HOLLY IP

Biotech Patents in Europe

Introduction

This circular relates to biotech patent practice in Europe. It is based on our experience of drafting and prosecuting biotech applications. The circular is written from the viewpoint of practice at the European Patent Office (EPO), though many of the issues that are discussed are also applicable to other territories.

The Patentability of a Biotech Invention

Assessing the patentability of a biotech invention is often more difficult than for other technology areas. As well as the usual analysis of the contribution over the prior art, it is more likely that there will be a need to consider whether European practice allows patent protection in that area and for that type of invention. In addition, it is not always straightforward to determine whether the available data is enough to comply with the disclosure requirements for an application.

The European Patent Convention (EPC)[1] excludes certain subject matter from patentability, for example for moral reasons. For other subject matter it is not possible to obtain patent protection due to the way that EPO practice and case law have developed, such as for a new medical use of a known device or for discovering the mechanism of action of a known drug.

Is there enough data to file?

Inadequate disclosure in an application can lead to objections of lack of support, lack of sufficiency, lack of industrial applicability or that the application does not show that the problem has been solved (which is an objection of lack of inventive step) . Such objections are more likely if the claims are broad, and for biotech cases they often are. Therefore it is important to ensure that the application contains appropriate disclosure and data to support the claims. For inventions concerning therapy it can take many years for clinical trial data to be produced. However EPO Examiners will normally accept *in vitro* data that demonstrates the technical effect. Post-filing data can be filed during examination and that is often helpful.

In general the more data there is the more convincing the application will appear to be and more likely to support broader claims. In addition, there is often more flexibility to change the problem being solved during examination. It is preferable for there to be exemplified embodiments across

[1] The European Patent Convention provides the legal system according to which European patents are granted

the breadth of the claims, particularly if the claims cover use of a broad range of compounds. In the case of gene sequences, the industrial applicability of the gene needs to be mentioned in the application.

Drafting Biotechnology Cases

When drafting a biotech case it is important to think carefully about the claim scope. Whilst broad claims are often appropriate, claims which are too broad can be detrimental to a case. Sometimes it is a case of striking the correct balance between inventive step and sufficiency to arrive at a scope which is credible from the available data. Essentially the claims as initially drafted should come across as a reasonable extrapolation from the Examples and with a clear distinction over the prior art. Whilst amendments are of course possible later, it is advantageous to have an initial position which is credible and potentially defensible.

EPO Examiners often focus on the technical effect(s) achieved by the invention. When drafting one should identify all of the technical effects to make sure they are reflected in the specification. For example a new product may have improved activity, but it might also be more stable, easier to make or have fewer side effects. Synergistic effects should in particular be identified and highlighted.

When assessing the contribution the invention makes the EPO will normally look at the problem being solved. However the problem being solved will depend on the prior art and if new prior art is discovered the problem may change. For biotech cases the problem can change substantially, and the application will need to be drafted in a way which bears this in mind. Essentially this means looking at inventions as something quite fluid which are only really defined during examination. It is therefore important, for example, to consider giving appropriate ranges for parameters which are used to define the invention.

The Claims

For biotech inventions the inventive concept often leads to many different independent claims, and so it is important to ensure that all possible independent claims are considered when drafting. An invention based on the finding of a gene polymorphism that causes a disease condition can lead to the claims to the following subject matter: a diagnostic test, a polynucleotide comprising the polymorphism, a protein comprising the resultant mutation, probes capable of detecting the polymorphism, an antibody capable of detecting the mutation, vectors, transgenic animals with the polymorphism, kits containing the probes or antibody, and possibly screening claims, such as use of the transgenic animals to identify substances able to reverse the effect of the polymorphism.

It is also important to identify all the different ways of putting the invention into practice. Given the complexity of biological systems this is not always straightforward. For example if the invention concerns a diagnostic test in which the presence of a specific polymorphism is detected, then one should consider whether there are other polymorphisms linked to the specific polymorphism that could also form the basis of the diagnostic test.

Lack of Unity

The EPO is strict on lack of unity, and lack of unity is often found on biotech cases. This is now more problematic given that the EPO has imposed stricter deadlines for filing divisional applications. When lack of unity is found Examiners will tend to split the claimed subject matter into different inventions along the lines of the sequences that can be used in the invention. Sometimes each sequence is deemed a separate invention, leading to a large number of inventions being identified. This is unfortunate as there are often other ways to define the inventions that lead to a lower number of total inventions. However given the present practice of the EPO, if the invention relates to multiple sequences then the most important sequence should be listed first (either in the claims or in the description).

It is important to think about unity when drafting. If possible, one should seek to highlight why the claims relate to a single invention and aim to draft the claims in a manner where the contribution of the non-sequence aspects is emphasised.

Problematic Subject Matter

As mentioned above certain subject matter cannot be patented in Europe due to exclusions from patentability or because of the way that EPO case law has developed. If this is relevant to the invention then European Patent Attorneys can advise on whether appropriate drafting of the claims will allow some protection to be obtained for the invention.

The Biotech Directive[2] defines subject matter that is excluded for moral or other reasons, such as parts of the human body, human embryos, methods of cloning humans, certain methods of changing genetic identity and certain transgenic plants.

Methods of *in vivo* diagnosis and therapy and methods of surgery are also excluded from patentability in Europe. For diagnostic and therapeutic inventions it is normally possible to obtain patent protection using other claim types, such as diagnostic or medical use claims. Medical use claims are directed to use of a therapeutic substance in therapy. European practice allows such claims to be additionally limited in many different ways, for example by patient group, dosages,

[2] European Parliament and Council Directive 98/44/EC of 6 July 1998 on the legal protection of biotechnological inventions

administration schedules or methods of administration, and so a wide range of inventions can be protected. However there are still problematic areas, such as new medical uses of known devices, particularly where an electrical impulse or electromagnetic radiation is delivered (instead of a substance). Other problematic areas are those where the invention is not restricted to use of a specific therapeutic substance or treatment of a specific condition, such as a new delivery system for example. This is because Examiners are reluctant to allow medical use claims which define substances functionally and which are not limited to treatment of a defined specific disease condition.

In cases where the invention has both *in vivo* and *in vitro* steps it can be unclear as to whether it can be worded as an allowable medical use claim. For example it is presently unclear to what extent medical use claims can encompass a diagnostic or screening step. For *in vivo* diagnosis the case law is complicated and continues to evolve.

EPO Examiners usually apply the exclusion of surgical methods from patentability broadly, so that taking a sample from a body, or administering via injection, or even by particles, can lead to objections. In many case the objection can be overcome by excluding the relevant step from the claims, but clearly for certain inventions this might not be possible.

In general, defining substances in the claims in a functional way is problematic. If this needs to be done then fall-back positions relating to specific defined substances should be present in the application. Reach through claims are not allowable (which define substances on the basis of them being identifiable using a specified screening method). In addition Examiners are increasingly strict on defining disease conditions in a mechanistic or functional way (such as 'a condition in which TNF-α levels are elevated'). If such a definition is used in the claims, then the application needs to contain details of how the skilled person can determine whether or not a given condition falls within the definition which is used.

Inventions relating to the elucidation of the mechanism of action of a known therapy are problematic since it can be difficult to draft a claim that will be considered novel over the known therapy. Essentially such cases are only allowable if knowledge of the mechanism will be reflected in the therapy being performed in a different way.

At present the position of the EPO is unclear on the novelty of medical uses claims where the patient group that is treated overlaps with that treated by a known therapy. For example if it is found that patients with certain biomarkers are particularly receptive to treatment with a known cancer drug, it is unclear whether a medical use referring to the treatment of patients with the biomarker will be deemed to be novel. This does of course have tremendous implications for the rapidly developing field of personalised medicines.

Polynucleotide and Polypeptide Sequences

Where an invention concerns a specific polynucleotide or polypeptide sequence then it is normally desirable to also cover variants. This is usually done by drafting claims that cover homologues of the sequences defined using percentage identity or homology. In such cases the description of the application should refer to an algorithm that can be used to calculate the identity/homology.

EPO Examiners are increasingly taking a strict view of variant sequences, and may want further limitations in the claims so that only useful variants are covered. Normally the variants are required to have a particular activity. However if possible the application should identify preferred variants defined by specific sequences and the application should include data for variants.

Antibodies

It is normally acceptable to define antibodies with reference to the epitope that is bound, and one finds that in general EPO Examiners will accept the term 'specifically binding' to distinguish over prior art antibodies. However if the prior art is very close, an Examiner may take a stricter view. In the case where an antibody is an important part of the invention one should consider providing further preferred features of the binding properties. In particular it is useful to define polypeptides which the antibody fails to bind. This can be done, for example, by referring to polypeptides having less than a defined percentage identity to the natural epitope sequence.

The European Patent Office (EPO)

The EPO has a highly developed practice and case law in biotech. It is a sophisticated patent office that is capable of properly assessing the patentability of biotech inventions, having Examiners who can understand complex biotech inventions and who take a consistent approach to patentability. Whilst there have been suggestions that the EPO grants too many biotech patents with broad claims, in our experience we find that EPO Examiners normally do find a fair balance between the rights of the applicant and the rights of third parties.

Dialogue with the Examiner on Difficult Biotech Cases

In our experience biotech cases can be the most challenging during examination. However it is important to realise that at the EPO a real dialogue is possible with the Examiner. Whilst the EPO does have an established practice and case law which seems quite strict, Examiners are open to the arguments made by applicants. They will change their initial view of a case and are flexible enough to adopt a case by case analysis when it is appropriate.

Perhaps one mistake that applicants make is to pursue claims which are too broad for too long in examination. It can be more effective to appreciate the Examiner's position and make limiting

amendments earlier when these will be inevitable for a case to be allowed. Amendments can be powerful way of changing the perspective of the Examiner on a case and are a sign that the applicant is cooperating.

Inventive Step

Inventive step on biotech cases is often complicated, and might involve many documents. Due to the nature of biotech research it is often possible to find a prior art document that has some suggestion of the invention. However the EPO will accept inventive step arguments based on an analysis of the likelihood of the invention working. Thus the test of 'reasonable expectation of success' is often used. This means that whilst an invention can seem obvious from one document, it is possible to show inventive step based on other documents which, for example, give reasons as to why the skilled person would not have expected the invention to work.

EPO Examiners are also receptive to arguments based on surprising advantageous properties, and the more surprising and advantageous the invention is, the more likely the case is to be allowed, though it might seem obvious from the prior art. Essentially the surprising advantageous property becomes part of the problem being solved. Thus the problem is not simply finding a compound with the required activity, but is to find a compound with high activity, for example. The skilled person would have less expectation of this second problem being successfully solved.

Sometimes it can be helpful to file evidence or an expert declaration during examination. These can be persuasive in showing Examiners the expectations of the skilled person at the priority date. Given that negative results rarely get published, it can be difficult to show through published documents that in a particular field there would have been no expectation of a certain approach succeeding.

Appeal from Examination

Whilst appeal should not be viewed as an opportunity for the entire case to be looked at again, in practice it is very helpful. Appeal Boards are open to the arguments presented to them and are prepared to take a different view from Examining Divisions.