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Biotechnology case law developments in Europe

By **Dorothea Majer** and **Caroline Pallard**,
Nederlandsch Octrooibureau, The Hague

This article analyses European case law on three specific biotechnological issues:

- The exclusion from patentability of essential biological processes applied to plants.
- The exclusion from patentability of diagnostic methods.
- The industrial applicability of a nucleic acid sequence.

Plant patenting and “essentially biological processes”

A plant variety may fall under a European patent for various reasons. For example, a patent may claim a process for obtaining a plant. Such a claim covers plants obtained directly by the claimed process (Article 64(2) of the European Patent Convention (EPC)), whereby plant varieties may fall under the scope of the patent. A prerequisite for allowing such a claim is that the process is not an “essentially biological process” (Article 53(b) and Rule 23b(5) of the EPC). According to Rule 23b(5), a process is essentially biological if it “consists entirely of natural phenomena such as crossing or selection”. But what does this mean? Does the word “entirely” imply that a certain degree of human intervention would make the claim patentable?

An answer to this question may soon be provided by the Enlarged Board of Appeal (EBA). The Technical Board of Appeal (Board 3.3.04), chaired by Ms Kinkeldey, is set to refer to the EBA questions of law which have arisen in Case T0083/05.

Case T0083/05 relates to European Patent EP 1 069 819 B1 (PBL), wherein claims were allowed for a method for the production of *Brassica oleraceae* plants with modified glucosinolate levels (comprising crossing and selection steps) and to plants with this new phenotype. At the end of the

opposition, the patent was maintained in amended form, with method claims containing a step which uses molecular markers for selection purposes.

The EBA may now be asked to confirm whether the use of molecular markers takes the claim out of the Article 53(b) exclusion, and to clarify the meaning of “entirely essentially biological”.

In Case EP 1 211 926 (State of Israel), the Opposition Division decided during oral proceedings that a method of breeding tomato plants comprising crossing and selection steps, and a final step of leaving the fruit on the vine past the normal ripening stage and screening the tomato fruit for reduced water content, is an essentially biological process and is therefore excluded under Article 53b. The Board followed Case T320/87, stating that the totality of human intervention and its impact on the result achieved must be considered when deciding whether a method is “essentially biological”. If the degree of intervention required amounts to routine breeding steps which are considered “trivial” in the sense of Case T320/87, then the method is essentially biological.

The proprietor and the opponent have appealed against the decision and the case is pending as T1242/06. The Technical Board of Appeal (Board 3.3.04) has now asked the appellants whether, in view of the referral of Case T0083/05 to the EBA, they would prefer to stay the proceedings until the EBA has decided on the points of law in Case T0083/05 or whether they would like corresponding questions arising in this case also to be transferred to the EBA.

It is hoped that the appellants will favour the second alternative and that, as a result, the EBA will provide a clear and comprehensive decision on this important point of law.

Diagnostic methods or knowledge of discrimination

Article 52.4 of the EPC, in its current wording,

stipulates that diagnostic methods practised on humans or animals shall not be regarded as inventions which are capable of industrial application, implying that these methods are excluded from patentability. The forthcoming version of the EPC, which will be effective by the end of 2007, simply states in Article 53(c) that such methods cannot be patented.

Article 53(c) was subject to debate in recent European case law. The meaning of the word “diagnosis” itself was disputed.

“Diagnostic method” was defined in Case T 385/86 as a method whose results immediately make possible a particular medical treatment. In other words, a diagnostic method comprises at least the following steps:

- Examination (technical step).
- Establishment of symptoms (non-technical step – comparison of data of the person examined with control databases).
- Deductive medical decision (non-technical step – intellectual exercise).

If one of these steps were lacking, the claimed method would not be regarded as a diagnostic method, since no diagnosis would be reached. Therefore, methods providing interim results would not be considered as diagnostic methods and could thus be patented. This was the so-called “narrow exclusion” theory.

Case T385/86 further emphasised that a method involving at least one step which only a physician would be able to perform could also be regarded as a diagnostic method.

Later, in Case T964/99, the Board concluded that the definition of “diagnostic method” in Case T385/86 effectively set a different standard for diagnostic methods from that established for other methods excluded from patentability, such as surgery or therapeutic methods (Article 52.4 of the EPC).

The established standard for surgery or therapeutic methods is that if a claimed method involves a single step which serves a purpose or related purpose excluded from patentability, then the whole method must also be excluded. The Board in Case T964/99 applied this standard to diagnostic methods as well. Therefore, contrary to the conclusion held in Case T385/86, a method providing interim diagnostic results would be excluded from patentability. Case T964/99 defined the so-called “broad exclusion” theory.

In contrast to Case T385/86, Case T964/99 concluded that a method may be regarded as a diagnostic method even if a

physician is not involved in any steps of the method.

In view of these two conflicting decisions, the EBA in Case G01/04 had to clarify the situation and confirmed the “narrow exclusion” theory of Case T385/86. Two main reasons were given, as follows:

- Article 52.4 of the EPC does not specify that neither individual steps of diagnostic methods nor methods relating to or of value for diagnosis should be excluded from patentability. On the contrary, Article 52.4 specifically excludes diagnostic methods as such from patentability.
- Surgery and therapeutic methods differ from diagnostic methods since they can be defined by a single-step method, whereas a diagnostic method or method providing the “knowledge of discrimination” comprises several steps as outlined in Case T385/86. Therefore, intermediate findings of diagnostic relevance do not amount to a diagnostic method as such.

In addition, the EBA confirmed the conclusion reached in Case T964/99 that qualification of a method as diagnostic should not depend on the identity of the person involved. The reasons given for this were twofold. First, Article 52.4 of the EPC specifically reads on the excluded method and not on the identity of the person who carries out that method. Second, having to define the identity and activities of that person for exclusion from patentability would create uncertainty.

Finally, the EBA clarified the meaning of the expression “practised on the human or animal body” by implying an interaction with a human or animal that necessitates the presence of the latter. Non-invasive methods could also be considered to satisfy this criterion. Therefore, if the technical step of a claimed potential “diagnostic” method necessitates the presence of a human or animal, this method will be excluded from patentability.

This means that “diagnostic methods” comprising the three steps as defined in Case T385/86 and which are not “practised on the human or animal body” are not excluded from patentability. One example of such method is a diagnostic method that is carried out *in vitro*. Another is a diagnostic method carried out by a device without involving any interaction with a human or animal.

The EPC excludes from patentability only diagnostic methods as such whose results

immediately make possible a particular medical treatment and with regards to which the presence of a human or animal is necessary for examination.

Industrial applicability of a nucleic acid sequence

Article 52.1 of the EPC states that an invention is patentable if it is capable of industrial application. This concept is further defined in Article 57, which states that an invention will be considered as capable of industrial application if it can be made or used in any kind of industry, including agriculture.

Rule 27.1(f) of the EPC further provides that if this is not obvious from the description of the nature of the invention, the manner in which the invention is capable of exploitation in industry must be indicated in the description.

As a consequence of EU Directive 98/44/EC, a new Rule 23e was introduced into the EPC, introducing a stricter patentability criterion for industrial applicability of nucleic acid sequences than for other products. Rule 23e EPC reads as follows: "The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application."

Therefore, nucleic acid sequences are now the only type of invention for which industrial applicability must be expressly stated in the application at the time of filing.

When is the industrial applicability requirement satisfied?

This issue was recently clarified to some extent in Case T898/05, which referred to three earlier decisions (T870/04, T338/00 and T604/04).

First, the fact that a claimed polypeptide can be produced (referring to Article 57 of the EPC) is insufficient to meet the requirement of industrial applicability (T898/05, T870/04). Indeed, as soon as a nucleic acid sequence has been cloned, the production of this nucleic acid sequence and/or of the encoded polypeptide has in principle been made possible.

In order to meet the requirements of industrial applicability, the application should specify some profitable use of the claimed polypeptide encoded by the nucleic acid sequence (T898/05).

What is a profitable use?

A profitable use is an immediate concrete benefit. "Immediate" implies that it may be derived from the application. "Concrete benefit" implies a practical exploitation in

the industry, as opposed to a purely theoretical possibility of exploitation.

Function may be the key to understanding the concrete benefits which may derive from industrial exploitation of the invention. Case T898/05 defines the concept of polypeptide function at several levels:

- Structural function – the amino acid sequence of the polypeptide itself can be seen as advantageous for an application (eg, animal nutrition)
- Molecular function – biochemical activity of the polypeptide (eg, a protease).
- Cellular function – function of the polypeptide in cellular processes (apoptosis, secretion).
- Biological function – influence of cellular processes within a multicellular organism (cancer).

Case T898/05 establishes a criterion for deciding on industrial applicability: elucidation of at least one of these function levels may result in straightforward industrial application, even where other levels remain unknown. What is decisive is that the "elucidated function level" establishes a link to an immediate concrete benefit. In this respect, the decision further concludes that a function level which is elucidated through computer-assisted methods is as valuable as one elucidated through classic experimental work.

Several examples are provided below to illustrate how this criterion has already been applied.

If a biological function of a claimed polypeptide is well known to be essential for human health, then identification of the polypeptide with this function will immediately suggest a practical application in the case of a disease or condition caused by a deficiency associated with this function (eg, insulin, erythropoietin, growth hormone).

If a molecular function of a claimed polypeptide is known from the application but no link is made in the application between this function and an immediate concrete benefit, and both prior art and post-publication evidence give no further concrete indication of possible use, industrial applicability cannot be acknowledged. Sometimes the results of interesting research cannot be directly translated into a practical industrial application. The only practical use suggested in such case might be to use the isolated nucleic acid sequence to find out more about its own natural functions.

The facts underlying Case T870/04 are an example of this. The amino acid

sequence of a new phosphatase was claimed. It is generally known that phosphatases are involved in cellular signal transduction and that some phosphatases play a role in fighting cancer. However, the application gave no immediate concrete use of the kind of role which this protease could play in fighting cancer. In addition, prior art on other phosphatases and post-publication evidence on this particular phosphatase suggested only a general role in cellular signal transduction but did not establish a link to an immediate concrete benefit; therefore, industrial applicability could not be acknowledged.

If, on the other hand, a cellular function of a claimed polypeptide is known from the application and a concrete practical use is suggested, industrial applicability can be acknowledged.

The facts underlying Cases T338/00 and T898/05 are an example of this. In Case T338/00, the amino acid sequence of a heterodimeric receptor (retinoic acid receptor RXR and members of steroid/thyroid receptor) was claimed, and its role in different physiological processes was explicitly described in the application as a transcription modulator. In addition, two uses were described: (1) use for modulating suitable transcription expression systems, and (2) use in screening for further compounds for the ability to modulate disclosed cooperative interactions. Hence, a link to an immediate concrete benefit was provided and industrial applicability could be acknowledged.

If a potential function of a claimed polypeptide is known from the application (based on computer alignment), concrete uses are suggested in the application based on this potential function and the prior art confirms the role of related polypeptides as a family in the pharmaceutical field, industrial applicability can be acknowledged.

The facts underlying Case T604/04 are an example of this. The amino acid sequence of a putative orphan chemokine receptor was claimed. The prior art confirmed that chemokines are known to act via their own receptor and are known, as a family, to be important mediators of inflammation. The potential biological function of the polypeptide could therefore be derived from the application. From the prior art and the application, it could be deduced that chemokine inhibitors could be effective as anti-inflammatory drug and that an agonist of chemokine could play a role in wound healing and tissue repair.

In conclusion, it seems that the indication of the immediate concrete benefit of a claimed nucleic acid sequence provided by the (potential) elucidation of at least one function level of the encoded polypeptide is sufficient to meet the requirement of industrial applicability.



Nederlandsch Octrooibureau

JW Frisolaan 13
2517 JS The Hague, The Netherlands
Tel: +31 070 331 2500
Fax: +31 070 352 7528

www.octrooibureau.nl

Dorothea Majer

European patent attorney
majer@octrooibureau.nl

Dorothea Majer works as a European patent attorney for Nederlandsch Octrooibureau. Her main focus lies in obtaining patent protection for biotechnological inventions, with a special interest in the protection of plants and plant-derived products. Ms Majer holds a PhD in molecular phytopathology.



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Caroline Pallard

European patent attorney
pallard@octrooibureau.nl

Caroline Pallard joined the firm as a European and Dutch patent attorney in 2006. Her technical background is in biotechnology, molecular biology, biochemistry, haematology and microbiology. She also has expertise in food ingredient-based inventions. She works for universities, small start-ups and international food concerns.

Ms Pallard holds a PhD in haematology and molecular biology and undertook two years of postdoctoral research on immunology and molecular biology. Before joining Nederlandsch Octrooibureau she spent eight years working in the patent department of an international concern.

Nederlandsch Octrooibureau

JW Frisolaan 13

2517 JS The Hague, The Netherlands

Tel: +31 070 331 2500

Fax: +31 070 352 7528

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