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Product patents on human DNA sequences: where do we stand in Europe?

Joseph Straus

Managing Board, Munich Intellectual Property Law Centre [1], *Marstallplatz 1, 80539 Munich, Germany*

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Presented by François Gros

Abstract

In July 1998, the Directive 98/44/EC was adopted by the competent European Community bodies. It should have been implemented into national laws of the member states by the end of July 2000. So far, however, most member states missed that deadline. One reason for resistance and hesitations are concerns about potential negative effects of product patents based on gene sequences. Reasons for this situation are analysed and solutions sought for minimising the prospects of increasing dependencies on dominant patents on genes. ***To cite this article: J. Straus, C. R. Biologies 326 (2003).***

Résumé

Brevets de produits sur les séquences d'ADN humaines : où en est-on en Europe ? En juillet 1998, la directive 98/44/EC a été adoptée par les organismes compétents de la Communauté européenne**.** Elle aurait dû entrer en vigueur dans le droit national des États membres avant fin juillet 2000. Mais jusqu'ici, la plupart des États membres n'ont pas respecté la date limite. Une des raisons de cette résistance et hésitation est l'inquiétude suscitée par les effets négatifs potentiels des brevets de produits fondés sur les séquences des gènes. Les raisons de cette situation sont analysées et des solutions recherchées pour réduire les perspectives de dépendance croissante des brevets dominants sur les gènes. ***Pour citer cet article : J. Straus, C. R. Biologies 326 (2003).***

Keywords: DNA sequences; integral part of the notion of invention; patents; scope of protection

Mots-clés : brevets ; étendue de la protection ; fonction intégrale de la notion d'invention ; séquences d'ADN

1. Introduction

After ten years of tense and controversial debates, the European Union, on July 6, 1998, adopted the Directive 98/44/EC of the European Parliament and Council on the Legal Protection of Biotechnological Inventions [1]. Then the decision of the European Court of Justice (ECJ), of October 9, 2001, [2] which explicitly confirmed the 'Légalité' of the Directive, seemingly had no impact on national lawmakers of the member states. On the contrary, in January 2002,

E-mail address: J.Straus@ip.mpg.de (J. Straus).
[1] http://www.miplc.de

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the lower house of the French parliament passed a bill, which, if adopted also by the senate, would ban from patent protection all inventions related to or involving biological material of human origin [3].

Although not bound by any legal mechanisms to the EU legal system, the Administrative Council of the European Patent Organization on June 16, 1999 [4], decided to adapt the Implementing Regulations of the European Patent Convention (EPC), to the rules set forth in the Directive to the extent they relate to patentability issues. Under Article 164(1) EPC the Implementing Regulations are an integral part of the Convention and therefore are equally binding on the EPO's Boards of Appeal (Article 23(2) EPC) and on national courts. Hence, for practical application of the Convention, only the interpretation of its provisions laid down in the Implementing Regulations is binding. A different interpretation of the Convention would be possible only if it is specially demonstrated that a particular rule of interpretation is inconsistent with the Convention itself [5]. Since the overwhelming majority of biotechnology patent applications in Europe is filed with the European Patent Office (EPO), this eventually means that they are examined and patents issued according to the principles set forth in the EU Directive.

2. Presumable obstacles for implementation

The reasons why the great majority of EU member states resisted until now to implement the Directive 98/44/EC into their national laws may vary from country to country, and may be due to differences in the understanding of ethics, as demonstrated by the action of the lower house of the French parliament, as well as to some specific economic interests. The Organization for Economic Cooperation and Development (OECD) identified basically the following concerns, which might be responsible for such hesitations of the EU member states: dependency resulting from DNA patents in general and from undue broad claims specifically; reluctance of researchers to enter fields with already patented genes; genetic testing; monopolistic genetic testing practices; royalty stacking and explosion of legal disputes. In fact the only sign of a negative impact of product patents on DNA sequences may be viewed in the fact that researchers in most cases refrain from research in further uses of a gene once they have realized that it had already been patented for a third party.

Professor Hubert Markl, the then President of the Max Planck Society for the Advancement of Science in a recently published article stated: "*... I wish to emphasize strongly that it is definitely desirable to limit the patent rights given to a well-defined and clearly proven useful function, since we know now that each single gene – of which we may have only 25,000 to 40,000 altogether in one human genome – may be involved in the production of a ten or twentyfold number of functional proteins, and many such proteins may be enmeshed in a number of different functions of an organism. Assigning broadly defined patent rights to a specific gene plus its protein, for which only one function has been described, in such a way that all additional functions described in the future are also covered – even though common practice when granting traditional patents on chemical or pharmaceutical substances – could be ruinous to an economic landscape of biotech startups, because the actual inventor of a completely new marketable use would immediately be subjected to serfdom under licence to someone who did not contribute his own creative intellectual or practical effort to a new development in that field. Sweeping genetic technology patents could thus all too easily brush a promising new industry down the drain*" [6].

The first consultations of the Bill implementing the EU Directive into national patent law in the German Parliament confirmed the expected resistance, which nearly exclusively focused on the issue of product patents on DNA sequences of human origin. In a nearly never experienced unanimity, representatives of all parties rejected that idea as unacceptable and unjustifiable.

Symptomatic is the statement of Margot von Renessee, Chairwoman of the Enquête Commission on Law and Ethics in Modern Medicine who emphasized "*the risk of over-rewarding the person who obtains a product patent, particularly evident in the case of genes, because they are multi-functional and in the field of natural products*". And she engaged the patent lawyers to help by telling them how to limit the product patent to the function discovered, while not sacrificing anything by so doing [7].

3. The case of product patents on DNA sequences

A look at the EU Biotech Directive shows that there are two reasons why the traditional case law related to product patents on chemical compounds, to which Professor Markl referred, and which allowed also that a specific industrial applicability could be indicated in the course of patent granting proceedings, can no longer apply where the patenting of DNA sequences of human origin is at hand. On the one hand, the disclosure of a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention (Recital 23), even if the method of manufacture is indicated. And on the other hand, the industrial applicability of the DNA sequence, in other words its function, cannot be submitted in the course of the examination process, but has to be *specifically* disclosed already in the patent application as filed (Recital 22, last sentence, Art. 5(3)). Where the use of a sequence or partial sequence of a gene for making a protein or part of a protein is claimed, the protein or part of protein and its function have to be specified (Recital 24). If therapeutic or diagnostic uses are claimed, the disorder to be diagnosed or treated must be specifically indicated. Thus, the European legislator has made the function of a claimed DNA sequence an integral part of the notion of an invention (inventive concept).

The EU Biotech Directive makes it clear that it is not creating any special patent law for biotechnological inventions, but is only making adaptations and amendments which the national legislator must also implement in order to take adequate account of the developments that use biological material, but at the same time also fulfil the patentability requirements (Recital 8) [8]. This is achieved, in addition to the clarifying amendment to the notion of an invention, in the case of DNA sequences, by the explicit clarification that the natural pre-existence of biological material alone does not constitute a patentability obstacle (Art. 3(2)).

Two other provisions of the Directive relating to the scope of protection and its effects need to be mentioned. Firstly, the provision that the protection of a product, which consists of or contains genetic information, i.e., a DNA molecule and its sequence, extends to any product – *except human* – in which this product is incorporated and in which the genetic information is contained and performs its function (Art. 9). In order to counteract the problem of far-reaching dependencies arising from the scope of product protection, the interpretation rule is then set forth in Recital 25, according to which patented DNA sequences, which only overlap in parts which are not essential to the invention, have to be considered as independent in terms of patent law. Under both aspects the (disclosed) function of the DNA plays a decisive role. To our understanding there can be no infringement under Article 9 of the Directive if the claimed DNA sequence in an allegedly infringing product performs a function, which is objectively also inherent to the sequence, but has neither been disclosed in the patent application nor in the patent itself.

4. The Biotech Directive in the light of the latest scientific developments

The European legislator adopted the Directive in July 1998 in order to achieve a harmonized interpretation of the patent law throughout Europe and to introduce protection standards in line with those of US and Japanese law.

It can be assumed that the European Parliament, the Commission and the Council have not only endeavoured to take account of current developments in science and technology, but that they have also actually taken them into account. But if Europe had a central patent jurisdiction of the US type, the Directive could be regarded dispensable. A court of this type could be responsible both for a Europe-wide harmonized interpretation of patent and for adapting it to the changing conditions in science and technology.

At present, the latest scientific developments are on proteomics where DNA is primarily used as the source for the production – expression in various hosts of therapeutically effective proteins. The determination of the complex 3D structure of proteins and their function has long been an extremely time consuming and cumbersome undertaking. Identifying proteins which are involved in human disease, as well as determining their 3D structure is of enormous importance [9,10]. This importance is best demonstrated by comparing genomics and proteomics: "*The genome tells you what could theoretically happen inside the cell. Messenger*

RNA tells you what might happen, and the protein tells you what is happening". Also the human genome does not vary much between individuals (99.9% homology), the expression of proteins demonstrates remarkable variations from tissue and even in the tissue of a specific person in the course of the process of aging [11].

5. Lessons to be drawn from these new developments

The patent law as defined by the German Federal Supreme Court is not only to protect individual interest but also to impose necessary limits on individual powers and rights in the interests of the common good and to create the correct *balance* between the rights of the individual and the rights of the general public.

Because of the high level of interactivity and interdependence of the processes involved and the present state of the sequencing technology, the inventive step must be seen in conjunction with the discovery of the one or several functions of a product that exists in nature, whose discovery and structure clarification as a rule are not based on any inventive activity. So limitation of the protection to the function(s) disclosed is clearly necessary in most cases. And it is logical that the function(s) must be specified in the patent claims, which will automatically affect the protective scope of the patent.

If the examination of the relevant state of technology reveals that the inventive merit "merely" lies in the clarification of the function, the applicant, therefore, may be required to include the details of the function of the claimed DNA sequence into the patent claims accordingly.

The result which purely and simply depends on the correct application of the patentability requirements by patent office and courts may well contribute to a balanced application of patent law and also comply with the EU Biotechnology Directive and the TRIPS Agreement of the World Trade Organization.

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