OECD-BMBF
Workshop on Genetic Inventions, IPRs and Licensing Practices

Berlin, 24-25 January 2002

The patentability of genetic inventions in EPO practice

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The role of the patent system

- While the patentability of genetic and biotechnological inventions, has never been questioned among experts, it is still subject to much public debate, in particular with regard to the issue of patenting DNA sequences isolated from the human genome. Much in this debate is due to misconceptions regarding the role of the patent system.

"The patent system adds the fuel of interest to the fire of genius„

Abraham Lincoln

The patent system is a regulation of competition

Three main features

- exclusive right of use:
  prohibition of free-ride, not monopoly
- publication:
  compelling case for competitors to innovate
- patents turn an invention into a tradeable commodity

Limits to the Patent System

- Technical character of invention
- "Industrial application„
- Free use of the state of the art belonging to the public domain
  ➥ novelty and inventive step!
- „Public order and morality"

EPO Practice

Statistics

- IPC: CN12N15
  “mutations or genetic engineering“

No. of applications for a European patent (EP + Euro-PCT)

1997	∨	2000
± 2000		> 5000

Claimed subject-matter

Claims in genetic applications cumulative or alternatively pertain to

- genes or partial DNA sequences such as ESTs
- proteins encoded by these genes and their function in the organism
- vectors used for the transfer of genes from one organism to another
- genetically modified, micro-organisms cells, plants and animals

Claimed subject-matter

- processes used for the making of a genetically modified product
- uses of the genetic sequences or proteins which include *inter alia*
  - genetic tests for specific genetic diseases or predisposition to such such diseases
  - drugs developed on the basis of the knowledge of proteins and their biological activity
  - industrial applications of protein functions

The "Product of Nature" Doctrine

- Material as found in nature
  - Can only be **discovered**, **not invented**
  - **Cannot** be **new**

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- **Art. 3(a)**
  "... biotechnological inventions shall also be patentable if they concern biological material produced by means of technical process, **even if previously occurred in nature**„
- **Art. 5(2)**
  "... the sequence as partial sequence of a (human) gene **may** constitute a patentable invention even if the **structure** of that element is **identical** to that of a natural element

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- **Art. 5(3)**
  "The industrial application of a sequence of a gene .... **must be disclosed in the patent application**."
- **Recital 23**
  "Whereas a mere DNA sequence without indication of function does not contain any technical information (teaching?) **(„keine Lehre zum technischen Handeln"**) and is therefore not a patentable invention"

Function requirement in EPO practice

- **Inventive steps and sufficiency of disclosure**
  - function assignment must be „specific", „credible", „non-speculative"
  - generalising function indications („receptor", „kinase", „probe") generally not sufficient
  - Bioinformatics:
    results of computer run to be confirmed by „real live" examples

Function as limiting feature in claims to DNA sequences?

- **EPO practice:**

  Function must be disclosed in the application but is not necessarily a limiting feature in claims to DNA sequences

  Same practice in national offices in Europe, USA, Japan

Function limitation in Claims?

Opponents	Proponents
• DNA sequences are chemical compounds, just like any other	• Informational character of genome ("Data base") function different from other chemical compounds
• Directive Art 5: Function must be **disclosed** in **application not** in claim	• Recital 23 Function is the essential technical contribution to the state of the art
• Huge investment in genetic research discouraged by function limitation	• Future research for new functions discouraged by "reach-through effect" of absolute product protection for DNA sequences

Opponents	Proponents
• Clear disadvantage for European industry versus overseas competitors	• denied
• Patents for further new functions remain available	• Results of further research will be dependent patents
• Dependent patents common in the whole field of chemistry	• Inventive new uses of known DNA sequence owe little or nothing to first DNA sequence determination

Opponents	Proponents
• Dependency is adequately dealt with through licensing and cross-licensing	• -
• Scientific research protected by experimental use exception	• Experimental use exception does not allow for actual use of research results
• Overlapping patents are often the basis for cooperation between SME's and larger entities	• Product protection for genes advantages large entities over SME's
• etc	• etc

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I. Introduction

1. Genetic engineering makes practical use of the fact that the genetic make-up of all living things, from the most primitive organisms through the entire plant and animal kingdom to mankind itself, is determined by genetic molecules (DNA or RNA) in which just four nucleotides are arranged in a certain sequence. Today, molecular biologists can not only identify these sequences and decipher their biological function, but also intervene to modify practically any genotype, isolate individual genes and, by transferring them to bioreactors, "industrialise" their metabolic functions. This has torn down the barriers of conventional biology, in which the genome was indivisible, and opened a new field for scientific and industrial research with breathtaking perspectives for society at large.

2. Biological material and biological processes were recognised as patentable subject-matter in the late 19th century, long before modern genetic engineering emerged at the industrial level.

In 1873, Louis Pasteur was granted a US patent for his method of removing pathogenes from beer yeast.
In 1969, the German Federal Court of Justice (BGH) held in its "Red Dove" decision that an invention was "not rendered unpatentable by the mere fact that its starting point, means and aim were living organisms".
In 1975, the same Court recognised the patentability of micro-organisms as such, and
in 1980, the US supreme Court, in its famous "Chakrabarty" decision, upheld the first patent granted for a genetically modified micro-organism, stating that "Congress intended statutory subject-matter to include anything under the sun that is made by man"

.

This is the background against which EPO practice has developed since the Office opened its doors in 1978. That practice, in turn, has been codified in the 1998 EU-Directive on the legal protection of biotechnological inventions.

II. The role of the patent system

While the patentability of genetic and biotechnological inventions has never been questioned among experts, it is still subject to much public debate, in particular with regard to the issue of patenting DNA sequences isolated from the human genome. Much in this debate is due to misconceptions regarding the role of the

patent system and this is the reason for which I count on your indulgence if I shortly turn to this item.

"The patent system adds the fuel of interest to the fire of genius"

I like to use this citation of Abraham Lincoln when I have to explain the patent system to non-experts.

The patent system is a regulation of competition. Three features make it a powerful driving force of technical innovation and economic growth in a modern economy.
The first feature is the exclusive right to use the invention granted to the inventor or successor in right. This must not be confused with a monopoly, as sometimes even experts do. Patents prohibit a free ride on somebody else's achievement and thereby make innovation rather than imitation, the condition of success in competition.

Secondly, publication of the invention as a prerequisite of protection not only keeps the general public informed as to the latest state of the art, but also creates a compelling case for competitors to innovate on their own, if they want to stay in the race. Today, the total research and development investment worldwide financed through the patent system amounts to hundreds of billions of US dollars or Euro. In the research-based pharmaceutical industry research and development expenses represent over 16% of turnover.
Thirdly, patents turn an invention into a tradeable commodity, which can be assigned or licensed to third parties. There is ample evidence that this mechanism fosters much wider use of new

inventions than free-ride imitation could ever achieve. Worldwide total income from licensing fees alone also tops a hundred billion US dollars or Euro yearly.

Of course, there must also be limits to the role of patents.
One inherent limitation is that the patent system can produce its effects only in the realm of industrial (or commercial) competition. This is the reason for which industrial application is one of the three basic patentability requirements and for which discoveries and creations which are of a non-technical character are excluded from patent protection.

Secondly, patents must not hamper the use by third parties of the state of the art belonging to the public domain. This is why, to be patentable, an invention must not only be new but also represent an inventive technical contribution to the state of the art.
Thirdly, patents must not be granted for inventions, the (commercial) exploitation of which would be contrary to public order or morality.
In the endless debate on patents and ethics, there is the ever-recurring erroneous assumption that it is the patent system which allows or disallows certain types of research or kinds of business. In actual fact, the patent system as a mere regulation of competition does not and must not interfere with the basic values of society and therefore does not extend protection to subject-matter which for ethical reasons cannot possibly become the object of lawful trade.

On the other hand, excluding from patent protection any subject-matter which may well become the object of lawful trade simply

amounts to encouraging free-ride imitation and to cutting off the adding of "fuel to the fire of genius" in that field. This is an issue we shall return to when discussing the patentability of human genes.

III. EPO practice

1. Some statistics

Since the EPO opened its doors in 1998, some 30,000 European patent applications have been filed in the area of biotechnology in the broadest sense of this term. More than 10,000 of these have been classified into the group C12N15 of the IPC pertaining to "mutations or genetic engineering". The activity in this field shows sustained growth, rising from some 2,000 applications in 1997 to over 5,000 in the year 2000. Some 40% of those applications pertain to micro-organisms, plants and/or animals, the other 60% relate to human or animal DNA sequences and concern inventions aiming to develop new therapies and medicines.

There are no official analytical statistics. The figures I have just quoted must therefore be appreciated as estimates which are subject to correction which a deeper digging in the complexities of the patent classification system may impose.

2. Claimed subject-matter

Claims in genetic applications cumulatively or alternatively pertain *inter alia* to

- genes or partial DNA sequences such as ESTs
- proteins encoded by these genes and their function in the organism
- vectors used for the transfer of genes from one organism to

another

- genetically modified, micro-organisms, cells, plants and animals
- processes used for the making of a genetically modified product
- uses of the genetic sequences or proteins which include *inter alia*
  - genetic tests for specific genetic diseases or predisposition to such diseases
  - drugs developed on the basis of the knowledge of proteins and their biological activity
  - industrial applications of protein functions

3. Patentable subject-matter

None of the claims I have just cited as typical examples *falls per se* under any of the three exceptions to patentability in European patent law, namely medical treatment practiced on the human or animal body, plant and animal varieties, and inventions, the exploitation of which would be contrary to public order and morality. Thus, the whole range of inventions in the genetic field, encompassing both processes and products, constitute patentable subject-matter and will actually be protected, provided that the general requirements of novelty, inventive step, industrial application and enabling disclosure are satisfied.

4. The products of nature doctrine

Before discussing the particularities of the application of these four requirements to genetic inventions, let me just say a few words with regard to the so-called doctrine of products of nature.This doctrine asserts that biological material is a product of nature and can therefore be discovered but not invented. Moreover, biological material as found in nature cannot be new.

In accordance with long-standing patent practice in all industrialised countries in Europe and around the world, this doctrine is expressly rejected by the EU Directive on biotechnological inventions. Indeed, Article 3(a) of the Directive provides that "biotechnological inventions shall also be patentable if they concern biological material which is isolated from its natural environment or produced by means of a technical process, even if it previously occured in nature". Concerning the human genome, Article 5(2) of the Directive is even more specific in providing that "the sequence or partial sequence of a (human) gene **may** constitute a patentable invention, even if the structure of that element is **identical** to that of a natural element".

The key to understanding this provision lies in the word "may", which places DNA sequences as patentable subject-matter in the context of the general patentability requirements. Article 5(3) of the Directive specifically requires that "the industrial application of a sequence or partial sequence of a gene must be disclosed in the patent application". The meaning of this paragraph is further explained by Recital 23 of the Directive which states that the "mere indication of a DNA sequence, without the indication of a function, does not contain any technical information (in German: keine technische Lehre) and is therefore not a patentable invention".

With this statement, the Directive seems to conform to classical patent practice in general chemistry, where it was always held that the mere disclosure of a new chemical compound without any indication of actual function or use is not patentable.
There is, however, a tiny but perhaps important nuance. In general chemistry, function or use indications can be very broad, such as "use of a new compound as a dye" (Farbstoff) and, where needed to illustrate such a function or use indication, evidence can be submitted after the filing date at any time during the examination process.

According to Recital 23 of the Directive, this is not so with DNA sequences. If the mere disclosure of a DNA sequence without indication of function is not a patentable invention, then function seems to be a constituent feature of any sequence invention and must therefore be fully disclosed in the application as filed. This is what is expressly stated in Article 5(3) of the Directive even if the reference made to "industrial application" made in this provision is perhaps somewhat narrow.

5. The function requirement in EPO practice

In actual EPO practice, the function requirement plays a fundamental and central role not only relative to industrial application but also to the requirements of inventive step and sufficiency of disclosure.
The test for inventive step attempts to answer the question of whether, in view of the state of the art, the invention entails a technical contribution which was not obvious to the person skilled in the art at the date of filing.
Whereas the Directive's requirements with regard to industrial

application seems to be satisfied by any plausible indication of function, EPO practice requires distinctly more than that before acknowledging inventiveness. In order to stand the test of inventive step, function assignments for genetic inventions must be sufficiently specific in view of the state of the art and must be credible and non-speculative, and usually supported by experimental or empirical evidence.
Resulting often from automated identification and annotation methodologies, function indications such as "receptor" or "kinase" or "probe to identify related DNA sequences" or "potential drug target" are not held to be sufficiently specific.

Modern bioinformatics are powerful instruments in genetic research, but they also carry a risk of findings of non-patentability under the aspects of both inventive step and sufficiency of disclosure. Functions or technical effects assigned to a given biological compound on the basis of a computer run are often speculative and non-credible, unless they are supported by concrete "real life" examples.

6. Function as a limiting feature in claims to DNA sequences?

The fundamental and central role of function in determining the patentability of DNA sequences has led distinguished experts in both science and law to propose that function should be systematically included as a limiting feature in any claim to DNA sequences and in particular to human genes.

In EPO practice as well as in the practice of national patent offices in Europe, the US and Japan, such limitations can be found in

individual cases but they are not imposed as a general rule.
Those in favour of maintaining this practice agree that genes are chemical compounds **just** like any other and therefore deserve the same treatment, namely absolute product protection. Their argument is that given the huge investment which is required between the identification, isolation and purification of a useful gene sequence or partial sequence and the putting on the market of any new therapy or medicine, systematic function limitations in sequence claims would discourage pioneer research. If such limitations were to be introduced in Europe alone, European industry would be at a clear disadvantage compared to their overseas competitors.
Outside Europe, such limitations do not exist and cannot be expected to be imposed by a change in legislation.
Also, absolute product protection would not prevent third parties from obtaining protection for new and inventive uses of the same or similar sequences. It is further argued by proponents of absolute product protection that the fact that further uses of a patented gene are dependent on the basic patent is a phenomenon common to the whole field of chemistry and is adequately dealt with by licensing and cross-licensing. Scientific research is protected by the experimental use exception and as far as SME's are concerned, overlapping patents are often the very basis for successful cooperation with larger entities.
On their side, **the proponents of function limitation** *inter alia* argue that assimilating genes to ordinary chemical compounds is a basic misconception. A gene can be defined as a chemical compound, but its function is categorically different. The genome is in fact a huge data base containing billions of pieces of information which is so programmed that it determines all the interactions of

the elements making up a living organism. With modern bioinformatics, isolating and purifying a gene sequence or partial gene sequence can no longer be considered an inventive contribution to the state of the art. Proponents of function limitation further argue that this principle is clearly entrenched in Recital 23 of the Directive, and that, as EPO practice shows, protection of a DNA sequence depends on a function being disclosed.
The opponents of absolute product protection for DNA sequences also argue that absolute product protection is likely to cover very soon the totality of about 30-40,000 genes present in the human genome and is therefore equivalent to a fantastic reach-through to future inventions waiting to be made in the coming years and decades, which will owe little or nothing to the initial isolation of a gene. Such a reach-through is argued to be incompatible with the fundamental role of a well-functioning patent system and to be likely to hamper rather than promote biotechnological research.

IV. Implementation of the Directive in national patent law

Returning now to the EU Directive and its enactment in national patent law, I wish now to conclude with two points:

First: Articles 3(a) and 5(2) merely state that genes, including human genes, and any other DNA sequences, are statutory matter, thereby rejecting the "products of nature" doctrine.

Secondly: Article 5(3) together with Recital 23 of the Directive make it clear that function is a constituent element of any DNA sequence invention. Whether or not that implies that claims to DNA sequences must be limited to the disclosed function(s) is a

controversy still debated in expert literature.

The practice to be followed ultimately in Europe by both national patent offices and the EPO is open to further debate and development, notably in response to the case law of the courts and appeal boards which, in applying and construing the relevant provisions, will have to determine the standards proper fo patenting genetic inventions and the scope of protection conferred by gene patents. The point is that this practice must be uniform throughout Europe, and can only be built on a common legal basis. To create that basis is the fundamental role of the Directive.