, since we still have to know what an overbroad patent is. An overbroad patent is a patent which claims more than it has given to the public in terms of

disclosure, the patent claimed is not commensurate with the disclosure made. That implies that in some cases broad patents are justified, if the disclosure made is of such a nature that it covers the invention claimed, for example because it discloses a general principle, applicable to an unlimited number of embodiments. If the invention consists of a number of discrete products or processes, without underlying principle, it would be overbroad to claim embodiments which have not been disclosed. That will be the case with most of the reach-through claims, which therefore alone will be rejected.

As already said earlier in this study, patent scope must thus be broad enough to recompense the cost of invention. On the other hand, patent scope should not extend further than is necessary to accomplish this objective, because patents restrict distribution of the invention and reduce incentives for others to make improvements, and they can thus reduce the social benefits of patented inventions. It has also been held in this context that the increasing breadth of the patent typically is increasingly costly, in terms of dead-weight loss,[222] as the patentee's market power grows. It has been claimed in the past that pioneering inventions deserve a broad scope of protection, in view of the fact that they are pioneering. Such reasoning is problematic in the sense that it does not sufficiently take into account the application of the patentability requirements, which require an equal application for all types of inventions. Applying those requirements on equal footing to all inventions is the best guarantee for a just and fair patent system, thus creating legal certainty for all market players. It is also the best manner to tackle opposition against certain types of patents, if one takes into account that it are exactly those modern technology patents which are the major cause of this

[222] Basically, the dead weight loss system for monopolies works as follows. Assume a monopoly price for a specific good. The level of the price makes some consumers search for substitute goods, goods that the higher monopoly prices makes more attractive. The substitution involves a loss in value. This can be seen if one considers that each substituted product is identical or similar to the monopoly product, but its cost of production is higher, and hence is priced higher than the monopolized product if this were to be sold at its competitive price, but is priced lower than the monopoly price. The effect of monopoly is then that some consumers switch and satisfy their demands with goods that are more costly for society to produce than the monopolized products. This added cost is a waste to society, and is called the dead-weight loss cost. The loss suffered by the consumer from ceasing to buy the monopolized product is not offset by any gain to the sellers, That is also why it is called dead-weight loss. See for this, POSNER, R.A., The Social Cost of Monopoly and Regulation, 83 Journal of Political Economy, 1975, 807-808; POSNER, R.A., Economic Analysis of Law, 4th edition, Little, Brown and Company, Boston etc., 1992, 272-273.

oppositional attitude, and that it are also exactly inventions in these modern technologies which are often called 'pioneering'. If a pioneering invention is the application of a general principle, and it fulfils the other patentability requirements, there is no objective reason to refuse broad patent protection. If this sort of protection is given, however, to a pioneering invention, merely because it is a revolutionary new technological development, and that one has to be lenient in order to stimulate technological development, of which the pioneering invention is an example 'par excellence', there is far less justification for the latter policy. This is because it has not been demonstrated that the invention would not have been made in the absence of that broad patent protection (broad patent protection, and not mere patent protection). This study merely recommends to apply those requirements which can have an influence on the scope of protection in a strict and transparent manner, so that one is capable of evaluating whether the protection claimed is overbroad or not. A central court and interpretation would considerably enhance the development of such a transparent policy with a clear standard of review.

7.2. Scope of protection provisions under Dir. 98/44/EC

With the advent of biotechnology, patent law has undergone some changes. Also in the field of scope of protection, some specific rules have been created to tackle some of the specific features of biotechnological inventions. Scope of protection comes into play in the context of the exclusive rights of the patent holder. In general, and oversimplifying matters to a certain extent, one could say that no one has the right to produce, use or put into circulation the patented product or process without the permission of the patent holder.[223] Knowing what falls under the scope of the patent, and thus within the ambit of the exclusive rights of the patent holder, is crucial to develop an appropriate research and development strategy.

What is so special then about biotechnology that it makes traditional patent provisions not perfectly fit for their purpose? Biotechnology is a special case because it deals with living matter, capable of self-reproduction. This means that if living matter has been patented, and it reproduces, the invention could still be present in the next generation. An example clarifies the point: if a patent has been granted for an animal that has been genetically manipulated (in the sense that a

[223] See e.g., s. 60 UK Patent Act 1977; Art. 53(1)(a) and (b) Dutch Patent Act 1995; Artt. 25-28 Community Patent Convention; Artt. 7-10 Proposed Community Patent Regulation COM(2000) 412 final, and Council Document 7119/04 PI 28.

gene has been inserted in the germ cell line of the animal), the next generation animals will still contain the genetic modification in their genes and cells. Does this imply that the scope of protection extends to all future generations of the patented animal? There has been considerable controversy in the literature on this subject, particularly for the cases of plants and animals. It suffices here to say that patent protection indeed extends to the further generation animals and plants if the genetic information is still present in the further generations and performs its function.[224]

In relation to inventions containing or consisting of genetic information, a similar, although not identical problem arises. What is the extent of protection of a patent for a DNA sequence which is inserted into the human body to perform its specific function, and which is later removed from the human body at the occasion of taking bodily fluids, e.g. blood? Evidently, the question is not whether the patent extends to the next generation human, since this would under all circumstances be excluded form patentability.[225] But nevertheless, a number of complications might arise which we will discuss in this study.

7.3. Art. 8 and 9 Dir. 98/44/EC and their scope

In Dir. 98/44/EC, some specific scope of protection provisions have been laid down, which should be capable of tackling some of the typical problems which come up when living subject matter is being patented. Art. 8 and 9 of the directive contain these provisions. These provisions are new in the sense that they were previously not found in most national patent acts. They do not create new rules, however, since similar solutions were developed in the past by interpreting the existing traditional patent law provisions. The advantage, at least at first sight, of

[224] For a detailed analysis of the issues relating to the patentability of genetically manipulated animals and plants and the scope of protection of such inventions, see, BOSTYN, S.J.R., 'The Patentability of Genetic Information Carriers; The New E.U. Directive 98/44/EC on the Legal Protection of Biotechnological Inventions' [1999] IPQ at 13-26, with further references; G 0001/98, "Transgenic plant/NOVARTIS II", Decision of the Enlarged Board of Appeal of 20 December 1999, OJ EPO, 2000, at 111 et seq.; See also Judgement of the ECJ of 9 October 2001, Kingdom of the Netherlands/Council and European Parliament, C-377/98, [2001] ECR I-7079 at points 42-49 of the reasons, and the Opinion of Advocate General Jacobs in case C-377/98, at points 113-41 of the reasons.

[225] See Art. 5(1) Dir. 98/44/EC.

these new provisions, is that they codify practices and policies which have been developed over time in court decisions.

Art. 8 directive 98/44/EC stipulates that:

> "(1) The protection conferred by a patent on a biological material possessing specific characteristics as a result of the invention shall extend to any biological material derived from that biological material through propagation or multiplication in an identical or divergent form and possessing those same characteristics.[226]
>
> (2) The protection conferred by a patent on a process that enables a biological material to be produced possessing specific characteristics as a result of the invention, shall extend to biological material directly obtained through that process and to any other biological material derived from the directly obtained biological material through propagation or multiplication in an identical or divergent form and possessing those same characteristics."

Art. 8(2) Dir. 98/44/EC does not only confer protection for the products directly obtained by the patented process, but also to any other biological material derived from the product directly obtained by the patented process through multiplication or propagation, in a different or identical form. The only condition is that the derived products or material still contain the same characteristics as the products directly obtained by the protected process. This is again within the framework of protecting all future generations of the product of the protected process. This provision could be said to go further than could be derived from the literal wording of Art. 64(2) EPC, which merely refers to products directly obtained by the protected process. Problems could arise here as to the exact meaning of the wording 'possessing those same characteristics'. Is it sufficient that the characteristics, whatever that may exactly mean, are present in the product, or is it required that those characteristics are also active in that product in order to be protected?

The Community legislator also sought to provide for a specific provision covering the extent of protection of a product containing or consisting of genetic information. Art. 9 Dir. 98/44/EC stipulates that "the protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material, save as provided in Art. 5(1), in which the product is incorporated and

[226] One can think of e.g. herbicide resistant plants, genetically manipulated animals, etc.

in which the genetic information is contained and performs its function."[227] This provision applies to cases where for example a patent has been granted for animal or plant cells. The scope of protection then extends to the plants and animals in which the patented cells are active. If the scope of protection would not extend to the material in which the protected material is incorporated, patent protection would be of little use in some cases.[228] Another example is a patent for a gene construct, which could be a plasmid with therein inserted a foreign gene which is capable of producing a protein of interest, used as a vector, to be inserted in a human or animal body, or in a plant.

Several conditions must, however, be met in order to obtain this extent of protection. The material in which the patented product is incorporated must contain the genetic information, and the genetic information must be expressed in that material. If these conditions are fulfilled, the scope of protection will extend to the animal or plant, but not, however, to the human body, because that is under all circumstances prohibited according to Art. 5 (1) Dir. 98/44/EC.

The provisions in Art. 9 might imply that the scope could be broad but it could also turn out to be narrow. Art. 9 not only prescribes that the genetic information must be present in the material, which could lead to a rather broad scope of protection if that were the only criterion, but it must also perform its function in the biological material in which it is present. This implies that if genetic information is present in biological material but does not perform its function in that material, the scope or protection will not extend to that biological material. Problem is, that the directive is not absolutely clear on this issue. Is the criterion that the function must actually be performed in the biological material, or is the criterion that the information must be capable of performing its function in the biological material? The latter interpretation would probably broaden the scope again.[229]

Some examples are given to illustrate the potential consequences of the application of the aforementioned rules for the scope of protection of DNA related inventions. A first example relates to gene therapy. Assume a patent granted for a

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[227] E.g. plasmids as vectors for gene expression, plant and animal cells, plant and animal genes etc.

[228] A patent for a gene construct to be inserted in an animal in order to modify this animal genetically, will only be of much value if the protection is extended to the animal. It must be admitted, however, that in most cases, patent applications will also include claims aimed at the protection of the material in which the protected material is inserted.

[229] See, BOSTYN, S.J.R., loc.cit., Medical Law Review, 2003, (67) 115.

DNA sequence. This DNA sequence is inserted in the human body, with the aid of a vector, which can also be patented. The DNA sequence finally arrives in human cells, and will produce there a useful effect, such as the production of a protein of interest. The DNA sequences are in the human cells, and assume they are also to be retrieved in the blood. Assume that later in time blood is taken from the patient in question. Applying the rules in respect of scope of protection implies that patent protection extends to the blood in which the DNA is to be found, and where it performs its function. If someone, after extraction of the blood, uses that blood for the production of blood products, he commits a patent infringement, be it contributory, because the manufacturer of those blood products or derivatives makes use of patented material, i.e., the DNA in the blood, without the permission of the patent holder, provided the genetic information still performs its function in the blood product.[230] Another example given here is also in the field of gene therapy. Assume that a patent has been granted for a virus, which will act as a vector to perform the gene therapy treatment. The virus is found in human cells. Cells are removed later in time, and they are used for further research and development, for example because these cells have interesting characteristics thanks to the virus, which is still present in the human cells. As soon as these cells are used for other purposes, except pure research, a patent infringement is committed, because the protection extends to the cells in which the virus is incorporated and performs its function.

7.4. Exact ambit of Art. 8 and 9 Dir. 98/44/EC not clear today

The abovementioned provisions are important for various reasons. On the one hand, it could be said that their conception was necessary in order to provide the patent holder with a scope of protection which is commensurate with what he has given to the public. If an inventor is capable of demonstrating that he has invented a genetically manipulated animal, why would he then not be entitled to obtain patent protection for all animals which have the genetic construct in their genetic material, and thus correspond to all elements of the patented invention? And why would the patent holder of a patent for a DNA sequence or a gene construct not be entitled to claim protection for the use of his patented invention once it has for example been removed from the human body and further research and development is pursued with the aid of that construct?

[230] See, BOSTYN, S.J.R., loc.cit., Medical Law Review, 2003, (67) 115.

On the other hand, it can be admitted that the consequences of broadening protection in the way Dir. 98/44/EC prescribes, could be far-reaching, in the sense that one knows where it starts with protection, but it is not always straightforward to determine where protection ends. And especially in the area of health care research, there might be important effects, in terms of royalty stacking, besides the (contributory) patent infringement claims one could face. Taking that into account, and being aware of the already present phenomenon of patent and royalty stacking, due to the increasing number of upstream patents, it would first of all be welcomed to have a uniform interpretation of these rules, in order to know what their exact ambit is, and secondly it might also make us reflect upon the consequences for health care research and development and the cost of health care in the future.

Chapter 8. Blocking Effects of Patents

8.1. Blocking patents, patent thickets, patent and royalty stacking and the effects on scientific research

In this study, we have hitherto analysed the question whether and to what extent patents for DNA inventions could be granted. We have occasionally already pointed to the effects which the grant of such patents might have on scientific research in its entirety. The advent of this new huge field of technology, with possibilities both in upstream and downstream areas, is indeed a reason for reflection on the future of the patent system as we know it today. What is/are the problem(s) here? There are various issues which deserve some attention in this connection. The grant of patents for upstream technologies, which is from the point of view of the patentability requirements possible under certain conditions, has the effect that further downstream inventions made, with a view to develop a medicament or cure against a disease, will depend on the upstream patent. This could cause patent and royalty stacking, in the sense that the final downstream innovator could be faced with a variety of upstream patents on which his invention is dependent.[231] He will then be forced to pay licensing fees in order to use these inventions, necessary and/or useful to make his own downstream product. From an economic point of view, it is said that transaction costs increase, because due to the licensing fees to be paid for each invention in the chain, not only become these inventions more expensive, but these costs are subsequently all accumulated in the final downstream product. A growing number of patents lead to a growing number of licenses, implying that the sum of all licensing fees increases. Shapiro stated it as follows: "thoughtful observers are increasingly expressing concerns that our patent (and copyright) system is in fact creating a patent thicket, a dense web of overlapping intellectual property rights that a company must hack its way through in order to actually commercialize new technology. With cumulative innovation and multiple blocking patents, stronger patent rights can have the perverse effect of stifling, not encouraging, innovation."[232]

In this context there is also the phenomenon called 'double marginalization': a monopolist (= patent holder) sells a product or process to another monopolist; the

[231] In this sense also recently, WALSH, J.P., ARORA, A., COHEN., W.M., Working Through the Patent Problem, 299 Science, 14 February 2003, 1021.

[232] SHAPIRO, C., Navigating the Patent Thicket, Innovation Policy and the Economy, 2, available at http://haas.berkeley.edu/~shapiro/thicket.pdf.

downstream monopolist incorporates the monopoly rent paid to the upstream monopolist into sales prices, which raises prices of the final downstream product, and in turn this reduces overall welfare.[233] Patent and royalty stacking and the increasing transaction costs might have a stifling effect on scientific research and development in the long run. This could lead to what Heller and Eisenberg[234] have called the tragedy of the anti-commons. The tragedy of the anti-commons arises when multiple players are involved in the use of resources. Each owner of one of the resources needed must give his permission before it can be used. This stacking of fees to be paid in order to use the resource necessary for own production leads to such a burden that the resource becomes underused. When we translate this into patent law language, innovation is stifled, because upstream resources are no longer used for new technological developments, because of the attached costs.

As such, dependency and as a consequence stacking, is not a new phenomenon in patent law. It has always been there, and has not caused the critical reactions in the past which it causes now. This can seem surprising, and one can also question whether we ought to put any effort into analysing its effects and to potentially remedy them. There is without doubt some value in that argument, but the fact that we deal here with a special type of subject matter, i.e., DNA, with its specific informational value and the central position it takes in whatever one tries to do or find about something based on that gene, is presumably a good reason to make that evaluation. And probably stacking and dependency is also a more important issue than in other areas of technology, in view of the size of the stacking and dependency. And combining this size effect with the specific and unique nature of DNA in scientific research in order to find cures and treatments for a variety of diseases, genetic or not, provides an even stronger argument to make that analysis.

From the point of view of economics, there are two problems playing here, i.e., the complements problem and the hold-up problem, which are both different, but which both have the similar effect of potentially stifling innovation. Under the complements problem, the accumulated costs for the use of two or more resources, owned by different monopolist-owners, for the production of a downstream product, will be higher than if the resources were in the hands of one owner only.

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233 BJORNSTAD, D.J., DÜMMER, C., An Introduction to Issues Underlying Patent Policy for the Emerging Genetic Information and Medical Treatment Industry, Joint Institute for Energy & Environment, Report JIEE 2002-05, 23.

234 HELLER, M.A., EISENBERG, R.S.; Can Patents Deter Innovation? The Anticommons in Biomedical Research, 280 Science,1 May 1998, 698-701.

This problem has been described by Cournot:[235] he considered the problem faced by a manufacturer of brass who had to purchase two key inputs, copper and zinc, each controlled by a monopolist. As Cournot demonstrated, the resulting price of brass was higher than would arise if a single firm controlled trade in both copper and zinc, and sold these inputs to a competitive brass industry (or made the brass itself). Worse yet, the combined profits of the producers were lower as well in the presence of complementary monopolies.[236] A similar situation arises today when multiple companies control blocking patents for a particular product or process.

Besides the complements problem, there is also the so-called 'hold-up problem'. The existence of a huge number of patents, even if they are narrow ones, gives rise to the payment of licensing fees. In case of some of these patents, the question can be asked whether they ought to have been granted in the first place. The issues involved in such a reasoning have been developed in detail when we discussed the patentability requirements. In the light of this reasoning, any tax (=licensing fee), even if it is a modest one, is counterproductive if a patent is being granted for innovations which should have not been patented. Another point is that, even if the patent was correctly granted, the cumulative effect of many small 'taxes' can become quite large, and will thus be an additional burden on the subsequent innovator.[237] In other words, for all of these reasons, the manufacturer is highly susceptible to hold-up by the patentee. This "hold-up" problem is present today, and both patent and antitrust policy makers should regard hold-up as a problem of significance in the years ahead.[238] The hold-up problem is worst in industries where hundreds if not thousands of patents, some already issued, others pending, can potentially read on a given product. In these industries, the danger that a manufacturer will "step on a land mine" is all too real. The result will be that some companies avoid the mine field altogether, i.e., refrain from introducing certain products for fear of hold-up.[239] Examples of these industries are the computer and software industry and, which is most relevant for this study, biotechnology, with a growing number of upstream patents.

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235 COURNOT, A., Researches into the Mathematical Principles of the Theory of Wealth (1838), New York, Macmillan, 1897.

236 SHAPIRO, C., Navigating the Patent Thicket, Innovation Policy and the Economy, 5.

237 SHAPIRO, C., Navigating the Patent Thicket, Innovation Policy and the Economy, 7.

238 This is also the point of view of SHAPIRO, C., Navigating the Patent Thicket, Innovation Policy and the Economy, 7.

239 SHAPIRO, C., Navigating the Patent Thicket, Innovation Policy and the Economy, 8.

8.2. Patent pools and cross-licensing as remedies

How can the inefficiency associated with multiple blocking patents be eliminated? There are basically two remedies which can be found. One is creating a patent pool,[240] where suppliers of two or more resources join forces in order to provide these resources to a downstream innovator at a lower price than it would be the case if they were all offering their resources separately. Due to the lower price, there is more chance that the downstream innovator will indeed continue efforts to produce his product or process, more than it would be the case if he was faced with a high burden of separate licensing fees to pay for the various resources. Hence, this is also advantageous for the owners of the resources, who will thus also benefit from such a situation. Another option, depending on the situation, is that a system of cross-licensing is developed so that the owners of the separate resources can via the cross-licenses also produce the downstream products themselves. In other words, without cross-licenses or patent pools, there is a tendency for products to bear "multiple patent burdens."[241]

8.3. Broad patents or purpose-bound patents to avoid blocking patents?

We have seen that patent pools and cross-licensing could be a remedy to avoid the possible stifling effects of patent thickets, definitely in case where so-called 'complements' are to be used in the downstream stage. However, such a solution does not take away the fact that there still remains the phenomenon of patent thickets. What could then be done in order to avoid patent thickets? Granting fewer narrow patents could be an option from a purely economic point of view. Fewer narrow upstream patents will clear the way for profitable downstream applications. A strict application of the patentability requirements, as described in this study, could achieve that goal. It is thus important for patent offices and courts to apply strictly those requirements, not only because that creates more certainty, and could meet a number of the objections voiced by opponents, but also because it creates better conditions for future inventions, and thus for R&D, and thus also for society at large.

Is granting broad patents, which will be fewer in numbers than narrow patents, then a better solution to avoid patent blocking? From the perspective of patent and royalty stacking it could be argued that it is indeed a better solution. Fewer patents

[240] On patent pools, see further below sub 9.

[241] SHAPIRO, C., Navigating the Patent Thicket, Innovation Policy and the Economy, 6.

create less dependency problems, and thus lower transaction costs. The total cost of licensing fees will also be lower if there are fewer licenses to be obtained. But even though broad patents could appear more desirable from the point of view of patent thickets, this does not necessarily mean that they are a positive contribution in the context of patent blocking in general. Patent stacking and royalty stacking is mitigated, but the blocking effect of a broad patent cannot be neglected in the sense that it becomes more difficult to make new developments that do not infringe upon the broad patent. Thus, even though patent stacking presents a burden for society, broad blocking patents are equally burdensome for society in terms of dead-weight loss attached to broad patents, and potential developments lost because of the broad patent which deters other innovators to enter the same field of research.

The tension which exists between a policy which is in favour of granting fewer patents, but broader patents, or a policy which by all means wishes to avoid broad patents, is well illustrated with the patentability of DNA sequences. As we have seen above, the absolute protection granted for DNA patents could lead to a situation where protection is broad in the sense that an upstream patent for DNA patents makes it impossible for downstream innovators to make new developments without being dependent upon the first patent holder.[242] Any subsequent innovator will thus be forced to acquire a license from the first patent holder for the use of that DNA sequence. This could have a blocking effect on subsequent innovators, as the licensing fees could be elevated, in view of the effective monopoly position which the patent holder has obtained, i.e., everyone who wants to pursue research with the patented DNA will be dependent upon his invention (with the limitations we have discussed earlier in this study), which might tempt the patent holder to charge more than moderate licensing fees. It could also be seen as an overcompensation to the first patent holder, since his contribution was merely limited to providing the DNA sequence to the public, without probably having any idea of the later found functions and applications. It is thus argued by some that the first patent holder would be overcompensated and is capable of (over-)using his monopoly power.

One of the solutions which have been discussed to prevent such a situation (and which has also been analysed in this study) is to limit patent protection for DNA sequence to the specific function disclosed, i.e., purpose-bound patent

[242] However, as we have emphasized earlier, this effect may not be overestimated, as a strict application of the disclosure requirement is capable of mitigating that effect to the extent that broadly claimed DNA patents might be rejected on the bases of insufficient disclosure of the embodiments and applications claimed.

protection. This type of protection necessarily leads to a narrower scope for the patent holder. This would bring justice to the efforts of the first and subsequent innovators, each receiving the benefits of what they have been giving to the public. It would bring justice to the first inventor, because the invention he disclosed to the public was in fact limited in scope. And it would bring also justice to the subsequent innovator, who has invented new functions and/or applications, without being necessarily dependent upon the first patent holder, thus giving that subsequent innovator more incentives to develop these new function and/or applications. The other side of the coin is, however, that it will make it less interesting for the first inventor to make the invention in the first place. But what is more important, such a policy would also lead to more patents, all purpose-bound, for the various functions and applications which could be conceived of the DNA sequence. And this brings us then to the problem that further downstream innovators are faced with a real patent thicket, a plethora of narrow scope patents which creates evidently royalty stacking. Patent and royalty stacking will only occur in such a scenario, however, to the extent that the downstream inventor needs various functions and/or applications in his downstream patent. The situation would be much easier in case the downstream inventor only requires one or a few patent licenses in the list of patents. Under the latter hypothesis purpose-bound patent protection would show to be the better option, since first of all there would be little or no stacking in the game, and secondly the licensing fee would most probably also be lower, in view of the more limited monopoly of the patent holder of the purpose-bound patent.

It is thus important that a thorough scrutiny is pursued by the patent offices in order to avoid that unnecessary patents are granted, which only increase the risk of patent and royalty stacking. Granting patents which should never have been granted, however narrow they might be, and however modest the licensing fee is, will always create a burden for society, since the cost could have been avoided if a proper analysis of the innovation had been made before patent grant. And this brings us back to a proper and strict application of the patentability requirements by patent offices and courts.

8.4. Putting information in the public domain a remedy?

Another option which could be thought of is to put more upstream information in the public domain. This has as an evident positive effect that patent thickets, patent and royalty stacking, and blocking effects are avoided. It will also be welcomed by public research institutions, which see this as an example 'par excellence' of furthering scientific research by exchange of research results

without financial burdens. It has as a potential negative effect, however, that investors could lose interest in investing in this area of technology, in view of the lack of return on investment. This can in turn lead to a stifling effect on technological development. However, practice has shown that a strategy of placing upstream information in the public domain has been pursued. It has for example been put into practice with the SNP Consortium. 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.[243] The work on molecular genetics supported by the Consortium is being performed at 4 major research centres.[244] 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 useful in finding genetic associations to diseases and therapies. The pharmaceutical companies hope the database will help them develop drugs to treat diseases whose genetic basis is revealed through the SNPs map. Consortium members agree not to seek to patent SNPs, but they are free to patent any downstream inventions.[245] It should be a subject of further research to analyse the positive and negative effects of such practices, in terms of accessibility of scientific data and investments and incentives for private companies, or the absence thereof, and to what extent such practices could also be expanded to other areas.

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

[244] Stanford Human Genome Center, Washington University School of Medecine, Wellcome Trust's Sanger Centre, The Whitehead Institute for Biomedical Research.

[245] OECD Report 2002, 67-68.

Chapter 9. Patent Pools

As we have seen earlier in this study, there is a risk that patent thickets will emerge. As a phenomenon, this is definitely not limited to DNA inventions, but it will also play a role in this area, and therefore some comments are considered useful. A large amount of patents for upstream inventions create the dense web where the downstream innovator must seek its way through. Patent stacking, and the accompanying royalty stacking can have a negative effect on the investment rate in technological development, since transaction costs and dependency licensing fees could raise to such a level that it is no longer interesting for innovators to invest in this field of technology. This increasing amount of patents for upstream inventions could thus become blocking patents, since they block the way for further downstream innovations.

Licensing and cross-licensing are a solution to the blocking effect of patent thickets, but these practices still have the potential drawback of keeping high licensing fees in place, thus leaving a blocking effect present to some extent. Another alternative, which might also be capable of tackling the issue of the price of licensing fees, is the creation of patent pools. A patent pool is an agreement between two or more patent owners to license one or more of their patents to one another or third parties.[246] In a patent pool, different companies jointly bring together a number of patents. All companies which have entered the pool or third parties can then obtain a license for the patents of the pool on a non-exclusive basis. The patent owners do retain ownership of their patents, however, the pool being created to facilitate licensing. There can also be some form of administration in the pool via an intermediary. The advantage of the pool is that it will be more easy for the members of the patent pool or third parties to obtain a license, and basically this license will be granted under more favourable terms than it would be the case without a pool, following the scheme developed by Cournot, described above. Since there will be more licenses granted, and there is the principle of mutual or cross-licensing, the price can be kept at a lower level, without losing anything at the level of total profits. The easy access to the technology in the patent pool can also facilitate a more rapid technological development. Another advantage of patent pools is that, since each party in a patent pool would benefit

[246] CLARK, J., PICCOLO, J., STANTON, B., TYSON, K., Patent Pools: A Solution to the Problem of Access in Biotechnology Patents?, USPTO, 5 December 2000, 4.

from the work of others, the members may focus on their core competencies, thus spurring innovation at a faster rate.[247]

However interesting the creation of a patent pool may look at first glance, both at the level of cost reduction and speed of technological development, it must be said that patent pools can be problematic in the context of antitrust law. This has bearing on the fact that first of all a patent is a type of monopoly right itself, and as such already theoretically suspect from the point of view of antitrust policy, even though it is a legitimately state-created monopoly. It becomes even more suspicious if a number of monopoly holders bring their monopolies together in a pool. Suspicious because it could have an even enforcing influence on the already existing monopolies, and thus hinder competition, instead of stimulating it, which is the rationale of antitrust legislation. Members of the patent pool could be tempted to make deals so as to offer the licenses at a price which is higher than it would otherwise be. But in the long run, such a strategy would mean the end of the patent pool for the sole reason that high prices will scare away potential licensees, thus ending up where it all started, i.e. blocking and stifling effects on technological development. It has been accepted, however, that patents in general and patent pools have the potential of stimulating innovation and competition, and not necessarily hindering it. However, thorough scrutiny remains to be exercised to avoid the risks mentioned.

One other potential drawback of patent pools is that they could lead to shielding of invalid patents. Companies who fear that their patents will be invalidated could settle by creating a patent pool. This would force the public to pay royalties on technology that would have been public if the patent would have been invalidated.[248] It is thus necessary in the construction of a patent pool system to provide guarantees that such practices cannot take place. That will probably require the involvement of an independent expert to evaluate whether indeed the pool has been created in order to shield invalid patents. It could be expected that such a practice would be applied in the information technology sector, where a considerable number of patents is said to be actually invalid. Whether it would also be applied on a large scale in biotechnology, is unknown at this very moment.

It has been held by the US Department of Justice that patent pooling can be procompetitive since those pools: (1) help integrate complementary technologies, (2) reduce transaction costs, (3) clear blocking positions, (4) avoid costly

247 Ibidem, at 8.

248 CLARK, J., PICCOLO, J., STANTON, B., TYSON, K., Patent Pools: A Solution to the Problem of Access in Biotechnology Patents?, USPTO, 5 December 2000, 10.

infringement litigation, and (5) promote the dissemination of technology.[249] Anticompetitive effects may occur if the pooling arrangement deters or discourages participants from engaging in research and development which is more likely when the arrangement includes a large fraction of the potential research and development in an innovation market.[250] Further additional guidelines have been set forth by the US Department of Justice: (1) the patents in the pool must be valid and not expired; (2) no aggregation of competitive technologies and setting a single price for them; (3) an independent expert should be used to determine whether a patent is essential to complement technologies in the pool; (4) the pool agreement must not disadvantage competitors in downstream product markets; and (5) the pool participants must not collude on prices outside the scope of the pool, e.g., on downstream products.[251]

Even though there are successful examples of patent pools in the electronics industry, it has been doubted in a recent OECD report whether patent pools are a feasible option for biotechnology: "While intriguing as a concept in biotechnology, for genetic inventions it is questionable whether the technologies and markets are amenable to pools. It is true that there is a growing interdependence among patents, that many patents are issuing with narrower claims, and that the patents are held by multiple owners. Licensing transaction costs are burdensome and freedom of operation is restricted, thus increasing the potential of conflict between researchers. However, the pharmaceutical biotechnology industry may be fundamentally different from the electronics sector. It is not an industry where defining standards is important, and assuring interoperability of technologies is not very important, especially not in the development of therapeutics. Company worth is tightly tied to their intellectual property fostering a "bunker mentality." There are likely to be disagreements between partners over the value of the different patents contributed to a pool, and dominant players may not have a strong incentive to join the pool. If a limited field of application and the essential patents can be defined in biotechnology, the patent pool model is worthy of consideration.[252] The suitability

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249 See US Department of Justice and Federal Trade Commission, Antitrust Guidelines for the licensing of Intellectual Property, 1995, § 5.5.

250 Ibidem.

251 See MPEG-LA Review Letter, <http://www.usdoj.gov/atr/public/busreview/1170.htm>

252 A review of potential patent pools in biotechnology has been done by MARKS, M., D. SCHMICKEL AND BEDNAREK M., "Unity in the Gene Pool," Intellectual Property, October 8, 2001.

of the patent pool for biotechnology patents certainly requires further study, as does the role of governments in their promotion."[253]

The European Commission has hitherto not yet developed guidelines concerning patent pools. It is recommended that such guidelines should be developed, in order to have a clear overview of when patent pools can be considered to be pro- or anti-competitive, and which criteria are to be used in determining such an effect. Together with the development of such rules, it would also be very useful if the European Commission would make an in depth analysis of advantages and disadvantages of patent pools, and the potential effects for scientific research policy, investment rate and profit ratio, and for society at large.

[253] OECD Report 2002, 67.

Chapter 10. Conclusions And Recommendations

This study has tried to give an overview of the various issues that play an important role in the context of patenting DNA related inventions. As will be clear from the reading, the field which has been examined looks more like a mine field if one looks at it through the eyes of a lawyer. Many of the questions which have now been raised, were most probably unthinkable a decade ago. On the other hand, some of these questions seem to bring us back to old discussions of a few decades ago, when chemical inventions caused a similar, but probably not that heavy a stir. This turmoil is not surprising, in view of the special nature of DNA and biotechnology in general. It is the viewpoint of the author that such a discussion is a positive evolution. DNA deals with the blueprint of us, human beings. It would be rather surprising if the grant of exclusionary rights for inventions based on these building blocks would not stimulate any discussion. But, having said that such a discussion is welcomed, it must also be stressed that such a debate should take place on the basis of a proper and full information and knowledge about the specifics both of the science behind DNA and the principles of patent law. This study has made an attempt to provide the necessary information relating to the patent law story. It has definitely not solved all the problems, nor has it given an answer to all the questions which arise when discussing the patentability and scope of protection of DNA related inventions. But it provides sufficient information to continue the debate with the necessary nuance. Patent law is in that sense also a particular field of the law, in that it influences and is influenced by science and economics. Understanding and applying patent law presumes a continuous balancing of interests: what is beneficial to society, without hampering too much technological and economic development? And how can technology be stimulated without causing a social cost which is disproportionate? These are difficult questions, which must be dealt with, however.

At the end of this study, a number of conclusions and recommendations are made, which should be capable of contributing in a positive manner to a better informed-based discussion on the future of the patent system and its application to biotechnological inventions.

10.1. Communicating the patent system to the public and research community

One of the conclusions which can be drawn is that the patent system remains a rather unknown field of the law, despite its importance in society. Presumably this

is partly due to the fact that it is a rather complicated area of the law. However, it has undoubtedly also bearing with the fact that apparently, the system and the way it functions, have been communicated poorly in the past. This calls for a fundamental change in the future. There is a need for a continued effort to explain the patent system, and inform the people at large and interested circles about the importance of the system for scientific and technological progress, and as a consequence its beneficial effects for society at large. There is no doubt that the patent system has proved its value for technological developments, and as a means to find the financial resources to make them. The patent system has also had an enormous stimulating effect on the development of medicaments and more generally cures for diseases. Without the patent system, our health care would not be at the level we can benefit from today. It would probably be cheaper, but one can wonder what the value of a cheap health care system is when it cannot provide an effective cure for a number of diseases. To some extent, society must be prepared to pay the price for the level of its health care. No one will doubt that for some types of innovations, the patent system is probably not the most suited system, but that does not take away the positive effects of the system in general.

In this effort to communicate the system, one should not refrain from pointing out to features of the patent system which might give rise to objections to the system. In view of the fact that a patent provides an exclusionary right, it could be used by patent holders in a way which is not necessarily beneficial to society, but is more concentrated on the financial interests of patent holders and/or investors. One should not pretend that such effects are non-existing, but it should also be clarified at the same time that such a use of the patent system is the exception more than it is the rule.

10.2. Strict application of the patentability requirements recommended

It is also necessary to further explain the checks and balances which are present within the patent system. The idea that anyone can obtain a monopoly right on whatever trivial invention he makes, does not do justice to the admittedly complicated checks and balances built within the patent system. The patentability requirements, if properly applied, provide a buffer against unjustified monopoly patent claims. However, a correct and strict application of these requirements is necessary in order to play the role they are capable of playing. It should therefore be a continued concern of patent offices and courts to strive for a transparent and just application of these requirements. Economic reasons make this task more

difficult, as there is an increasing pressure to examine and grant patents more rapidly, which inevitably influences the quality of the evaluation. It is easier to grant a patent, which has a plethora of possibilities of being revoked later (opposition, appeal, court proceedings in first instance, appeal, and final instance), than refusing to grant a patent, which has a more definitive character (with the exception of appeal possibilities). Such a policy shifts the burden – and thus also the cost – to society.

But irrespective of these concerns, and coming to DNA related inventions, it should be emphasised that a correct application of the patentability requirements of novelty, inventive step, industrial application and sufficient disclosure is capable of tackling some of the potential side effects of patenting DNA, as we have discussed at length in this report. As has become clear in this study, DNA is from a patent law point of view not a most peculiar item. The principles which are applicable to chemical inventions are mutatis mutandis also applicable to DNA inventions, which are considered chemical substances. Hence, the objective must be to apply those principles to DNA.

10.3. Overlapping sequences remain patentable under certain conditions

In respect of overlapping sequences, Dir. 98/44/EC has laid down the rule that if there is overlap between an earlier patented sequence, and a later application for a DNA sequence, the scope of the earlier patent will not extend to the later disclosed sequence, if the overlap is not situated in that part which is essential to the invention. Besides the fact that it is not very clear what is meant by the wording 'essential to the invention', it must also be clear that recital (25) does not give an answer to the question of patentability of overlapping sequences, but is merely confined to extent of protection. In respect of patentability, application of the patentability requirements will provide the solution. In some cases, it will be possible to obtain selection patents.

10.4. The industrial application requirement under Art. 5(3) Dir. 98/44/EC creates confusion

The Directive has unnecessarily made things somewhat more complicated when it comes to the industrial application requirement. The text of Art. 5(3) Dir. 98/44/EC is not the most fortunate one could have conceived. Due to its wording, it might give rise to various interpretations. Some might see it as a justification for a

purpose-bound product protection, since the text refers to 'the industrial application'. Even though it can readily be said that the framers of the directive did not have this option in mind when they wrote this provision, the mere text suffices to come to a different conclusion. It would have been a much better and clearer option if the text would have referred to 'an industrial application', since that could only have led to one conclusion, i.e., that it was a mere clarification of the industrial application requirement as we know it under Art. 57 EPC.

10.5. The choice between full product protection and purpose-bound protection remains strongly debated

In the context of the type of patent protection best suited for the protection of DNA inventions, taking into account the interests of society at large and investments in R&D, this study has given an overview of the various arguments which can be invoked to take a stand in the discussion as to whether purpose-bound patent protection could be the better solution, with all its positive but also negative effects. In the view of the author, the discussion on this issue is not finalised yet. The arguments forwarded by the proponents and opponents are not always consistent, and even sometimes contradictory. Purpose-bound protection has the obvious advantage that it could avoid at least part of the dependencies, and due to its narrow scope, it might give the idea of more legal certainty. Question remains of course whether limiting patent protection in such a manner would not have negative effects on the investment rate. This is even more so in view of the fact that purpose-bound protection is not capable of avoiding dependency entirely. And it must also be admitted that purpose-bound patents could add to the already existing stacking problem, in view of the fact that such a patent scope limitation might lead to more narrow scope patents for each individual function. Also worth evaluating in this connection is the argument that the real effect of purpose-bound protection is limited, in view of the fact that, at least in some cases, it is almost impossible to specify the use very precisely, so that it covers only a very well defined, narrow purpose (e.g., only breast cancer instead of cancer). And what is even more important, even if this were possible, would it not unduly limit protection for the patent holder if he obtains for example only protection for breast-cancer, while the invention can also be applied to other forms of cancer? The so-called legal certainty which purpose-bound protection would bring, can thus, as demonstrated in this study, become illusionary, in view of the fact that in some cases it will be difficult to determine the exact scope of a purpose-bound patent, in terms of the applications which fall under it. Besides, while making this evaluation, the question must also be raised why such a solution would apply only to DNA and

not to other inventions. It must also be clear that if the decision is taken, granting practice can only change once the EPC has been amended. This would be required in view of the fact that this new approach would deviate from well established practice and case law not to discriminate on the basis of the type of invention.

10.6. Research tools are patentable

In respect of the patentability of research tools, it is submitted that the checks and balances present in the patent system are capable of tackling most of the potential problems that might arise. Such an innovation cannot be considered to be an invention, in the absence of a specific function, or could fail on the basis of the industrial application requirement. It could also fail on the level of inventive step, if the mere preparation is the key feature. Also the disclosure requirement will be an insurmountable hurdle in many cases. A strict application of the patentability requirements is capable of filtering out the most speculative claims. In other cases, patents could be granted. However, in view of their nature as being upstream inventions, research tools patents add to patent and royalty stacking and blocking. Would purpose-bound patent protection be of some avail here? Presumably not at the level of stacking, and once again the drawbacks of purpose-bound protection as explained earlier must be taken into account in the evaluation.

10.7. Reach-through claims are in most cases rejected

With regard to reach-through claims, a lenient granting policy of patent offices is capable of adding to stacking and blocking effects, something which this type of patents will easily lead to. It is then also important that patent offices scrutinise this type of claims very carefully, so as to make sure that the products identified by the patented tool are indeed sufficiently described in the patent application, and not mere speculation. The strict granting practice at the EPO will ensure that in most cases no patents are granted for such claims. There is no reason, however, to exclude this type of patent claims as such, as there is no legal basis for doing so.

10.8. Predictive diagnostic DNA testing method patents require thorough scrutiny and evaluation of their effects

(Predictive) diagnostic testing methods have already been patented, and have caused considerable arousal. This was an understandable reaction, since the patents had an immediate impact on research and clinical use. The subsequent wave of ‘attacks’ on the patent system is less easy to appreciate. Even though it can be

admitted that the BRCA1 gene patents, and more in particular the way in which the patent owner exercises his patent rights, are capable of having serious consequences for scientific research and clinical testing, this is not sufficient, however, to overhaul the whole patent system. In the maelstrom of the heated discussions, arguments from a not recent past live a second life. Especially those arguments relating to the distinction between invention and discovery seem to be rather popular again. But new ideas and demands have also been launched, amongst others that the diagnostic method exception should be extended to ex vivo methods, an urge for broadening the research exemption, and the request that the compulsory licensing system should be expanded so as to allow more easily that such licenses be granted. Interesting to mention in this context is that all these proposals and demands are being expressed based on speculation about the potential negative consequences of the BRCA1 gene patents, even though hitherto there is no established evidence of negative effects, also in view of the fact that the patent holder does not seem to be aggressive in suing patent infringers. And one reads very seldom the comment that these patents might be invalid in the first place, leaving the negative effects after rectification reaching the bottom level.

What are the potential side effects? One of the problems is that this type of patents basically covers the DNA sequence of the gene of interest, a number of predictive test methods, and in some cases also gene therapy methods. This leads to stacking, since the patent also covers the DNA sequence, indispensable for the development of any further test or therapy. To that extent, they could be categorised as reach-through claims, for which it has been submitted that if the patentability requirements are being applied in a strict manner, the patents should be refused in most cases. But, as we have also discussed in this study, the mere fact that most applications will face a rejection during examination, does not by definition mean that there will be no stacking anymore. In case of a patent which covers both the research tool and further products or methods, there will inevitably be stacking involved. As such, this effect is not special for predictive diagnostic test inventions, which leads to the conclusion that stacking should be discussed in a broader context, since it is a general feature of patents based on fundamental scientific research.

What seems to be clear, however, is that research institutions, who are active in clinical use of this type of predictive diagnostic testing, with an aim to pursue further research, are now faced with a new situation where they have to pay elevated licensing fees. This is capable of having a negative effect on their research output, in view of the simple fact that there are less financial resources left for the actual research. Even though it is not exactly clear yet what the precise

effects might be, it is worth considering some options. One argument could be to say that these ex vivo diagnostic methods ought to be excluded from patentability, as in vivo methods are, since the rationale for exclusion could be considered similar. Regard has to be taken, however, at the long term consequences of such a remedy, in terms of investment rate and technological progress. In view of the importance of diagnostics in the business community, it can be expected that consequences will be substantial. And these substantial consequences will have their effect on health care, i.e., if there is less investment, there will be fewer diagnostic methods available, which is not exactly a positive development from the point of view of health care. Another reason why excluding only predictive DNA diagnostic testing is not necessarily a preferred option is the fact that it is not straightforward to say that the exception would not count for other types of diagnostic testing. In the view of the author, a debate should be started which evaluates the pros and cons, and this study has tried to give a first shot to such a debate. If the decision would be taken to exclude ex vivo diagnostic testing methods, this will require an amendment of the EPC, and will thus not be a matter for the European Union only.

Interesting to observe is also that some of the patents granted in this field are owned by universities or publicly financed institutions or companies. And one of the consequences reported is that information sharing has decreased and ability to develop new tests was also, be it modestly, influenced.[254] This actually means that, knowing that it is the research community which is most active in being against this type of patents, it is that same research community which is largely responsible for creating the problem in the first place. This should make us reflect upon the desire that also universities and publicly financed research institutions should be stimulated to patent more of their inventions, since they seem to add to a considerable extent to problems relating to secrecy and less communication of research results, patent and royalty stacking, in view of the fact that they by definition will seek upstream patents, and hence cause potentially blocking and stifling effects. Instead of overhauling the whole patent system, it is worth analysing whether the problem could not be more effectively tackled by changing the policy of encouraging universities and publicly financed research institutions to seek patent protection, and e.g. stimulate more publication of research results without patent protection. Another strategy could be to include contractual obligations in the research contracts, according to which, in case patent protection is obtained, non-exclusive licenses are provided to all interested users under

[254] See CHO et al., cited earlier (see footnote 188).

reasonable terms, possibly by making also a distinction between fees charged for universities and companies, such as to stimulate dissemination and use of the research results.

10.9. A uniform interpretation of the research exemption in Europe is urged for

It is further submitted that a uniform interpretation of the research exemption is urged for. The existence of the research exemption is not very well known in the university research community, let aside its exact scope. The fact that most patents are granted in the United States, and that in that country no statutory research exemption exists, has not made the issue any clearer. The legal position in Europe can thus not be compared to that in the United States. Having said that most European countries have a research exemption in the statute is only one side of the coin, however. Unfortunately, and as we have seen in this study, this exemption is not uniformly interpreted. This makes things unnecessary complicated, and creates an atmosphere of uncertainty within the research community. It is unnecessary, since it could be easily done away with by creating a uniform interpretation. But that would require a uniform statutory rule for the whole of the European Union, and a uniform interpretation of that rule by a centralised court, in order to avoid the discrepancies we are faced with today. This is not only important for research institutions, but for all market players, who are entitled to know which activities are exempted and which are not. Legal certainty must be accomplished in this area.

In that context, it is also necessary to consider whether it would be better to extend the research exemption to clinical use. Such a policy would in any event be capable of tackling the problems faced by research institutions offering predictive genetic diagnostic tests, which can under the present system be sued for patent infringement if they use the test without consent of the patent holder. If they wish to avoid that risk, they find themselves in a situation where they are not capable of carrying out these tests. For both patients and the institutions mentioned it would be the better solution. Problem with this solution is that it makes the distinction between what is exempted and what is not, already problematic under the current research exemption, even more difficult to make. This is even enhanced by the absence of a uniform rule and interpretation relating to the research exemption. And another question is then what it would mean for the industry developing these tests, and their potential return on investment with the aid of the patent? It is thus important to balance the advantages in the short term for patients and research institutions to have access to these tests at affordable prices, against the

disadvantages for patients in the long run that in the absence of patent protection, fewer tests will be developed. Further research is required in order to analyse the trade-off between the social benefits and the social costs, the precise negative effects and their magnitude, together with similar effects of the options presented, in order to find the optimal solution, if any.

It must be said, however, that the hypothesis formulated above relating to the accessibility to diagnostic tests presumes that the price level of patented tests will be such that they are too heavy a burden for research institutions and patients. It can be questioned, however, whether such a strategy is a sound one from the point of view of the business who has developed and patented the test. In the absence of the financial resources to apply the test, it will not be used, and consequently the patent holder will receive less revenue. And if the patent holder maintains the licensing fee level, it could always be argued that the patent holder refuses to grant a license under reasonable terms, thus opening the possibility for the grant of a compulsory license. Government interference with the price level of such tests could be a means to determine easily and straightforwardly what reasonable terms might be.

10.10. Compulsory licensing should remain a last resort solution, and no lenient application is recommended

Compulsory licensing is nowadays also often invoked to be a solution for potential 'over the edge' practices of patent holders. It can be doubted, however, whether the compulsory licensing system is that much of a help for those situations some might think it can be of some avail for. It must be remembered that the compulsory licensing system has been developed for use in exceptional circumstances only. It should also remain that way, if one does not want to erode the patent holder's rights to such an extent that very little remains of the monopoly power which a patent is supposed to provide, with the well considered aim of providing a return on the investment made for innovation. The argument used for a broader application of the compulsory licensing scheme is for example that if predictive genetic tests are too expensive for users, a compulsory license ought to be granted. Such a solution is most probably not in conformity with the text of the present compulsory licensing provisions as we can find them in national patent acts and in the proposed Community Patent Regulation. A compulsory license can in principle only be granted if the patent holder does not practice the invention, or if no voluntary license can be obtained, except in cases of emergency or crisis, or, as it is laid down in some patent acts, in the public interest. The standard situation is

thus that a voluntary license must be asked for first, and only if that is refused under reasonable terms, a compulsory license can be granted. Major difficulty here is determining what exactly is meant by 'under reasonable terms'. It is not clear which factors should be taken into account in order to make this evaluation. It can easily be seen that most potential licensees will invoke unreasonableness in order to influence the price of the license downwards. But that is not enough to declare a term as unreasonable. As soon as the patent holder has been granting licenses, be it exclusive ones, it will be very difficult to invoke unreasonableness, since the terms were apparently not unreasonable for the already existing (exclusive) licensees. It would be most welcomed if further study would clarify this.

It can also be questioned to what extent the public interest provisions in some national patent acts are in conformity with TRIPs, which only allows exceptions to the normal procedure of trying to obtain a voluntary license first, in cases of national emergency or other extreme urgency. The somewhat broader term 'public interest' does not seem to fit into this narrow definition.

Summarizing the compulsory licensing issue, it is submitted that the system as it is conceived today, is impracticable for the situations it is invoked for. Besides the fact that it is impracticable for these situations, it can also be strongly doubted whether there is a need to use the system for these situations, also in view of the potential effects for later developments. Once one starts broadening the application of the compulsory licensing system, it is impossible to narrow it down later, to the contrary. The Doha WTO access to drugs issue illustrates this very clearly. Once one admits that the system is applicable to a specific situation, there will be attempts to broaden the application of the system to a larger catalogue of situations.

10.11. Scope of protection provisions require further monitoring

The scope of protection rules under Dir. 98/44/EC deserve the credit that they have made some issues at least clearer than they were before. This is more in particular the case for inventions consisting of living subject-matter capable of reproduction. In the past, debates have been pursued on the question as to whether protection for living subject-matter, such as e.g. plants or animals, should not only extend to the generation which is created by the inventor, but also to further generations, as long as those further generations still contain the characteristics which was the core subject-matter of the original invention. The provisions of the directive now give an answer to these questions. And in case the core of the invention consists of genetic information, protection extends to all material in which the genetic material is present and performs its function. In view of the fact

that the directive has not yet been transposed in the majority of the member states, it is too early to tell what the exact consequences of these provisions are on patent practice. The said provisions could potentially lead to a broad scope of protection, and if that occurs, it is to be awaited what the consequences might be for scientific research and technological development. Because of this uncertainty, it is submitted that these provisions require further monitoring in order to evaluate their consequences in practice.

10.12. Effects of patent and royalty stacking on scientific research require further study

Important, but also hard to quantify, are the effects of patent and royalty stacking in terms of technological developments lost. Patent stacking as a phenomenon is present, this is beyond doubt. But it is not a new phenomenon. It is already amongst us for some time, and is more in particular a feature of technologies where there is a high degree of dependency of innovations on certain basic building blocks. It is evidently a phenomenon that dominates some technologies more than others. Gene technology appears to be one of those in which patent stacking has a strong presence. Patent stacking causes rising transaction costs, and hence higher development costs. If patent stacking reaches a certain level, it becomes a thicket, and it can then develop into a blocking factor. There are at present insufficient data to evaluate whether there is a serious problem in this respect, but as there is a trend in DNA technology of stacking, it will presumably be only a question of time before we end up with a thicket and blocking effects.

How could we tackle this phenomenon if it occurs? Limiting patent protection to the specific purpose disclosed in the patent application leads to narrow scope patents. This does not take away the phenomenon of patent and royalty stacking, since the fact that the patents granted will be of narrow scope will most presumably lead to more patents, and thus more stacking. To the extent that subsequent innovators need to use different of these patents to carry out their own invention, which will be the case if their downstream patent avails itself of various functions claimed, the problem remains unsolved. But to the extent that the majority of downstream innovators use only one function, stacking is reduced by allowing only purpose-bound claims. But we have also seen in this study that the certainty envisaged with purpose-bound protection, i.e., protection limited to a well defined purpose, can be illusionary in some cases, and if that turns out to be the reality, the envisaged solution becomes at the least less valuable. Allowing full product

claims, with potentially broad scope patents will as such not have a negative effect on patent stacking, since fewer patents will be granted. However, broad scope patents can have blocking effects in the absence of stacking. Broad scope patents can block the entry for subsequent innovators who consider a particular line of research as being no longer profitable.

A broader research exemption could also partly mitigate the effect of patents and dependency, and thus patent stacking. This is because by allowing some activities, as falling within the scope of the research exemption, royalty stacking is prevented. However, for downstream inventors who wish to commercialize downstream products, a broader research exemption will be of no avail. And it must also be emphasized that a broader research exemption can have negative effects on the investment level of innovation, as we have seen in this study.

Another option to mitigate the potentially negative consequences of patent and royalty stacking is to place more information in the public domain. It requires more research to examine the overall effects and the feasibility of such a strategy. On a limited scale, it is profitable for all market players involved, since also businesses are faced with stacking, and placing information in the public domain prevents patents from being granted, and leads thus to less stacking, and it consequently prevents blocking effects. There is insufficient information to date, however, to evaluate the effects on research and development and investment rates. But it is probably a strategy worth taking for making available information, which would otherwise be claimed as research tool at the very top of the product development process. It might turn out that there are sufficient possibilities for companies to receive return on investment if they decide to patent only products or methods somewhat further in the process, i.e., more downstream.

10.13. There is a need for uniform European guidelines on patent pools

Patent pools are also capable of having a positive effect on royalty stacking. But at the same time they are also capable of having antitrust consequences, however. Thorough scrutiny is therefore required to evaluate these pools. Uniform guidelines for the evaluation of such pools should be drafted by the European Commission, who has been silent hitherto. In view of the important positive effects these pools can potentially have on the serious problem of royalty stacking and rising transaction costs, and thus potentially also on research and development and technological progress, expedient action is recommended.

10.14. Evaluating the current patent system: checks and balances are capable of tackling many of the problems which are previously discussed

This study has demonstrated that the directive has succeeded in providing a balanced view on the patentability of DNA inventions. We have also seen that the practice of the EPO, and the current patent system, are capable of providing solutions for most of the problems which were discussed in this report. It is therefore important to emphasize that it would be a bad idea to change the patent system dramatically, which has proved to work well, with its proper checks and balances. This study has demonstrated that there are a number of unclarities which require further analysis or clarification, with a view to make the system even more balanced, and to improve legal certainty. Statutory texts are not always clear beyond doubt, and that has also happened with Dir. 98/44/EC. This study has given the first shot to start an exercise in clarifying and further explaining the issues which require clarification or explanation. It has also tried to point to some potential future negative effects of patent and royalty stacking. Clear evidence is lacking at this very moment, but the phenomenon and its development require continuous attention, so that one can interfere by fine-tuning in due time.

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