EXHIBIT H

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Genetic Inventions and Patent Law

An Empirical Survey of Selected German R & D Institutions

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Foreword

The impact of intellectual property rights (IPR), especially patents, on the progress of life sciences and biotechnology has been at the center of interest of the public at large and the academic community for some time. Politicians have focussed on this issue in the course of their deliberations related to the implementation of Directive 98/44 of the European Parliament and the Council on the Legal Protection of Biotechnological Inventions of July 1998, due by July 31, 2000, but missed by the vast majority of the EU Member States. One key reason for the hesitation observed was the rule in Article 5 (2) of the Directive providing, *inter alia*, for product patents on DNA sequences of human origin if isolated from the human body or otherwise technically produced.

Since concerns related to product patents on DNA sequences have been expressed and supported by a number of well-known scientists, who predicted a serious negative impact of such patents on further developments in the area of genomics and life sciences in general, the OECD Working Party on Biotechnology took up this issue and organized an expert workshop on "Genetic Inventions, Intellectual Property Rights, and Licensing Practices", which was hosted by the Federal Ministry for Education and Research in January 2002 in Berlin and opened by Minister Edelgard Bulmahn. In order to provide the workshop with the reliable empirical data necessary for discussions and further OECD actions, the German Federal Ministry for Education and Research commissioned an empirical survey of selected German R&D institutions, which was carried out in 2001 by Henrik Holzapfel and Matthias Lindenmeir under my supervision. The results of that survey were presented at the OECD Berlin Workshop and briefly summarized in the OECD publication "Genetic Inventions, Intellectual Property Rights and Licensing Practices – Evidence and Policies" (Paris 2002, pp. 45-49). Due to repeated enquiries for more information on that survey, we decided to publish it in full length with some additional general comments. We are very indebted to the Federal Ministry for Education and Research for the financial support that enabled this publication.

Joseph Straus

Table of Contents

Abbreviations

AIPA	American Inventors Protection Act
DNA	Deoxyribonucleic Acid
e.g.	for example
EC	European Community
EPC	European Patent Convention
EPO	European Patent Office
EST	Expressed Sequence Tag
EU	European Union
GenTG	Gentechnikgesetz
HGP	Human Genome Project
i.e.	id est
IIC	International Review of Industrial Property and Copyright Law
IP	Intellectual Property
IPR	Intellectual Property Rights
JPO	Japan Patent Office
Ltd	Limited
NIH	National Institute of Health
OECD	Organization for Economic Cooperation and Development
PCT	Patent Cooperation Treaty
pp.	following pages
R&D	Research and Development
rDNA	Recombinant DNA
SNP	Single Nucleotide Polymorphisms
U.S.	United States
USPTO	United States Patent and Trademark Office
UTTOs	University Technology Transfer Organizations
Vol	Volume

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I. Introduction

As diverse a definition of biotechnology[1] could be as sundry seems to be any biotech subcategory like genetic engineering combined with intellectual property rights, and here especially with patent law and licensing features. Granting of patents on genetic inventions was one of the first and most controversial legal and societal developments of biotechnology. The issue was raised when Genentech first filed patent applications on genes encoding already well known examined proteins. In 1991, when the NIH sought patents on ESTs[2], the stormy debate refreshed anew and is continuing today when innovations in DNA sequencing technology made high-throughput sequencing feasible and in response genomics companies start in race filing tsunamis of whole gene patent applications[3]. However, there has to be mentioned, that it is not solely the patent and licensing systems that determine how consecutive biotech research at universities, start-ups and even giant pharmaceutical companies is transferred to both the public and private sectors, but it is also essential to keep in mind that in the life cycle of genetic engineering, from research to the market-place, there are other fundamental legal regulations (e.g. Genetechnikgesetz in Germany) that are critically important for facilitating, constraining and guiding the evolution of gene research[4]. Besides, to understand systems of reward exchange in research and development one has to consider that in the biotechnology and pharmaceutical industries, where joint ventures, licensing, and other transactions are common, there might be many traps for the careless patent owner and licensor. Enforcing patent rights in a proper way defines a valuable asset and could help a company to establish a profitable transaction pipeline.

[1] The US Definition of Biotechnology, proposed at the OECD Meeting, Paris, May 2003: "A diverse collection of technologies that both capitalize on the attributes of manipulate organisms, tissues, or cellular, sub-cellular, or biomolecular components to discover new knowledge, to solve problems and create models thereof, goods, products, services and therapies".

[2] Cf. Straus, J., Intellectual Property in Human Genome Research Results, OECD STI Review No. 19 (1996), pp. 46, 50 ss.

[3] Nuffield Council on Bioethics, "The ethics of patenting DNA", Nuffield Foundation (2002), paragraphs 3.42 and 5.38.

[4] Gentechnikgesetz (GenTG), introduced in Germany 1990 with the purpose of control of risk and dangers through genetic engineering.

Although, the numbers of patent applications and patent grants on genetic inventions show a significant increase[5], only little information is openly accessible about the interrelationship between patent law and the licensing practices to whom and under what contractual conditions they take place and about the general impact of patent law on scientific research. Transfer of research and technology and transformation into the development and marketing process underwent severe changes during recent years, where only powerful pharmaceutical companies could afford widespread internal research and development activities. Medium sized smaller companies are forced to enter into R&D partnerships as the mandatory financial input volume seems to explode. In response to this development complementary research platform technologies have to be licensed in to compete with other players and to gain access to novel enabling technologies assigned to modify the own in-house production activities, e.g. with "in-silico" genomics. The individual contributions to the complex genomics evolution are mostly covered by patents, implicating that a company involved in R & D activities will be compelled to acquire licenses with the side-effect of piling up additional financial obligations[6].

Whether patent law, often denounced as being inhibitive to the scientific progress, indeed has such a negative impact on the dynamics of research and development has so far not been well investigated. This the more, since the information pipelines in this area are mainly kept dry.

Nevertheless, for clarifying the alleged and the real impact of patent law in focus through an empirical study on "Genetic Inventions and Patent Law" the impetus was to gain information from an objective viewpoint concentrating on the challenges of potential patentees for patenting genetic inventions and to provide evidence about the licensing practices in respect of genetic inventions. Furthermore, it was to elucidate whether specific problems arise from the application of patent law on genetic inventions, in particular from patents on DNA-sequences.

[5] World Health Organisation. Advisory Committee on Health Research. Genomics and World Health. 2002: http//www3.who.int/whosis/genomics/pdf/genomics_report.pdf.

[6] European Commission, Community research, Workshop Report on Managing IPR in a knowledge-based economy-Bioinformatics and the influence of public policy, Brussels, November 2001.

II. Conception of the Survey

In co-operation with the Federal Ministry of Education and Research a sample group consisting of pharmaceutical companies, biotechnological companies, biotechnological research institutions and clinical institutions associated with universities performing research and development in the field of genetic engineering was selected.
It has been agreed upon to conduct personal interviews with the representatives of these genomics-associated firms and institutions. All of them were involved in this interrelational interface between genomics and the patenting and licensing systems as potential proprietors of patents, licensees and/or licensors, or even as plaintiffs and defendants in legal conflicts.
The applied questionnaire encompassed five key-categories:

1. Formal business profile of company.

This category included questions on the marketed product, yearly turnover, financial background, merger acquisitions and cooperative structures with other companies.

2. Patents

This category focused on the number of filed and granted patents, especially claiming DNA sequences and taking into account the significance of own patents as well as the competitors` patents interacting with the company's business.

3. Licenses

In analogy to the second key-category, the number of granted and refused in-licenses were ascertained. Questions on applications for compulsory licenses and cross-licenses were posed.

4. Patents and R&D

The main points here were questions on the annual investments in R&D, policies controlling situations where any dependent patents were available and dominated by competitor's patents, or how research tools for the own R&D are tackled. Other questions included the scientific publications and the impact of patent law on time, quality and quantity of publishing research findings. Developments based on patents and R&D, as e.g. spin-offs of genomics R&D were also examined.

5. Patents and Patent Litigation

This category dealt with the possibility of law-suits in the light of alleged patent infringements and potential consequences thereof for R&D. The influence of in-depth knowledge of patent law also in relation to external legal consultation taken. A broader survey should have been gained through questions on special patent characteristics of genetic patents. Other issues here were the justification of absolute protection of a substance, independence of disclosed use and the comparison of the legal framework for R&D in the field of biotechnology in Germany and other countries.

6. The Method Applied

The interviews have been conducted in a seven-months period from July 2001 to January 2002. Taking into account the differing activities and needs of the individual interview partners for each key category the questionnaire was adaptively modified, being in this very sense of a questionnaire more of a guideline than a strict frame for each interview performed. This procedure seemed to be appropriate in order to discuss delicate questions of patent law and biotechnology with the addressees directly and to avoid any misunderstandings. Moreover, an individual personal conversation enabled further investigation of topics that had been raised unexpectedly. Due to an extensive method of investigation and the given personnel and financial resources the number of institutions to

be interviewed was limited. Bearing this aspect in mind, the significance of statistical data obtained has to be considered in the light of this flexible way of interviewing and reflecting as well the relatively small sample group. This notwithstanding, the primer to identify and judge trends and developments could be accomplished.

III. Results of the Survey

1. Financial Dependency on Patents and Patent Lawsuits

In recent years investors have been piling into biotechnology stocks creating a new emerging stock sector with all the ups and downs of the indices. When it came to the situation that pressure had been exerted on the EPO or the USPTO to restrict their practices for granting gene-related patents, mainly those companies were at risk of sliding biotech indices having patent portfolios stiffed with broad claims on DNA or DNA fragments like ESTs[7]. However, even if the patent offices grant broad claims on genes, such patent-owners might be exposed to costly law-suits to defend them for the future. Another economic aspect might be influenced by such patents creating a prospect function, so-called pioneer patents, that introduce new and promising technologies and thereby stimulate greater venture support through the investors[8]. But it might not only be the patent portfolio setting the venture capital on a high scale, what matters could also be the existence of real products tightly associated to patents. Although it is hard to quantify and evaluate such dynamics the economic importance of patents is undisputed as our findings suggest.

[7] Seen as an effect of the introduction of the new "written description guidelines" by the USPTO.

[8] Kenneth W. Dam, "The Economic Underpinnings of Patent Law", Journal of Legal Studies, Vol. 23, (1994), 247-271.

a. Pharmaceutical Companies

The interviewed pharmaceutical companies did not believe that patent applications and patent lawsuits in the field of biotechnology specifically affected their stock exchange rate or the acquisition of venture capital, even if considerable turnover was generated in marketing biotechnological or biotechnologically made products. Large pharmaceutical companies rather regard patent rights as a mechanism for prevailing research in specific scientific field and as pawn in negotiations with potential partners. The decisive variable there was seen in a successful end-product, related or not related to in-house patents.

b. Biotechnological Companies

Biotech companies without or with few ready for sale products stated that patent applications, patent grants or patent lawsuits affected their stock exchange range or the acquisition of venture capital substantially. In the first place because a fundamental pioneer patent in most cases was the essential asset for start up companies. In the second place every lawsuit filed against a company forced downs of the stock exchange rates markedly. The development of the stock exchange rate was particularly essential for small companies, because among those stock transfers were a common mode for merging with other companies.

One principal issue here was to bridge the gap between the potential of science and the expectations of the investors implicated by legal proceedings. There existed criticism that venture capital firms could asses properly the implications of neither patent applications nor of patent lawsuits, i.e. some investors were blinded by high numbers of patent applications not recognizing that the majority of applications belonged to a single family of gene sequences. Companies could possibly take advantage of this fact by primarily filing a multitude of patent applications in order to combine various applications into a single patent in order to save patent office's fees. Besides that from the investor's perspective the prospects of a pending lawsuit due to patent infringement or patent invalidity were overshadowed by the mere fact of filing an action. On the contrary it was pointed out that the scrutiny preceding the entry into the stock market was more profound.

Two biotechnological companies, that had been active in the market for a longer time, felt that in the long run qualities like qualification of the employees, after-sales service and quality management will increase in importance compared to the patent portfolio.

2. Significance of Patents for the Co-operation or Merging of Companies

In the face of increasing costs and risks of high-tech innovations, one means of transacting knowledge could be through alliances between companies in form of sporadic associations or even stable joint ventures as active promoters for acquisition, development and exchange of technology.

Despite this positive list of benefits through allying the disadvantages may also lay at hand, since a company as alliance partner would consequently agree or may be obliged to transfer control over internal activities and technological resources[9]. This could turn out as a mechanism where a cooperating partner company could be cast for the part of the dependent partner risking the loss of technological knowledge to those partners which without alliance would be competitors itself.

In an increasing manner, the value and the importance of intangible assets, among them the traditional intellectual property assets like patents, seem to be the incentives for mergers, acquisitions and takeovers.[10] The critical point in such a manifestation of corporate restructuring through merging is the issue that the consecutive acquisition of patents as intangible assets could lead to antitrust violations by eliminating competition between major players within a certain domain. However, it is anticipated, that in the global development of a knowledge-based economy the driving force for future merger and acquisitions proceedings might be dominantly manifested in the technological value of patents[11].

[9] Sergio Speranza, Strategic alliances and licensing the transmission of knowledge, Les Nouvelles, Vol. 35 No. 2. (2000), pp. 82-85.

[10] Lanning G. Bryer and Scott J. Lebson, Intellectual Property Assets in Mergers and Acquisitions, Les Nouvelles, Vol. 35, No. 3. (2000), pp. 124-128.

[11] Biotechnology Statistics in OECD Member Countries: Compendium of Existing National Statistics, Second Ad Hoc Meeting On Biotechnology Statistics, Paris, OECD, 3-4 May 2001.

a. Pharmaceutical Companies

Some pharmaceutical companies pursued a strategy of "buy, not make", i.e. they bought intermediary products, production assets as well as research tools from biotechnological companies or used external services for screening or purification procedures.

In this respect intellectual property issues were of limited significance as far as the ownership of patents could not be secluded from the – not legally protected – know-how that was acquired by realizing the patented invention. Sometimes the know-how was regarded as even more crucial:

The question was rather who could implement a certain method than who had the permission to do this. However as permission and ability regularly coincide the intellectual property situation was attributed at least a secondary importance.

Whether relevant patent rights existed and whether the contractor owned these patent rights was not always examined meticulously. A slightly different situation was observed in respect of research tools such as expressed sequence tags (ESTs) or single nucleotide polymorphisms (SNPs). Costly developments of pharmaceuticals and diagnostics relied on these research tools. To avoid a tiring "rat race", the pharmaceutical companies tried to monopolize the innovative activity based on such research tools. For this purpose the intellectual property issues were screened more accurately and an exclusive license was sought.

b. Biotechnological Companies

Some biotechnological companies admitted that co-operations with other companies had failed or were complicated because of unresolved intellectual property questions.

c. Co-operations

As regards the ownership of prospective patents co-operations between companies including joint research projects differed to a high degree, depending on individual

circumstances. In most cases the parties agreed on the distribution of intellectual property prior to the co-operation, at least on a preliminary basis. According to the ex-post estimates of the value of the invention, the preliminary arrangement could be subject to changes.

Predominantly the co-operating parties agreed upon which one should become sole proprietor of expected patents, combined with the obligation to license the invention for free or within an agreed range of royalties to partners in the co-operation. Within co-operations between companies and research institutions the company usually became proprietor of the invention. Only in cases where inventive contribution of the research institute was clearly predominant and the contribution of the company
was limited to financial support or supply of equipment the situation was different. In general research institutions were interested mainly in publishing their results and did not want to procure the costs associated with patent application and enforcement of royalties themselves.

Within co-operations between companies mostly that company became patent owner whose core business was affected by the patent. An advantage of a clear assignment of patent rights was the well-defined responsibility. Further handling of patents, e. g. enforcement and licensing, did not require extensive negotiations between several parties.

d. Mergers

In mergers with an other company the intellectual property situation played an important, if not dominating role. Sometimes the existence of a patent right was the key incentive for merging.

3. Purpose of Patenting

As indicated in the introduction of this paper the patent system had been most controversial through the granting of gene sequence patents and therefore is particularly vulnerable to criticism. It is a fact that a patent may be an extensive right, however it is not admissioned without restrictive examination both, for qualifying criteria and validity

requirements. This is ensured for all types of technical and scientific innovation, and particularly true for biotechnological inventions. Major confusion and misunderstanding is provoked by the putative nature of a "monopoly" represented by a patent[12]. This is not true for the real purpose of the patent, since it does not confer the right to exploit the invention. One principal reason for patents is to be an initial filter for scientific and technological regulation, thus claiming to be the basis for contracts, rewards and incentives directing to future benefits to allow the inventors to enjoy their returns on the generation and application of knowledge.

From the perspective of some companies patenting seemed to be rather an option, to enable and secure further research by the company and to facilitate future co-operations as means of negotiation and exchange, compared to the intention to monopolize the market. This was partly due to the not promising and complex enforcement of rights.

This was especially true for research tools, since a drug possibly discovered by the use of e. g. ESTs would be a "small molecule" allowing in most cases no detection of its origin. Moreover patent infringement lawsuits often resulted only in the grant of reasonable royalties as remedy for the use of the research tools. Usually lawsuits did not result in a participation in the profits derived from selling the drug that had been developed using the research tool.

Some biotechnological companies indicated that they felt a kind of "peer group pressure" towards patenting. Companies did not want to fall behind competitors filing many patents at any rate, although the real benefit of patenting was not always recognized.

For one clinical center the purpose of patenting of genes consisted mainly of donating the commercial revenue to those patients concerned with a genetic disorder (e. g. Nijmwegen breakage syndrome).

4. Genetic Inventions and Licensing, Compulsory Licenses

As a fact, the time for licensing a patent regularly falls some years behind originating and disclosing a patented invention, therefore the momentum when a patent could be licensed

[12] Warren Jones Amanda, Patenting rDNA, human and animal biotechnology in the United Kingdom and Europe, Lawtext Publishing Ltd. 2001, p. 74.

may not be well-timed. Immense complications when dealing with patents in any licensing or collaboration proceedings are especially striking within the disputable biotechnology and drug discovery industries. Indeed, most companies that have substantial portfolios of patents do not fully understand what they have and what its value is[13]. Far-reaching potentially fatal consequences could arise for smaller companies, if they fail to handle their patent rights adequately, i.e. mining the patent portfolio for licensing opportunities in a sophisticated way. In this context the deal-makers in charge should be well aware of the technological value of a patent and also deny licensing if the conditions for rent seeking tend to be asymmetrical[14].

Governments can opt to issue, or threaten to issue compulsory licenses which provide as liability rules in a sense a potential defense to patent infringement obliging the patentee to grant a license to a potential infringer[15]. Although the patentee would lose his patent rights to some degree he could be reimbursed by license fees, which appear to offer little real benefit. Provisions for compulsory licensing are implemented as a common feature in most patent law systems, however applied very rarely, since problems of valuation and compensation seem to turn out rather complicated[16].

a. License Negotiations

There was unanimous consent that no special problems arose negotiating licenses for genetic inventions. With genetic as with other inventions the patent proprietor was usually aimed at commercializing his invention as profitable as possible. As licensing fees created income and the patentee himself possibly could not exploit all conceivable uses of his invention, the full potential of the invention could only be commercialized by licensing

[13] Robert S. Bramson, Mining the Patent Portfolio for Licensing Opportunities and Revenues, Les Nouvelles, Vol. 35, No. 3., (2000), pp. 109-115.

[14] Patrick Duxbury and Diane Mellett, License and collaboration agreements: Protecting your most valuable asset, nature biotechnology, Vol. 20, No. 1, January 2002, pp. 91-92.

[15] Trevor Cook, Catherine Doyle, David Jabbari, Pharmaceuticals Biotechnology & Law, Stockton Press 1991, pp. 322-323.

[16] Genetic Inventions, Intellectual Property Rights and Licensing Practices, Evidence and Policies, OECD, 2002.

the invention at least partially, making licensing the economically more attractive choice than denying a license. Patent owners acted rationally ("could calculate") while reaching a deal on licenses. Licensing gave the patent owner the possibility to generate revenues with minor risk than developing marketable products himself. Some licensors were too demanding and overestimated the values of their inventions. This dilated license-negotiating significantly, however the prospects of future licensing were still positive. Often there was competition among potential licensors, e. g. when various equally suitable gene expression systems existed. In such constellations alternative pathways enabled the licensee to bargain a reasonable royalty. Finally licensors depended on the commercialization of their research tools and therefore would have to renounce on revenues completely without a license contract.

b. Royalty Stacking

Despite regular license negotiations the problem of royalty stacking emerged, e. g. many licenses had to be paid to market a single monoclonal antibody.

Genuine in-house developments hardly ever occurred in the field of biotechnology. One to three licenses per marketable product could be tolerated, but increasingly often seven or more licenses were mandatory, endangering the commercialization of the final product.

It was desirable that, like in the United States, complete license packages were on offer. Besides it was feasible to include royalty-stacking clauses in license contracts, with the effect of reducing costs for each individual license if the total number of licenses to be taken exceeded 10 per cent of the turnover of the final product.

c. License Disapproval

In most of the cases where a license had been denied it was that a license had been sought from direct business competitors. Not different from other types of inventions the patent owner did not want to support his competitor's business activity.

d. Exclusive Licenses

In some fields of genetic inventions, e. g. some kinds of research tools, almost only exclusive licenses were on demand, guaranteeing the licensee for the left patent period the exclusivity of research building upon the licensed invention. This offered the licensee a better chance to recoup his invested capital.
This was why in some cases an exclusive license had been denied, i.e. if the would-be licensee was not given the confidence of realizing a commercially successful innovation.

As a consequence of that the patentee did not want to waste the exclusive license on contracting with such a license seeker.

e. Patent Pooling and Cross-licensing

Patent pooling and cross-licensing were not popular. Only three companies participated in cross-licensing or patent pooling. In their opinion such arrangements were not very effective: The fear of the participating companies of unbalanced contributions and profits from the arrangement increased the level of license fees. Nevertheless for researchers patent pools could be more attractive.

f. Compulsory Licensing

Compulsory licensing was not seen an very essential issue. Compulsory licenses were perceived as a more hypothetical alternative compared to successful license contracting, regarding the restrictive way of granting compulsory licenses by the patent offices or courts, respectively. Some wondered if there existed a kind of gentleman's agreement not to apply for compulsory licenses, as oneself did not want suffer himself from a compulsory license either.
One company discussed applying for a compulsory license twice. However it finally had not applied as essential investments could sometimes not be based on a non-exclusive

license. Likewise the consecutive existence of the compulsory license could not be relied on, since the mandatory public interest in the compulsory license could be inapplicable if the patentee began with the commercialization of a competitive product by himself.
Four companies suggested to facilitate compulsory licensing, e. g. when certain patent protected targets were integrated in the development of a medical drug. After all, the first drug to be discovered rarely was the most important one. Every one should be entitled to use an invention –especially research tools for reasonable royalties. One did not want to use the invention for free, the patentee rather should appropriately participate in the commercial success of the marketed product. Other companies stated that further facilitating compulsory licensing raised the question of the remaining value of a non-exclusive patent right. Respective to DNA-sequences they explained that the potential benefit of gene sequences was too hypothetical to establish the public interest in a compulsory license.

5. Effects of Patents on End Products on Research Activity

Functional genomics technologies is a fast-accelerating field where new products and services are developed from accumulating and complex composites of emerging *de novo* technologies. Various end-products might include DNA sequences, i.e. diagnostic tests like DNA-microarrays[17] or pharmaceuticals designed by proteins that were originated from corresponding gene expression profiles via the drug discovery value chain[18]. However, not only the end-product is eligible for patent protection, but also their use or production-methods including intermediaries[19]. These intermediary products could as well serve as end-products and thereby occupy a prominent role in the dynamic

[17] Diagnostic tests: With the recent completion of the human genome sequence and the fast-moving proliferation of the DNA-microarray-technologies, there will be a wide variety of high-quality diagnostic tests based on DNA and protein microarrays.

[18] Mark Schena, Microarray Analysis, Wiley-Liss 2003, pp. 21-25.

[19] Straus Joseph, Patenting Genes and Gene Therapy: legal and ethical aspects, in: From Genome to Therapy: Integrating new technologies with drug development, John Wiley and Sons, Ltd. 2000, p. 115.

interplay involving research activities in molecular biology, genetics and medicine as well as engineering sciences and applied bioinformatics.

a. Examination of Patents

All companies indicated that they examined patented inventions of competitors concerning novelty, disclosure and function, at least when the invention influenced their own core business. This examination was performed in view of possible opposition and invalidity procedures as well as possible license negotiations. Nonetheless these examinations could be carried out even after taking the license if an option period or cancellation opportunity had been agreed on. Competitors of the patentee were often the first to discover the lacking patentability of a patented invention.

b. Comparison of Products

Tests were performed in order to compare own products still under development to products that were already marketed by competitors. The comparison with this state of the art provided information on the patentability of own inventions. Especially when competing products proved to be superior the further investment in the development of the own end product could be re-reviewed.

c. Improvements of Inventions

Experiments serving the improvement of inventions were often conducted with own inventions. Herewith the practical applicability of the invention should be advanced or the experimental results achieved leading to dependent inventions. In this context it was reminded that the second medical indication of a drug was often more precious than the first. At the same time the companies mentioned, on principle, not to perform experiments in order to upgrade alien patents. Then only a dependent patent was available, by which the dominant patent of a competitor would have been increased in value.

Two companies admitted to work on an improvement of foreign patents only in an exceptional constellation, i. e. when the major part of the investment in an innovation had already taken place or an agreement with the proprietor of the dominant invention (patent) seemed probable. This consent could be a cross-licensing or selling of the dependent invention to the owner of the dominant patent. However an amicable settlement became the more expensive the later on in the innovation procedure one became aware of existing patents relating to the own innovation work and the more investments in the use of a dominant patent had already been made.

d. Patent Dependency

A pragmatic way of avoiding the effects of patent dependency was mentioned by one company: Buying the dominant patent. This was the way of choice if a patent obtained exclusive dominance in a field of technology that was of major value for the company's business activity.

6. Effects of Patents on Research Tools on Research Activity

In the future, the use of patented research tools by pharmaceutical or biotechnology companies is most probable within the development of novel therapeutics, since this will involve the examination of databases of gene-related biochemical substances corresponding to designated biochemical sites as well as their application to the interaction with targets. In such early-stage research activities functional genomics research tools (broad range of genes and gene functions with their expression products[20]) will be of a major interest for the scientists of the private or public sector to narrow down defined research procedures in order to reach a scientific goal. Nonetheless, currently it

[20] This could be proteins which encompass an cumulative functional diversity providing a large set of molecules including enzymes, antibodies, transcription factors, receptors, hormones or other mediators and targets.

[21] Nuffield Council on Bioethics, "The ethics of patenting DNA", Nuffield Foundation (2002), paragraph 5.38, 5.43 – 5. 47.

seems to be an open question, if the use of patented gene-related research tools by other parties with research objectives in drug discovery or diagnostics will cumulate infringement proceedings and/or damages[21].

a. Application of Research Tools

The application of research tools so far did not present a disputable issue. Firstly research tools like certain enzymes were easily available staple goods which could be bought without declaring the intended use. Purchasing the research tools leads to exhaustion of the patent right. Therefore the direction of the own research activity could remain discrete. Furthermore it was pointed out that as a rule patent infringement in making and utilization of research tools remained undetected "behind locked laboratory doors". That was why the patentee was unaware of such infringements, so that he could raise claims only against contributory infringers. The suspicion of infringement could only occur when a product was marketed that could have been developed by infringing e.g. a research tool patent. Only few of the interviewed biotech companies had reached the stage of commercialization.

b. Awareness of Legal Implications for Patented Research Tools

The research institutions complemented that their employees might not be aware of legal implications of making or using patented research tools. This was due to the fact that patent infringement law suits were not often filed against research institutions. There was little economic incentive for the patentee to file such a lawsuit, because the research institutions generated no revenues through patent infringement.
In a single case it was speculated that patent owners might fear to lose reputation when suing a publicly owned research institution. Accordingly lawsuits enforcing patents on the enzyme taq-polymerase had caused a loss of renommée.

c. Copyright Implications

One research institution believed that a kind of copyright would have sped up the sequencing of the human genome. With the legal status quo discovered gene sequences would have been kept secret temporarily. Preferably anyone should be entitled to use gene sequences given that part of the revenue to generate was passed on to the copyright proprietor.

7. Effects of Patents on Publication Activity

A significant primer for most scientific research work may be the publication of research findings for peer review. In this context however premature publication activities could create adverse effects upon subsequent endeavour to acquire patent protection for the methods and results disclosed in a paper[22]. Whereas in most European Patent Systems pre-publication collides with the objectives of the patent systems, in the United States of America patent protection is still available if a patent application is filed with the United States Patent and Trademark Office (USPTO) within one year of the publication date, so-called Grace Period[23].
Although reluctance in respect of premature publishing predominates for good reasons[24], it is not unusual to have scientists publish research details before any patent considerations have been made[25]. As the pros and cons for a Grace period are still going to be discussed

[22] Straus Joseph, Grace Period and the European and International Patent Law, Analysis of Key Legal and Socio-Economic Aspects, IIC Studies 2001, p. 77.

[23] Straus Joseph, Grace Period and the European and International Patent Law, Analysis of Key Legal and Socio-Economic Aspects, IIC Studies 2001, pp. 45.

[24] Bill Barrett, Defensive use of publications in an intellectual property strategy, nature biotechnology, Vol. 20, No. 2, February 2002, pp. 191-193.

[25] A prominent example is the publication of the results achieved by Stanley Cohen and Herbert Boyer which led to the granting of U.S. Patent 4,237.224.

the impetus within the scientific community for the continuous race to be the first appears to be unbroken. And this requires publication.

a. Companies

All the companies stated that scientific publishing of experimental results had no priority for them. On the contrary they established formalized prepublication procedures in the course of which the patent department had to agree with the intended publication. This prohibited publications precluding novelty.

b. Grace Period

The interviewed companies opposed the introduction of a grace period into German and European patent law. The legal certainty that existed without a grace period was perceived as more important than the incentive to early publication. At least the grace period of one year provided by U.S.-law was considered too long. On the opposite side the research institutions favoured the introduction of a grace-period. They were unable to establish pre-publication procedures like the companies as the individual researchers were rarely willing to consult the patent department (if one existed) before each and any speech or conference. On the whole scientific researchers were not sensitive for the fact that those talks and conferences could constitute prior art. Publications in scientific magazines were not regarded as that problematic since a patent application could still be filed during the time-consuming peer-review process, i. e. prior to the actual publication.

8. Lawsuits Dealing with Genetic Inventions

One main issue for reasonably policing an invention also true for genetic inventions concentrates on the value of a patent which on the other hand depends itself on the capability to anticipate others from applying the claimed invention without prior licensing. The reasons that patent protected inventions are infringed by using them without

authorization are multiple, however, due to such a diversity of products or processes in certain fields of biotechnology the predominant motivation to do so is the belief of potential infringers that the patent owner would never become aware of their illegal use[26]. But when occurring infringement has become evident to the patent proprietor, it is possible for him to terminate the illegal use through legal proceedings. Since litigation could be a financial high-risk[27], this approach should be kept in mind as *ultima ratio*. Furthermore, during a litigation the validity of a patent might be jeopardized by the alleged infringer in the sense that the patent could be revoked or the economically decisive claims could be narrowed to insignificance through the appealed court. Besides alternative dispute resolutions[28], the parties could agree to resolve the problem by licensing the invention under reasonable contractual terms.

a. Pharmaceutical Companies

The well established pharmaceutical companies emphasized that lawsuits dealing with genetic inventions had not occurred to any larger extent than in other fields of technology. Most biotechnological companies were too ambitious to co-operate with pharmaceutical companies to sue the pharmaceutical companies.

Some uttered the opinion that mainly in the United States lawsuits accumulated, despite the doubtful validity and scope of certain patent claims.

This was due to the heavy competition among biotechnological companies with the intention to reach a dispute settlement leading to an opportunity of licensing the own invention to the sued company. In this respect the doubtful validity and scope of certain patent claims propagated lawsuits.

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[26] Saliwanchik Roman, Protecting Biotechnology Inventions, A Guide for Scientists, Brock/Springer Series in Contemporary Bioscience (1988), pp. 61 following.

[27] James D. Myers and Robert Glatz, Procedural Aspects of Patent Litigation, in: The Law and Strategy of Biotechnology Patents edited by Kennth D. Sibley, Butterworth-Heinemann (1994), pp. 231-232.

[28] As a result of the long delays and the high costs associated with resolving disputes by traditional trial mechanisms, there is an increasing emphasis on negotiating settlement or applying alternative methods of dispute resolution like arbitration or mediation.

b. Biotechnological Companies

All but one biotechnological companies testified they never had been involved in a patent lawsuit. This could result from the fact that a great proportion of them did not market any products yet, so that any proprietor of a possibly infringed patent had difficulties in realizing that his patent could have been infringed and had little economic incentive to file a lawsuit.

Possible motivation for nevertheless filing a lawsuit preceding marketing by the alleged infringer were urgent financial need as well as the intention to arrange a licensing agreement or to advance competition from the level of marketing to the level of research and development. The latter could lead to a preventive suppression competition.

In general, the concern to be sued appeared greater than the inclination to file a lawsuit. In other words, especially the smaller companies made use of a defensive strategy for enforcing patent rights. This was justified on the one hand by high expense of manpower and financial resources, on the other hand by uncertain outcome of a patent infringement or invalidity trial. The economic incentive was also diminished by reasonable royalties, that were granted as maximum remedy in most patent infringement cases. An inhibition for filing lawsuits was also very often the vagueness of law concerning validity and reach of claims in gene-related patents, e. g. microarrays. Above all few precedents existed that would make the outcome of a patent infringement lawsuit more predictable. For this reason only written reminders were exchanged that might lead to a dispute settlement. Furthermore possible plaintiffs and defendants of patent infringement trials were potential licensors and licensees who did not intend to negatively affect their business relationship. This was why the opinion was expressed that the tendency to file a lawsuit was more obvious between biotechnological companies than between biotechnological companies and pharmaceutical companies. One was more likely to sue a direct competitor from whom a license would be difficult to obtain.

c. Lawsuits

In one case lawsuits by a direct competitor from a foreign country had been filed. The sued company wondered whether such lawsuits served the legitimate interests of the plaintiff or constituted an abuse of a patent right on order to expel a competitor from a market of common interest. E. g., in one case a lawsuit was not only filed the day after the patent grant. Also it was sued because of a claim describing more the technology of the defendant than of the plaintiff. In this case the broadest claims had been "hidden" in the last parts of the patent.

d. Trial Duration

There were complaints as to the long duration of trials, especially in the United States. The persisting legal uncertainty and the uncertainty of further business action as well as the impact on potential investors burdened especially the small companies. A trial duration of several years exceeded the average life expectancy of biotech start-ups.

9. Patenting and Secrecy

Heavy financial efforts are underway in the public and private biotechnology sector to determine research information and restrict access to its use by patenting or secrecy, e.g. depending on the degree of implemented confidentiality during the research and development stage. Other considerations refer to the prior art to which the subject matter of the invention relates or to the requirements of patentability[29]. Patenting provides a strategy for protecting inventions without secrecy. Within the sector of industrial research, the patent system promotes more disclosure than would occur if secrecy were the only means of excluding competitors. In some sectors patenting is relatively inefficient when it

[29] Margreth Barrett, Intellectual Property, Cases and Materials, Second Edition 2001, American Case-book Series, West Group, p. 337.

comes to secure the rents due to an invention therefore secrecy is favoured as a non-legal protective mechanism within a competitive environment[30].

a. Research Tools

Because of the difficult protection and enforcement of research tool inventions one company wondered whether to keep research tool discoveries secret in the future.

b. Secrecy vs. Patent Protection

Other companies advocated the view that at least for process patents, that are difficult to enforce, secrecy could be more effective than patent protection. Recently patent protection was encouraged by sophisticated analyzing tools which allow more and more deductions from an end product to the complete production process, e. g. by identifying catalytic converter remains. To protect the owner of process patents it would be desirable to provide for a regimen in which potential infringers would have to provide for more information on the actually used methods.

c. Secrecy for Important Inventions

In one case secrecy was mandatory as important discoveries were excluded from patenting. Secrecy would have been successful because it would have taken a great amount of effort to discover the secret knowledge, even from the marketed end product. The classified knowledge could have been licensed similar to a patented invention.

[30] Carine Peeters and Bruno van Pottelsberghe de la Potterie, Strategic Management of Innovation and Patenting Performances, September 2003, p. 7, http://www.iir.hitu.ac.jp-/file/WP03-17bruno.pdf.

10. Importance of Legal Knowledge and Business Strategies

For initial securing the protection of inventions as well as exploiting them legal professionalism is the key factor for successful competition. The type of patent professional with whom the inventor is likely to get into contact might depend on whether the inventor is independent or is employed by a large or a small company or an university[31]. However, a high degree of sensitivity of the scientists concerning legal knowledge to determine the patentability of an invention seems to be the first step in patenting an invention. The next step should be a close cooperation between the patent agent, in-house or not, even before a research development is at the stage of a formal invention report[32], otherwise creating a defining strategy for obtaining strong global patent rights might be too difficult.

Besides, after patenting and licensing, the commercialization of know how and technology could only be successful, if institutions were exposed to the dynamics of business competition.

a. Large Companies

While large companies maintained in-house patent departments, smaller companies at least co-operated with external lawyers on a permanent basis. This was partly due to the emphasis venture capital firms put on the protection of intellectual property. The co-operation between companies and patent lawyers often extended to patent search, which was then demanded as an external service. The great advantage the internet provided for patent search was stressed.

[31] Larger companies, which may file multiple patents applications a year, will normally have established a working relationship with a particular law firm, and often with the own patent attorney employed in the firm. Smaller companies will regularly deal directly with a patent attorney in private practice. Technology transfer agencies handle the technology transfer for research institutes such as universities.

[32] Grubb Philip W. Patents for Chemicals, Pharmaceuticals and Biotechnology, Fundamentals of Global Law, Practice and Strategy, Clarendon Press, Oxford (1999), pp.273 – 287.

The interviewed institutions pointed out the fact that not all of their employees were completely sensitive in respect of the implications of patent law. As early as in their university classes natural scientists should be confronted with the basics of patent law. Even established scientists should be given more opportunities to undergo special legal training in patent law. In so far the United States set a good example.

b. Smaller Companies

One smaller company's representative outlined the impression that patent attorneys showed only minor interest in solving legal problems of their clients, as they made a living by exactly those problems. A possible countermeasure would be standardized fees for classes of cases.

c. Public Academic Institutions

The representatives of public academic institutions emphasized that contrary to some statements that they lanced too few patent applications the opposite was true. A multitude of patent applications, especially for genetic inventions, was filed. Yet they partially had been filed not in the name of the academic institutions but in the name of co-operating companies. The academic institutions did not file the patent applications themselves because they lacked managerial staff qualified in dealing with patent applications, licensing and enforcing patents.

11. Patent Document and Patent Scrutiny

In an ideal fashion, the patent claim language is so clear and unambiguous that its meaning is out of dispute. Nevertheless, this goal is difficult to accomplish and fairly often due to the fact that claims are written by people providing just a very incomplete understanding of the precise nature of the subject matter of an invention. As a result, the significance of words implemented in a patent is often the focus of patent litigation

referring to validity or infringement unless such language was sorted out by the patent examiner[33]. Resulting from such a high research activity in the field of biotechnology in recent years still large numbers of biotechnology patent applications were filed. Therefore, waiting time from the date of filing to the initial examination of the application could be up to several years interfering negatively with the long-term planning of a biotech company, otherwise, in certain circumstances companies might regard this aspect as an advantage[34].

a. Language Barrier

Criticized was the language barrier between natural scientists and lawyers. Scientific publications were easy to read and understand, patent documents were not. On the contrary patents had been successfully challenged because of their alleged ambiguity, although their meaning was easy to understand for a person skilled in the art.
In some instances the impression had arisen that patent attorneys had tried to hide the broadest claims in patent applications, e. g. as "patent claim number 48". In other cases unusual word spelling of biological terms had been applied on purpose to hide the gist of inventions.

b. Patent Documents

Some complained that patent documents were not very substantial compared to scientific publications. To master the scientific peer-review process a scientific paper had to be consolidated by sophisticated experimental data. Patent examination seemed to be comparatively superficial, making many granted patents appear speculative or emerging

[33] Chisum Donald S., Craig Allen Nard, Herbert F. Schwartz, Pauline Newman, F. Scott Kieff, Principles of Patent Law, Cases and Materials, Second Edition 2001, University Case Book Series, Foundation Press, pp. 836 – 839.

[34] For the pharmaceutical industry in particular, where the registration of a new drug is a long-lasting and costly procedure, deferred examination is a practiced standard to lower the financial risks for the case that a pharmaceutical is abandoned during clinical trials.

from a mere "educated guess". The generous way of examining patents by German or European Patent Office derived presumably from understaffing.
In addition, on the one hand the patent offices employed more chemists than biologists, on the other hand the staff had ended their scientific education years ago so that they could not always appropriately judge recent discoveries in the field of biotechnology. It was suggested to establish a peer-review program for patent examinations resembling the one for scientific publications with a high impact factor. However secrecy could become a problem if patent examiners sought external advice from publicly appointed experts. Meanwhile the whole branch suffered from doubtful validity and scope of certain patent claims, e. g. risky lawsuits, or with whom to negotiate a license if several rivalling patents existed?

c. Extended Granting Period

Criticism was voiced concerning the extended duration until the grant of a patent. Having several years of limited protection until the granting of a patent a claimed DNA-sequence could already have been used by others at the time of granting. The long waiting period exceeded the planning frame of biotech start-up-companies.

d. Patent Search

Patent search for patent examiners as well as inventors became increasingly intricate, time-consuming and costly by patents covering multiple members of a sequence family in a single patent and by claiming molecules described as "hybridizing with" the claimed ones. This way easily 1,000 - 2,000 patent applications could become relevant, exceeding the capacity of present patent search tools.

12. Statutory Clarity with Genetic Inventions

Although there is much greater statutory clarity with gene patents, e.g. through the Revised Guidelines on the Examination of Patent Applications[35] in the United States of America including also gene patents that must disclose specific, substantial and credible utility or in Europe through the EU Directive 98/44/EC[36] claiming a specified function for DNA sequences within a patent, there is still evident concern about associating property rights with human biological materials regarding the genome as common human heritage or opposing the inventive element when identifying the utility of genes. Others pronounced practical implications of gene patents that include impediments to research information, to the creation of other innovative products or to clinical information in a clinical setting, so-called "access issues"[37]. For those reasons some propose special laws for genetic inventions also codifying against absolute protection of gene sequences.

a. Special Regulations for Genetic Inventions

All of those interviewed did not support an idea for special regulations for genetic inventions. In particular a discrimination of genetic and chemical inventions was denied. Even the European Directive on the legal protection of biotechnological inventions (EU Directive 98/44/EC) could prove outdated shortly, as science in the field of biotechnology progressed dynamically. It was unsatisfactory that naturally occurring substances could be patented without disclosure of utility, gene sequences, however, not.
In any case the specificities of genetic inventions could diminish in future the importance of patents in this field, bearing in mind, e. g., that even analyzing the function of a gene could be performed automatically. Under such conditions the requirement of an inventive

[35] Introduced by the USPTO in 2001.

[36] EU Directive 98/44/EC of the European Parliament and of the Council of the European Union of July 6, 1998 on the legal protection of biotechnological inventions.

[37] Genetic Inventions, Intellectual Property Rights and Licensing Practices, Evidence and Policies, OECD 2002, pp. 10 following.

step could be met only by downstream technologies for which protection would be available along the lines applied for conventional inventions such as medical drugs.

b. Absolute Product Protection of Genetic Inventions

Pharmaceutical companies stressed that absolute protection of substances had proven successful. This kind of protection was essential in order to pay tribute to the fact that e. g. with the development of a medical drug about 40 % of engineering expenses were caused by the proof of non-toxicity, metabolization and non-allergic characteristics. These costs were related to providing an active substance, not to the discovery of a certain medical indication.

Competitors could be prevented from building upon these results only by the absolute protection of the provided substance. In addition, only the provision of the substance put a competitor in a position to search for new medical indications.

The biotechnological companies characterized the value of absolute protection not as essential. Absolute protection was not advocated *per se*, but a discrimination of genetic and chemical inventions was denied. Above that absolute protection of DNA-sequences was regarded as a facilitating means of enforcing patents disclosing certain utilities of genetic information. On the contrary others criticized absolute protection of inventions including single DNA-sequences since all claims should be restricted to the inventor's contribution to the state of the art.

The discussion on absolute protection of genetic information was neutralized by the fact that genetic information generated by the Humane Genome Project (HGP) was publicly available, depicting only the protection of newly found functions.

13. Reach-through Claims

As a recent phenomenon in biotechnology an increasing number of patent applicants aim at patent protection for future downstream inventions by means of "reach-through-claims"[38] providing the patentee a dominant control over future inventions by obtaining exclusive rights to the first in line patent owner by way of legal enforcements rather than as the outcome of negotiating reach-through rights[39]. While some remain sceptical about further existence of reach-through claims other practitioners are startled by the negative economic implications[40] of protecting prospective inventions by this mode d'emploi. Since this technique of creating broad biotech patents is a global phenomenon, the Trilateral Project B3b[41] has been performed as a comparative study on "reach-through claims" to analyse the factual impact of reach-through claims. Though the economic arguments on both sides have theoretical merit, the empirical evidence by the project would presume that prior generations of gene patents have not significantly hindered progress in the genomics domain.

Among our interview partners the problem of reach-through claims was discussed controversially: Some asserted that worries about such claims were unjustified, because reach-through claims did not exist or were invalid. Others replied to have been confronted with such claims and that it was unresolved until the decision of an Opposition Division of the European Patent Office (EPO) if reach-through claims were valid or not.

Reach-through claims as intended parts of license contracts, e. g. for microarrays, could sometimes be defeated, but in any way the license negotiations became more cumbersome by the demand of reach-through royalties.

[38] For example, in genomics research the identification of gene expression patterns of a new drug target that controls metabolic events in the human body may lead to the use of that target (receptor) within different drug discovery value chains.

[39] Stephan G. Kunin, Mark Nagumo, Brian Stanton, Linda S. Therkorn, Stephan Walsh, Reach-Through Claims in the Age of Biotechnology, American, University Law Review 2002, Vol. 51, pp. 616-619.

[40] Concerns evoked about reach-through royalties that increase royalty stacking, thus making project management more complex and the cooperations more delicate when costly negotiations become necessary.

[41] Trilateral Project B3b, Mutual understanding in Search and Examination, Report on Comparative Study on Biotechnological Patent Practices, performed by the USPTO, EPO, JPO 2001: http://www.uspto.gov/web/tws/B3b_reachthrough.pdf.

14. Comparison of Laws, Harmonization of Laws

Through the introduction of some of the provisions of the European Biodirective into the EPC, the requirements for obtaining patents for genetic inventions in Europe have been clarified and recent case law has supplied guidelines for interpreting these provisions[42]. However, the situation in Europe has not yet been harmonized as several member states, whose national courts might set different standards with regard to what can and cannot be patented in biotechnology, have failed to implement the European Directive. At the moment there seems to be considerable political pressure to install an EU patent ("Community Patent")[43] to secure patent protection with same effects throughout the single market, i.e. the territory of the entire European Union. An international central body facilitating applicants' filing applications in 123 States is the regulatory framework of the Patent Cooperation Treaty (PCT), which is administered by the International Bureau of the World Intellectual Property Organization (WIPO)[44]. Even if a number of international patent agreements with harmonized patentability criteria were achieved, further harmonization activities should be performed to facilitate the enforcement of patent rights.

a. International Harmonization

The necessity of international harmonization of law became apparent. The impression persisted that the guidelines for patent examiners of different countries as regard to genetic inventions varied in detail. That constituted a drawback since important key inventions were applied for a patent and enforced in several countries in any case. Divergence existed e. g. concerning the requirements of proving genetic functionality. Differences existed as well relating to the possibility of including multiple members of a sequence family in single patent application.

[42] Gerald Kamstra, Marc Döring, Nick Scott-Ram, Andrew Sheard, Henry Wixon, Patents on Biotechnological Inventions: The E.C. Directive, Special Report, Sweet & Maxwell 2002, pp. 1-8.

[43] Commission of the European Communities, Proposal for a Council Regulation on the Community Patent, Brussels August 2000, http://europa.eu.int/comm/internal_market/en-/indprop/patent/412en.pdf.

[44] Patent Cooperation Treaty: http://www.wipo.org/treaties/registration/pct/

b. National Patents

Disapproved was also that in Europe after uniform decision to grant patents by the EPO, these patents split up in various national patents each treated according to national legislation. Undesirable was the hypothetical situation where a patent on a DNA-sequence was first granted by the EPO, but then was in some countries protected as a substance independent of a certain use, in others only in connection with a specific use.

c. National Applicants

Few of the interviewed deplored, that national patent offices tended to prefer national applicants or that the general patenting policy was directed the way that suited mostly the national industries.

d. Submarine Patents

As a delicate question two companies stressed that under the former American Inventors Protection Act (AIPA)[45] inventions were published only at the time of grant of a patent, not within a certain period of time after application (so-called submarine patents).
At the time of a grant of a patent already considerable investment could have been made that then proved not to be usable without infringing the patent. European firms did not profit from any delayed publications as they applied their inventions for patent protection in Europe where patent applications had been published after eighteen months from application or priority date.

[45] American Inventors Protection Act AIPA, November 1999, http://www.uspto.gov/web-/offices/dcom/olia/aipa/

15. Genetic Inventions and Ethics

As mentioned above in the introductory lines genetic inventions are subjects of controversy, challenged by the lack of public acceptance and strong pressure from public interest groups. In many instances the situation is shaped due to distorted individual and social features of risk perception and how risk perception is linked to the open debate of concern. Thus, the amplification of the ethical discourse might have significant consequences on how genomics research and medical applications of modern biotechnology might be processed in the future. Some biotechnological companies noted that they suffered from the ethical debate on dealing with genetic inventions and the distorted perception of the impact of patenting genetic inventions. Not commonly known was that patent rights did not confer any license to practice the invention. However it was observed that the political environment had improved since the introduction of special legislation on genetic engineering in Germany (Gentechnikgesetz), making public protests negligible. The general clauses of patent law, e. g. the exclusion of inventions from patenting that could only be practiced in contradiction to ordre public or morality were sufficient to enable using genetic inventions in a responsible way.

IV. Summary

The essence of this investigational project was to assess how the interrelationship of patent law and research on the one hand as well as in the interplay between patent law and licensing practices (business strategies) on the other hand influence developments in science and technology in the area of genomics.

The most important conclusions, at least for Germany, were that so far companies do not count so much on filing law suits rather than to come to terms on reasonable royalty rates or equivalent co-operations. This as a fact that infringement events are hard to identify due to that patent thicket in the field of biotechnology. The other aspect is that so far not very many end-products have reached the market which could be potential targets of legal actions.

One high ranking issue mentioned was the lack of sensitivity in respect of legal knowledge and expertise on business strategies among scientists, especially at universities. There, much is still left to be done to install a coherent IP strategy and infrastructure consisting of educational approaches towards the researchers as well as the instalment of university technology transfer organizations (UTTOs).

None of the interviewees were in favour of special regulations for gene-related inventions as from the practical point of view this would not be desirable since biotechnology is not as far apart from other technologies that are well patentable. Moreover from a technological standpoint, the coincidence of genetics and technology within a gene patent does not influence the technique of the patenting procedure and the bottleneck of patent examination that special laws for genetic inventions are justified. Concerning ethical considerations the existing patent system proves sufficient legal clarity and legally binding towards universal human rights. However, the need for harmonized international laws was given unanimous emphasis.

Most of the other difficulties and challenges discussed with the specialists *in praxi* were found to be solvable under the individual circumstances between the parties not demanding any external intervention.

Appendix 1: The Questionnaire

1. Profile of company

a) Marketed product
b) Company established when
   Since when active in the market
c) Turnover/year world-wide
   Development since establishment of company
d) Number of employees world-wide
   Thereof in R & D
   Source of recruitment
e) Size of company in relation to direct competitors
f) Origin of financial sources, participation in the stock-market
   Financial dependency on potential patent rights
g) Mergers with other companies
   Significance of patents for merging
h) Co-operation with other companies
   Purpose of Co-operation
   Significance of patents for merging

2. Patents

a) Number of filed patents
   Thereof with claims on gene sequences
   Development since establishment of company
b) Number of granted patents
   Thereof with claims on gene sequences
   Development since establishment of company
c) Company exclusive owner of patents
d) Participation in patent pools
   Attitude towards patent pools
e) Significance of own patents for the company's business
   Thereof with claims on gene sequences
f) Significance of competitor's patents for the company's business
   Thereof with claims on gene sequences

3. Licences

a) Number of granted licences
   Thereof with claims on gene sequences
   Development since establishment of company
b) Licensees
c) Number of used licences
   Thereof with claims on gene sequences
   Development since establishment of company
d) Have licences been refused in the past
   Reasons
   Applied for compulsory licence
e) Cross licensing

4. Patents and R & D

a) Annual investment in R & D
b) R & D continued, when only dependent patent was available
   R & D continued, when no patent was available
c) Significance of competitor's patents for own R & D
   Field with competitor's patents excluded
   Significance of research tools for own R & D
d) Significance of data bases for R & D
   Satisfied with access to data bases
e) Subject of competitor's patents tested
f) Public funding of R & D
   Significance of patents
g) Scientific publications
   Impact of patent law on time, quality and quantity of publication
   Attitude towards grace period
h) Spin-offs of genomic R & D

5. Patents and patent litigation

a) Lawsuits because of alleged patent infringement
   Success
   Costs
b) Consequences of lawsuits for R & D
c) In-depth knowledge of patent law
   External legal advice taken
d) Special qualities of genetic patents, that should be dealt with by patent law
e) Significance of dependency of a patent
f) Justification of absolute protection of a substance, independent of disclosed use
g) Comparison of legal framework for R & D in the field of biotechnology in Germany and other countries

Appendix 2: Statistics

1. The Sample Group (n=25)

– 4 large pharmaceutical companies
– 9 small and medium sized biotechnological companies
– 7 research institutes
– 5 clinical institutions

2. Specialization of the Interviewed

interview partner	specialization
1. pharmaceutical companies	development and marketing of medical drugs
2. biotechnological companies	development of medical drugs (no marketing yet); partially services like purification, sequencing, target identification, screening, expression analysis, development of expression systems
3. research institutions; scientific administration	tumor immunology, molecular biochemistry; administration of research institutions
4. clinical institutions	genetic consulting, basic research in anti-retroviral therapy, molecular cytogenetics, gene therapy

3. Age of the Interviewed

Interview partner	foundation year
1. pharmaceutical companies	prior to 1900
2. biotechnological companies	2001: 1 2000 - 1998: 2 1997 - 1994: 3 1992; 1988; 1985
3. research institutions, scientific administration	1964 (genome research since 1987); 1970; 1970; 1975; 1990
4. clinical institutions	1970; 1970; 1972; 1976; 1985 genome research since mid-80's

4. Turnover/Year Worldwide

Interview partner	turnover/budget per annum
1. pharmaceutical companies	€ 3,000 - 6,900 million
2. biotechnological companies	no marketing of drugs yet partially turnover in services of € 1.75 - 60 million
3. research institutions, scientific administration	€ 0.75 - 105 million
4. clinical institutions	€ 1.1 – 7.5 million

5. Number of Employees Worldwide

Interview partner	Employees
1. pharmaceutical companies	24,000 - 117,300
2. biotechnological companies	4.5 - 1,600
3. research institutions, scientific administration	40 – 620
4. clinical institutions	60 – 120

6. Number of Applications for Genetic Inventions

Interview partner	patent applications
1. pharmaceutical companies	about 100*
2. biotechnological companies	25 – 180**
3. research institutions, scientific administration	50 – 100**
4. clinical institutions	1 – 20**

* per annum

** total number

7. Number of Granted Genetic Patents

Interview partner	granted patents
1. pharmaceutical companies	500 - 1,100
2. biotechnological companies	0 – 55
3. research institutions, scientific administration	30 – 110
4. clinical institutions	1 – 6

8. Number of Granted and Obtained Licenses

Interview partner	granted licenses	obtained licenses
1. pharmaceutical companies	n. a.	
2. biotechnological companies	0 - 28	1 - multiple
3. research institutions, scientific administration	0 - 83	0 - 10
4. clinical institutions	0 - 3	0

9. Number of Lawsuits on Genetic Inventions

Inter view partner	lawsuits
1. pharmaceutical companies	0 - 2
2. biotechnological companies	0 - multiple
3. research institutions, scientific administration	0 - 4
4. clinical institutions	0 - 1

10. Number of Co-operations

Interview partner	co-operations
1. pharmaceutical companies	many
2. biotechnological companies	0 - many
3. research institutions, scientific administration	2 - 91
4. clinical institutions	0 - 5

11. Spin-offs

Interview partner	spin-offs
1. pharmaceutical companies	-
2. biotechnological companies	-
3. research institutions, scientific administration	3
4. clinical institutions	1 - 3

Appendix 3: The Sample Group

Pharmaceutical Companies

1. Bayer AG
51368 Leverkusen

2. Merck KG aA
Postfach
64271 Darmstadt

3. Schering AG
13342 Berlin

4. Boehringer Ingelheim GmbH
55216 Ingelheim am Rhein

Biotechnological Companies

5. Atugen AG
Robert-Rössle-Str. 10
13125 Berlin

6. Epigenomics AG
Kastanienallee 24
10435 Berlin

7. GeneScan Europe AG
Engesserstr. 4b
79108 Freiburg/Breisgau

8. GPC Biotech AG
Fraunhoferstr. 20
82152 Martinsried/München

9. MediGene AG
Lochhamer Str. 11
82152 Planegg/Martinsried

10. metaGen Pharmaceuticals GmbH
Oudenarder Str. 16
13347 Berlin

11. MorphoSys AG
Lena-Christ-Str. 48
82152 Martinsried/Planegg

12. Rhein Biotech GmbH
Eichsfelder Str. 11
40595 Düsseldorf

13. Qiagen GmbH
Max-Volmer-Str. 4
40724 Hilden

Research Institutions, Scientific Administration

14. Ascenion GmbH
85764 München/Neuherberg

15. BioM AG
Am Klopferspitz 19
82152 Martinsried/München

16. Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280
69120 Heidelberg

17. Garching Innovation GmbH
Hofgartenstr. 8
80539 München

18. Max-Delbrück-Centrum für Molekulare Medizin
Robert-Rössle-Str. 10
13125 Berlin

19. Max-Planck-Institut für Molekulargenetik
Ihnestr. 73
14195 Berlin

20. Max-Planck-Institut für Biochemie
Am Klopferspitz 18a
85152 Martinsried

Clinical Institutions

21. Klinikum Grosshadern
Ludwig-Maximilians-Universität München
Marchioninistr. 15
81377 München

22. Institut für Humangenetik
Charité – Humboldt-Universität
Augustenburger Platz 1
13353 Berlin

23. Institut für Humangenetik
Universität Heidelberg
Im Neuenheimer Feld 328
69120 Heidelberg

24. Institut für Humangenetik
Ludwig-Maximilians-Universität München
Goethestr. 29
80336 München

25. Institut für klinische und molekulare Virologie
Universität Erlangen
Schlossgarten 4
91054 Erlangen