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Patents in Europe 2011/2012

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Ralph Minderop, Arwed Burrichter, Meikel Diepholz and Natalie Kirchhofer

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By patenting a biotechnological invention via the European Patent Office, a patent owner can ensure the protection of its patent across Europe

By **Ralph Minderop, Arwed Burrichter, Meikel Diepholz** and **Natalie Kirchofer**, COHAUSZ & FLORACK, Dusseldorf

As one of the key enabling technologies of the 21st century, modern biotechnology has become a major source of innovation and a global driver of economic growth in various industries, including healthcare, diagnostics and agro-food. With annual net sales exceeding US\$90 billion and double-digit growth rates in the last five years, biopharmaceuticals and diagnostics are of paramount importance to the pharmaceutical industry today.

The biotech industry largely depends on a strong patent system. In its 2010 EU Industrial Research & Development (R&D) Investment Scoreboard, the European Commission identified the biotechnology industry to have the highest R&D intensity (21.2%) of all industries. In comparison, according to the report the automotive and parts industry had an R&D intensity of 2% to 5%. In addition to skyrocketing R&D costs, the biotechnological sector is confronted with high regulatory burdens which must be counterbalanced and remunerated by patent-enforced market exclusivity. Finally, solid IP protection is the cornerstone for the business model of many small biotech start-up companies, which often build on a single invention as their major intangible asset. Therefore, from an economic perspective, strong and harmonised IP protection for

biotechnological inventions in Europe is indispensable.

In 1998 the European Parliament passed Directive 98/44/EC, which provides the legal framework for the protection of biotechnological inventions in the European Union. The directive was subsequently implemented into both national laws and the European Patent Convention (EPC), and is therefore binding for patent prosecutions concerning biotechnological inventions before the European Patent Office (EPO).

Under the EPC, biological material isolated from its natural environment or otherwise technically produced is considered patentable. This includes inanimate biologically active material such as proteins (eg, antibodies or enzymes), genes and DNA and RNA sequences. On the other hand, animate matter (eg, microorganisms, genetically modified animals) are considered patentable under the EPC.

The EPC contains several exceptions to patentability which pertain to biotechnological inventions in the wider sense. In contrast to the United States, where, according to the Supreme Court's decision in *Diamond v Chakrabarty* (447 US 303 (1980)), "anything under the sun made by man" is considered patentable, the following biotechnological inventions are generally excluded from patentability in Europe, mostly in view of moral or ethical considerations:

- Inventions contrary to public order *public* or morality (Article 53a of the EPC), in particular those listed in Rule 28 of the EPC:
 - Processes for cloning human beings.
 - Processes for modifying the germ-line genetic identity of human beings.

- Uses of human embryos for industrial or commercial purposes.
- Processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal.
- Plant or animal varieties (Article 53b).
- Essentially biological processes for the production of plants or animals (Article 53b).
- Methods for treatment of the human or animal body by surgery or therapy (Article 53c).
- Diagnostic methods practised on the human or animal body (Article 53c).

Despite these limitations, the protection afforded by the EPC is generally viewed as strong and adequate.

DNA and gene patents

There is no *a priori* bar to the patentability of genes or DNA sequences under the EPC. In fact, Rule 29(2) positively acknowledges that human gene sequences are patentable. However, as for all patent applications before the EPO, biotechnological inventions must meet the basic criteria of patentability (ie, novelty (Article 54), inventive step (Article 56) and industrial applicability (Article 57)). Moreover, the invention must be sufficiently disclosed in the specification and claimed in a clear manner (Articles 83 and 84).

To date, the majority of genes claimed in patent applications are derived from nature. Similar to new chemical compounds, genes as well as proteins are considered novel if they are isolated or produced for the first time, even if they are already present in nature (Rule 27(a)). In the post-genomics era, where the sequence of the human genome has been unravelled and most human genes have been cloned, patentable inventions can be expected to shift from original gene sequences as such to genetically modified sequences, special splice variants with surprising technical effects or purposeful selections of sub-sequences.

For human gene sequences, Rule 29(3) requires the applicant to disclose the industrial application (ie, function) in the patent application. Mere DNA sequences without indication of a function or practical use are considered to contain no technical teaching and are therefore not patentable under the EPC.

The particular function of the DNA sequence may also have an effect on the scope of the claims in patent litigation. In

Monsanto (C-428/08) the European Court of Justice held that in order to be protected, a gene must be fulfilling its function at the time of the alleged infringing act. The decision may change how such patent claims will be construed in the future when it comes to assessing their protective scope in litigation; patent practitioners may try to draft basic chemical-type claims on industrially produced inactive DNA, which would not be encompassed by the definition of genetic/biologically active material stipulated in the directive. However, many patent practitioners view *Monsanto* as a setback to the enforceability of patents directed to DNA sequences.

Peptides and proteins (enzymes and antibodies)

In claims, proteins and peptides are often characterised by structural features, their physiological activity and/or particular functional facts. In the prosecution of such applications before the EPO, the allowable breadth of the claims greatly depends on the detail of the disclosure of the claimed protein or peptide in the description of the application.

Proteins may be structurally defined by their full amino acid sequence or just by the sequence of that part of the protein that is necessary for its function. Regarding claims directed to antibodies, the minimum structural information necessary would be the heavy and light chain variable region sequences of the antibody, or at least the sequences of the complementarity determining regions of the heavy and light chain. The EPO is rather reluctant to grant patents directed to antibodies which, for example, are defined by the heavy chain variable region sequence or by single chain variable fragments only. If sufficient sequence determinants are included in the claim, the EPO will often grant protection of the antibody as such. However, patent protection is thereby limited to antibodies containing exactly these structural features.

An even narrower scope of protection applies to an antibody defined by reference to the deposition of a cell line producing the new and inventive monoclonal antibody with a recognised depositary institution (Rule 31(1)(a)). Such definition is generally accepted by the EPO, but provides protection only for the specific antibody produced by the deposited cell line.

To obtain a broader scope of protection, the applicant may try to claim antibodies or proteins with a minimum identity to specific sequences of the antibody or protein. For this, the applicant may disclose

in the application several sequences with modifications in one or more amino acids, all providing the same desired technical effect. The question is whether under such conditions the claims must be directed to the specific embodiments disclosed, or whether the scope of the claims can be broadened by defining a minimum identity to one of the disclosed sequences or allows protection for the disclosed embodiments only.

A generalisation beyond the exact sequence of a monoclonal antibody or peptide (eg, by using the phrase “at least 90% identity with...”) is possible for a claim which also includes a functional feature of the antibody or the peptide which cannot be derived from the state of the art. Thus, applicants would be well advised to include such functional features in the application in addition to the sequence data, since this may enable them to seek claims with a generalisation of the subject matter beyond the exact antibody sequence disclosed in the application.

In summary, generalisations in claims directed to antibodies are allowable only if the solution of the problem underlying the invention was made credible over the full range of claimed antibodies or proteins.

Microorganisms

The majority of patents in the field of microbiology are directed to either a microorganism itself or a method employing a microorganism for the generation of a specific product. In contrast to the scientific definition of “microorganism”, in patent law the term also includes animal and plant cells as well as viruses and prions.

The patenting of microorganisms generally requires deposition of the microorganism at an international depository authority (IDA). This is necessary since it is not usually possible to define a newly generated microorganism by a written description in enough detail to enable third parties to carry out the invention as required by Article 83. The Budapest Treaty ensures that deposition at one IDA is sufficient for all member states and organisations. However, this would mean that the deposited microorganism would become available to any third party upon publication of the patent application. In order to protect the rights of the applicant, the EPC has adopted the so-called “expert solution”, where the deposited sample may be made available only to an expert nominated by the applicant. Under the EPC, these samples then become freely

available only at the time of publication of the grant of the European patent or, where no patent is granted, 20 years from the date of filing.

Stem cells

Stem cells are particularly promising for the development of novel therapies. There are two types of stem cell: embryonic and adult. In principle, like all parts of the human body, cells are patentable only in an isolated form and in case the provision of the cell goes beyond a mere discovery.

While products or methods related to adult human stem cells were always principally regarded as patentable, the patenting of products or methods related to human embryonic stem cells was a highly debated topic which was recently clarified by a decision of the Enlarged Board of Appeal. In Case G2/06 the board had to decide on a patent application by the Wisconsin Alumni Research Foundation on a method for obtaining embryonic stem cell lines which, at the filing date, could be prepared exclusively by a method which necessarily involved the destruction of the human embryos from which they were derived. Although the patent application did not include the step of isolating cells from a blastocyst, which inevitably leads to the destruction of the blastocyst, the board regarded this method as a case of “uses of human embryos for industrial or commercial purposes”, which is excluded specifically by Rule 28(c). Thus, products and methods related to embryonic stem cells are excluded from patentability. Methods and products related to the use of adult human stem cells do not fall under this prohibition and are thus patentable under the EPC.

Transgenic plants and animals

According to Article 53(b), “animal and plant varieties or essentially biological processes for the production of plants or animals” are excluded from patent protection for lack of technical character. A process for the production of plants or animals is considered essentially biological if it consists entirely of natural phenomena such as crossing or selection (Rule 26(5)). On the other hand microbiological processes *per se* are not excluded from patentability under Article 53(b).

The definition of “essentially biological processes” according to the EPC was recently clarified when the Enlarged Board of Appeal ruled on two referrals relating to processes for the production of tomatoes (G2/07) and broccoli (G1/08). Decision

G1/08 dealt with a patent application claiming a process for crossing and selecting broccoli hybrids which allegedly prevented cancer. In the claimed method molecular markers were used for the selection of specific hybrids for further breeding. The board decided that the mere fact of using technical means such as molecular markers in a breeding process was insufficient to confer technical character onto the process as a whole. However, the board concluded that a method for breeding plants which comprises a technical step that by itself adds a trait to a plant or an animal (eg, a step involving genetic engineering) is still to be considered patentable under the EPC. The same applies to transgenic plants and animals which are the products of genetic engineering.

In Decision G1/98 the Enlarged Board of Appeal held that patent protection of transgenic plants is allowable as long as the transgenic plant is not considered a plant variety. This ruling was later confirmed for the patenting of transgenic animals (T315/03), although there is no *sui generis* protection system for animal varieties.

Finally, moral issues present an additional bar to the patenting of transgenic animals. Rule 28(c) excludes from patent protection processes for modifying the genetic identity of animals which are likely to cause them suffering without substantial medical benefit to man or animal and animals resulting from such processes. To address this exception, the EPO has developed a utilitarian balancing test which aims to assess the potential benefits of a claimed invention against its negative aspects. In T315/03 the Technical Board of Appeals had to decide on the patentability of the OncoMouse®, developed by Harvard researchers in the early 1980s for cancer research. The board held that the benefits outweighed the suffering of the animal and granted a patent.

Diagnosics and therapy

In contrast to US patent law, methods for treatment of humans or animals by surgery or therapy and diagnostic methods are excluded from patentability under Article 53(c).

Under the EPC, only diagnostic methods

performed on the human or animal body *in vivo* are excluded from patentability. Substances or devices for use in such methods, as well as all *ex vivo* or *in vitro* diagnostic methods, are patentable.

Article 53(c) does not exclude products (in particular, biotechnological subject matter), pharmaceutical compounds and compositions for use in methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body.

According to Article 54(4), known substances already comprised in the state of the art can still be patented if the invention constitutes the first use of such substances as a medicament. In addition, second (and further) medical use claims are allowable under Article 54(5) if the substance has already been used as a medicament, but only in a different medical indication. Instead of the Swiss-type claim, which was commonly used in the past, according to a recent Enlarged Board of Appeal decision (G2/08), claims directed to a second (or further) medical application should read “Sequence/Biopharmaceutical X for use in treating disease Y”. In the same decision the board ruled that claims directed to a known medicament for use in a known treatment of a disease are protectable by a second medical use claim, even if the only distinguishing feature with respect to the prior art is the provision of an – inventive – novel dosis regimen.

Outlook

Patenting of biotechnological inventions has come a long way since its advent in the early 1970s. With the expiry of the first patents on recombinant drugs (eg, insulin), generic products are surging onto the market. Biopharmaceutical innovator companies must weather this storm through smart patent lifecycle management and cultivation of a broad biotechnological patent portfolio. Recent years have shown that biotechnology offers cures and technologies beyond the reach of conventional small molecules. The patent protection offered for biotech inventions in Europe allows these innovations to translate into economic success stories. **iam**



Ralph Minderop is a senior partner with the law firm COHAUSZ & FLORACK. He has wide experience in the prosecution and litigation of cases in chemistry, pharmaceutical chemistry and biochemistry on behalf of German and international clients and gives strategic IP advice. He obtained his PhD in biochemistry.

Ralph Minderop
Senior partner
rminderop@cohausz-florack.de
+49 211 90 490 0

COHAUSZ & FLORACK
Germany
www.cohausz-florack.de



Arwed Burrichter is a senior partner with the law firm COHAUSZ & FLORACK. He is a renowned and highly experienced European and German patent attorney. Having obtained a PhD in chemistry from the University of Southern California, Los Angeles, he prosecutes and litigates patents in the fields of chemistry, polymer chemistry, pharmaceutical chemistry and biochemistry and gives advice on strategic IP decisions.

Arwed Burrichter
Senior partner
aburrichter@cohausz-florack.de
+49 211 90 490 0

COHAUSZ & FLORACK
Germany
www.cohausz-florack.de



Meikel Diepholz studied biotechnology in Braunschweig and San Diego and received a PhD at the European Molecular Biology Laboratory Heidelberg in the field of cryoelectron microscopy, protein structure and biochemistry. Dr Diepholz has authored and co-authored several high impact scientific publications. He joined COHAUSZ & FLORACK in September 2009 and is currently being trained as a patent attorney.

Meikel Diepholz
Technical expert
mdiepholz@cohausz-florack.de
+49 211 90 490 0

COHAUSZ & FLORACK
Germany
www.cohausz-florack.de



Natalie Kirchhofer obtained a graduate degree in biochemistry from the University of Tübingen. As a Fulbright scholar she attended Rockefeller University, New York and subsequently obtained a PhD at the Max-Planck Institute of Biochemistry in Munich, investigating DNA double-strand break repair mechanisms. Dr Kirchhofer joined COHAUSZ & FLORACK in October 2010 and is currently being trained as a patent attorney.

Natalie Kirchhofer
Technical expert
nkirchhofer@cohausz-florack.de
+49 211 90 490 0

COHAUSZ & FLORACK
Germany
www.cohausz-florack.de