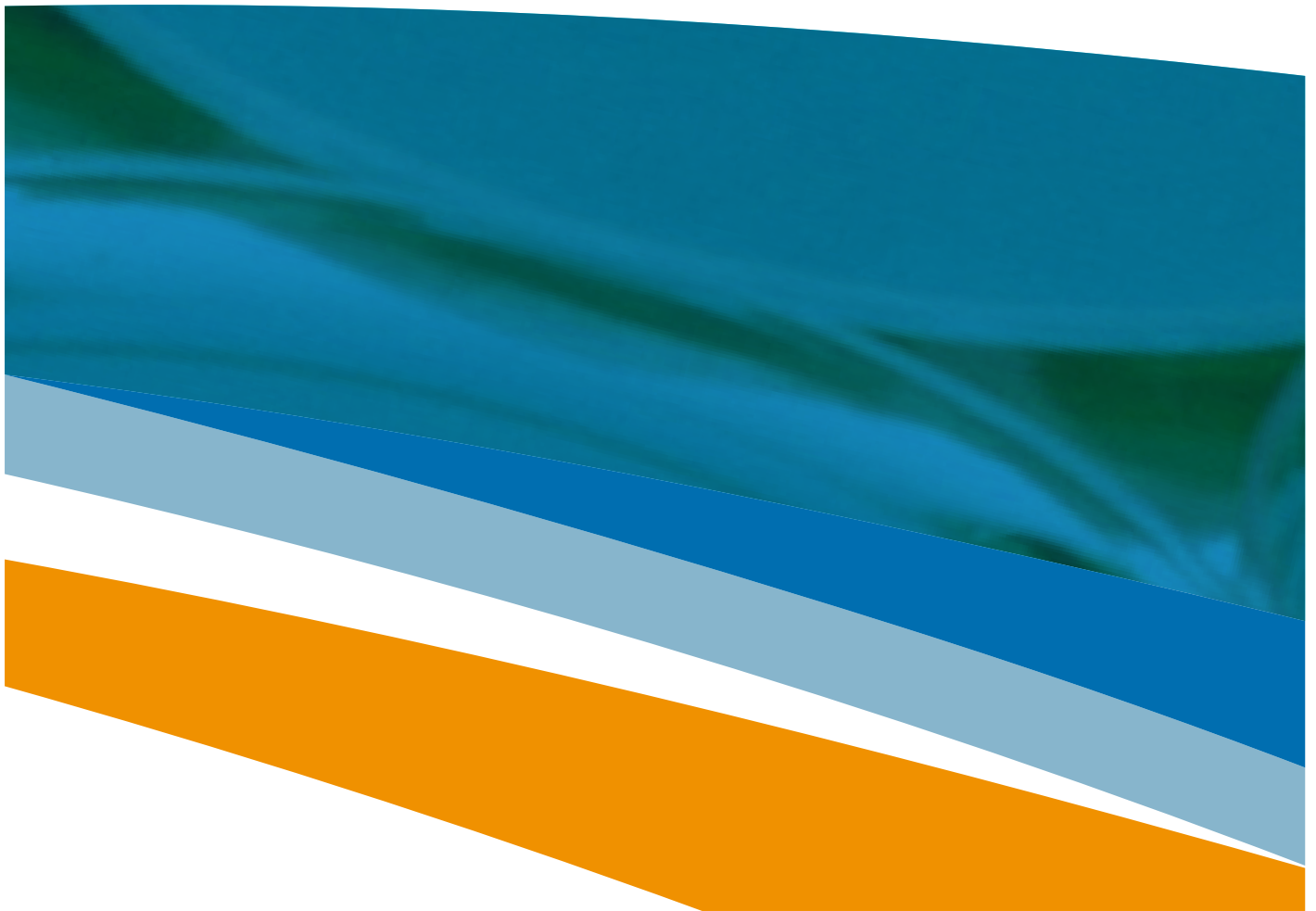




Intellectual
Property
Office

Examination Guidelines for Patent Applications relating to Biotechnological Inventions in the Intellectual Property Office



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Introduction

1. These Guidelines set out the practice within the Intellectual Property Office as it relates to patent applications for biotechnological inventions. The relevant legislation is the Patents Act 1977, as amended by the Patents Regulations 2000 (SI 2000/2037), and the Patents Rules 1995, particularly as amended by the Patents (Amendment) Rules 2001 (SI 2001/1412). The 2000 Regulations came into force on 28 July 2000 and implemented the provisions of Articles 1 to 11 of the European Directive 98/44/EC on the legal protection of biotechnological inventions (“the Biotech Directive”). These provisions relate to the patentability requirements for biotechnological inventions and so are arguably the most important provisions of the Directive. The 2001 (Amendment) Rules came into force on 6 July 2001 and implemented Articles 13 and 14 of the Biotech Directive, which relate to the deposit, access and re-deposit of biological material. The Guidelines do not address the practice in The Office stemming from the Patents and Plant Variety Rights (Compulsory Licensing) Regulations 2002 (SI 2002/247), which implemented Article 12 of the Biotech Directive on 1 March 2002. These 2002 Regulations concern compulsory cross licensing between patents and plant breeders’ rights and do not have a direct bearing on pre-grant matters.
 2. This edition of the Guidelines is an update of the Guidelines published in July 2012. All significant amendments are indicated by side lines.
 3. **Any comments or questions arising from these Guidelines should be addressed to Rowena Dinham, Room 2.Y35, Concept House, Cardiff Road, Newport, South Wales, NP10 8QQ (Telephone: 01633 814995).**
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Background

4. Agreement on the European Patent Convention (EPC) in the 1970s led to important harmonisation of the requirements for patentability amongst the EPC Contracting States, as well as with the European Patent Office (EPO). Patent practice in the UK during the 1980s and 1990s grew up on the back of precedent cases from the UK courts and the Boards of Appeal of the EPO. However, despite the harmonisation provided by the EPC it became apparent during the 1980s that Member States of the European Union (EU) were interpreting this harmonised law differently, particularly when applied to biotechnological inventions. This led the European Commission to propose a Directive on the legal protection of such inventions with the aim of greater harmonisation within the EU. The Biotech Directive was eventually adopted in July 1998 but only after an earlier Directive had been rejected by the European Parliament. Although the UK has implemented the Biotech Directive fully as noted above, this is not currently the case in all Member States of the EU. However, the Implementing Regulations to the EPC, which regulate the grant of European patents by the EPO, have been brought into agreement with the Biotech Directive even though the European Patent Organisation had no obligation to take account of any Directive because it is not a Community institution.
5. In the UK the Patents Regulations 2000 confirmed and clarified that inventions concerning biological material, including gene sequences, may be legitimately the subject of patent applications. In other words, these Regulations have established beyond doubt the legitimacy of biotechnology patents in the UK.

“An invention shall not be considered unpatentable solely on the grounds that it concerns -

- (a) a product consisting of or containing biological material; or*
- (b) a process by which biological material is produced, processed or used”*

Paragraph 1, Schedule A2 to the Patents Act 1977

6. Despite the guidance provided by the Biotech Directive, patent offices in Europe face a continuing challenge when examining patent applications for biotechnological inventions. Researchers are using ever more ingenious tools and techniques to probe the mysteries of biological processes and have at their disposal vast amounts of the information which may provide the key to new medical treatments, improved crops and so on. This means that the bench marks used by examiners to assess the patentability of biotechnological inventions are forever changing as the technology itself moves forward at considerable pace. For example, with the publication of the human and other genomes and the number of bioinformatics tools now available, patent applicants are seeking to protect polynucleotides and polypeptides which have been or could have been identified by in silico methods rather than traditional ‘wet biology’. Such methods involve what is sometimes called “data mining” and at the most basic level involve a homology search for genes listed in a databases or identified by random sequencing, and assigning a function to these genes based upon the closest matching protein of known function.
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Computer programs for carrying out such homology searches are well known and the data bases containing the relevant information are widely available on the world wide web. There are also computer programs which recognise certain patterns and profiles in proteins, for example transmembrane regions, as well as programs which can recognise certain motifs in nucleotide sequences, such as transcription factor binding sites, thereby aiding the identification of regulatory sequences of DNA.

Basic considerations

7. It is easy to focus on the contentious issues surrounding biotechnology patenting, such as the criteria for patenting plants and animals, the patenting of gene sequences and morality issues and forget that the majority of biotechnology patent applications will be decided on the basic issues of novelty, inventive step and industrial application, as well as on the requirements that the description should be sufficient and should support the claims. The Manual of Patent Practice is the examiner's main source of information regarding current practice in the Intellectual Property Office under the Patents Act 1977, and these Guidelines are intended to supplement the guidance given in the Manual of Patent Practice. Biotech inventions are considered in the same light as other technical inventions. However, often the application of even the basic issues to biotechnology patent applications can place considerable demands on the judgement of the examiner. Therefore, these Guidelines seek to help by looking not only at how the basic issues of protecting biotechnological inventions have been applied in the past but also at how they should be applied, subject to guidance from the courts and the EPO Boards of Appeal, in the context of recent developments in the technology, such as those described in the previous paragraph. The results of the Trilateral Projects (see Annex D) of the EPO, the Japanese Patent Office and the United States Patent and Trademark Office on biotechnology practices also provide a useful insight into how the EPO addresses some of these basic issues.
 8. Before you can determine whether a claimed invention is novel, inventive or has industrial application, it is important to decide exactly what is being claimed. Annex A provides guidance on how to construe claims commonly encountered in applications for biotechnological inventions.
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Novelty

9. Section 2 of the Manual of Patent Practice sets out the practice in the UK concerning the novelty requirement under the Patents Act 1977. However, the application of the novelty test to biotechnological inventions deserves special consideration, not the least because many biotechnological inventions are based on natural material. In this respect it is important not to confuse the objection that e.g. a polynucleotide sequence lacks novelty with the objection that the polynucleotide is unpatentable because it is merely a discovery. Basically, it is established practice that a natural substance which has been isolated for the first time and which had no previously recognised existence, does not lack novelty because it has always been present in nature ¹.

“It is common ground amongst the parties that until a cDNA encoding human H2-relaxin and its precursors was isolated by the proprietor, the existence of this form of relaxin was unknown. It is established patent practice to recognise the novelty for a natural substance which has been isolated for the first time and which had no previously recognised existence.”

Howard Florey Institute’s Application / Relaxin OJEPO 1995, 388 (V 0008/94)

Discovery is dealt with in paragraphs 102- 104 below.

Enabling disclosure

10. It is now well established that a novelty destroying disclosure must be “enabling” if what it discloses is to be regarded as being “made available to the public”.

“..... I do not see how an invention can be said to have been made available to the public merely by a published statement of its existence, unless the method of working is so self-evident as to require no explanation.”

Asahi Kasei Kogyo KK’s Application [1991] RPC 485 (at page 539) (House of Lords)

11. This principle has been established in the context of a number of biotechnology cases ^{2,3,4} and on this basis a disclosure only destroys the novelty of a later invention if the information it contains, when understood by a person skilled in the art, is sufficient to allow reproduction of the later invention.

1 *Howard Florey Institute’s Application / Relaxin* OJEPO 1995, 388 (V 0008/94)

2 *Asahi’s Application* [1991] RPC 485 (House of Lords)

3 *Collaborative / Preprorennin* OJEPO 1990, 250 (T 0081/87)

4 *Genentech’s (Human Growth Hormone) Patent* [1989] RPC 613 (Patents Court)

“Whilst it may theoretically not be absolutely impossible to proceed on the basis of the citation, a novelty destroying document must according to standard practice, be enabling without undue burden to a person skilled in the art. In such circumstances, inventions might require an actual demonstration of reduction to practice and corresponding detailed instructions to the public in a document, to become available for the purposes of Article 54 EPC as part of the state of the art.”

Collaborative / Preprorennin OJEPO 1990, 250 (T 0081/87)

12. However, an earlier enabling disclosure could destroy the novelty of a later invention even if this earlier disclosure has not actually been “enabled” or “reduced to practice”⁵. Actual prior identification of a process or product claimed is not in itself necessary to find a lack of novelty, merely instructions which, if followed, would inevitably result in the use of the claimed process or product. In *SmithKline Beecham Plc’s (Paroxetine Methanesulfonate) patent*⁶, the House of Lords considered that a person skilled in the art must be able to perform the invention, even if it was not precisely described in the earlier disclosure. In this case, the earlier disclosure used a solvent that was unsuitable for the crystallisation of paroxetine methanesulfonate, but a person skilled in the art would know to change the solvent in order to generate the crystals. (“Person skilled in the art” is dealt with in paragraph 29).

“If an inventor through clever foresight or lucky guess work describes something which works and how to do it, his disclosure is enabling. It is nihil ad rem that he never carried out the experiments themselves or faked the results. The more complex the area of technology, the less likely it is that the inventor will be able to predict the results of experiments he never carried out or that he will strike lucky, but what is important is what the document teaches, not how the contents got there.”

Evans Medical Ltd’s Patent [1998] RPC 517 (at page 550) (Patents Court)

13. The Office practice in relation to a document that outlines the steps to obtain a desired end product, is to assume that the disclosure is an enabling disclosure of that end product. An applicant against whose application such a document is cited can challenge this assumption by argument and/or evidence. If they do, the Office will decide, on the balance of probabilities, whether the disclosure is enabling or not.

⁵ *Evans Medical Ltd’s Patent [1998] RPC 517 (Patents Court)*

⁶ *SmithKline Beecham Plc’s (Paroxetine methanesulfonate) Patent [2006] RPC 10 (House of Lords)*

Product by process claims

14. *In Kirin-Amgen v Hoechst Marion Roussel* the House of Lords⁷ disagreed with the view of the Court of Appeal⁸ that a claim to any product can be characterised by a method of producing the product, and that the product of a claimed method will be novel if that method itself is novel. The EPO does not recognise that novelty can be conferred upon a known substance by a novel process for producing that substance⁹, and the ruling by the House of Lords led the Intellectual Property Office to change its practice and follow that of the EPO, thus rejecting product by process claims where the product is known, on the basis that it is not novel. In light of this, the Intellectual Property Office now takes the view that a claim to a product obtained or produced by a process is anticipated by any prior disclosure of that particular product per se, regardless of its method of production.

“I think it is important that the United Kingdom should apply the same law as the EPO and the other Member States when deciding what counts as new for the purposes of the EPC... It is true that this means a change in practice which has existed for many years. But the difference is unlikely to be of great practical importance because a patentee can rely instead on the process claim and article 64(2). It would be most unfortunate if we were to uphold the validity of a patent which would on identical facts have been revoked in opposition proceedings in the EPO”

Kirin-Amgen Inc. and others v Hoechst Marion Roussel Ltd and others [2004] UKHL 46 (House of Lords)

Section 60(1)(c) of the Act, which corresponds to Article 64(2) of the EPC, states that the protection provided by a claim for a process extends to the product of that process. Therefore, the patentee will still have some protection for the products of his novel process under this section of the Act.

15. The EPO does allow product-by-process claims in certain circumstances, and the Intellectual Property Office now follows this practice. Therefore, a claim to a novel and inventive product defined by its method of production is acceptable provided that there is no physical, chemical or biological means for distinguishing that product from the prior art. However, a claim to a novel and inventive product defined by its method of production is considered to lack clarity if there is an alternative chemical, physical or biological way of defining that product.

⁷ *Kirin-Amgen Inc. and others v Hoechst Marion Roussel Ltd and others* [2005] RPC 9 (House of Lords)

⁸ *Kirin-Amgen Inc. and others v. Transkaryotic Therapies Inc and others* [2003] RPC 3 (Court of Appeal)

⁹ *International Flavours & Fragrances Inc* [1984] OJEP0 309 (T 0150/82)

“A product-by process claim is interpreted according to the jurisprudence of the Boards of Appeal as a claim directed to the product per se, since the reference to a process serves only the purpose of defining the subject matter for which protection is sought, which is a product. Whether or not the term ‘directly obtained’ or any other term, such as ‘obtained’ or ‘obtainable’ is used in a product-by-process claim, the category of that claim does not change as it is directed to a physical entity and the subject matter of that claims, for which protection is sought, remains the product per se..... Therefore, irrespective of how a product-by-process claim is worded, it is still directed to the product per se and confers absolute protection upon the product, precisely as any other claim to a product per se. That product claim, hence, confers protection upon the product regardless of the process by which it is prepared”

Amorphous TPM/ Enichem (not reported) (T 0020/94)

16. As product-by-process claims are considered to relate to the product per se, a claim to a product ‘obtainable’ by a process is also acceptable, provided the product is new and inventive and cannot be otherwise defined. Whilst the term ‘obtainable’ does not limit the claim to a product when made by a particular process, this is not necessary as the claim is treated as a per se claim. This is consistent with Part C, Chapter II, para 4.7b of the EPO Examination Guidelines.

Sequence claims

17. The context in which a polynucleotide sequence is published can have a bearing on whether such an earlier publication will destroy the novelty of a later claim for that sequence. For example, the prior publication may be of the polynucleotide sequence as it occurs, i.e. as it is embedded, within the human genome. This prior publication would not impugn the novelty of the sequence when it is claimed in an isolated state. Similarly, a cDNA which corresponds to a naturally occurring polynucleotide, would not be anticipated by the prior disclosure of the natural polynucleotides because cDNAs do not occur in nature.

“....., the claimed DNA fragments encoding relaxin and its precursors (prepro- and pro-forms) are cDNAs, ie DNA copies of human mRNA encoding relaxin. cDNAs do not occur in the human body. The sequences of claims 1 - 7 are hence novel for this reason alone.”

Howard Florey Institute’s Application OJEPO 1995, 388 (V 0008/94)

18. On the other hand, a claim to a polynucleotide sequence that was available e.g. as part of a library, before the relevant date, lacks novelty, even if the sequence of the polynucleotide has not been previously determined¹⁰. However, a claim to a sequence does not lack novelty if the complete full length sequence is not present in a library, even if it is represented by overlapping fragments of a genome within several library clones¹¹.

¹⁰ *F-Hoffmann- La Roche* AG BL O/192/04 (not reported)

¹¹ *Ajinomoto/ Amino acid production* (not reported) (T 2352/09)

19. If a claim for an isolated polynucleotide embraces the polynucleotide as part of an unrestricted larger sequence (see Examples 3 and 4 in Annex A), it might be anticipated by a larger isolated polynucleotide, possibly even the associated chromosome if this has been isolated. On the other hand, a claim generally to any isolated fragment of an identified sequence (see Example 5 in Annex A) would lack novelty because it would be anticipated by a single, isolated nucleotide. However, a claim to a specific fragment might be allowable as a “selection invention” where it can be shown that the fragment has some advantage or useful quality not previously recognised, such as a specific polymorphism.

Implicit disclosure

20. It is normally required that the features of the claim under consideration are explicitly disclosed, for example in an earlier publication. However, the teaching implicit in a document can be taken into account, as guided by paragraph 2.07 of the Manual of Patent Practice.
21. Sometimes, claimed sequences are qualified by their activity. An earlier disclosure of the same sequence but without any indication of its activity would *prima facie* constitute a novelty anticipation of the claimed sequence. The assumption must be that the earlier sequence inherently possesses the activity of the later sequence. Here it should be noted that although there is a requirement that an earlier description must be enabling, there is no requirement that the skilled worker should be able to determine the activity of the earlier sequence from the earlier disclosure if the claim merely seeks to protect the sequence.
22. The same assumption can be applied to polypeptides when claimed by their tertiary structure if the same polypeptide previously has been isolated from the same source, with the same function, and with approximately the same molecular weight; it can be assumed that the earlier polypeptide has the same tertiary structure as the claimed polypeptide. However, a claim to a crystallised form of a known polypeptide may be novel if the prior art does not disclose crystals of the polypeptide or methods of making the crystals.
23. Whilst it could be argued that it is implicit that the sequence of a protein, which by name and function is identical to the polypeptide claimed, would also be identical in sequence, it could also be argued that due to the extent of variation between peptide sequences of the same family the sequence may differ significantly. Therefore, a document should not be cited under novelty unless it is certain that only one unique form of a particular polypeptide exists. If this certainly does not exist, then a document should only be cited under novelty if the peptide sequence is explicitly disclosed.
24. A claim to an isolated and purified molecule which comprises the binding pocket of a known protein, which is defined by structural coordinates, is not considered to be novel as the isolated known protein would inherently comprise this binding pocket. However, an isolated polypeptide consisting of the binding pocket, and which is demonstrated to retain the binding and signalling activity of the protein may be novel if no such isolated polypeptide fragment is known in the prior art.
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Inventive step

“Whenever anything inventive is done for the first time it is the result of the addition of a new idea to the existing stock of knowledge. Sometimes, it is the idea of using established techniques to do something which no one had previously thought of doing. In that case the inventive idea will be doing the new thing. Sometimes it is finding a way of doing something which people had wanted to do but could not think how. The inventive idea would be the way of achieving the goal. In yet other cases, many people may have a general idea of how they might achieve a goal but not know how to solve a particular problem which stands in their way. If someone devises a way of solving the problem, his inventive step will be that solution, but not the goal itself or the general method of achieving it.”

Biogen Inc v Medeva plc [1997] RPC 1 (at page 34) (House of Lords)

25. Section 3 of the Manual of Patent Practice outlines the practice in the UK concerning the requirement for an inventive step under the Patents Act 1977. When determining inventive step the four steps of “Windsurfing”¹², as reformulated in *Pozzoli SPA v BDMO SA*¹³ are used. The four step approach of *Windsurfing/Pozzoli* is intended to address the concept of inventive step without the benefit of hindsight, by ensuring that the examiner assesses the invention through the eyes of the person skilled in the art, with the benefit of his common general knowledge. The inventive concept of the claim in question is then construed, and the differences between the state of the art and the inventive concept of the claim are identified. This then enables the examiner to approach the final step and ask “is it obvious”. Section 3 of the Manual discusses these steps in detail, and therefore each step of this test will not be discussed in detail here. Instead these Guidelines will review the requirement for an inventive step in the light of judgments of the UK courts and decisions of the EPO Boards of Appeal as they relate to biotechnology in particular, and by their relevance to a specific step of the *Windsurfing/Pozzoli* test.
26. In general terms whether e.g. a sequence comprises an inventive step is determined in a similar fashion to that which applies to chemical compounds, i.e. whilst identity of structure will be enough to prove lack of novelty, similarity of structure will not be enough to prove lack of inventive step unless the activity is identical in at least qualitative terms. There is another way in which a sequence may be shown to lack inventive step and that is where an earlier disclosure points to the inevitability of arriving at a particular sequence even though the actual structure of the sequence is not determined until sometime later.
27. In the case where an applicant has prepared a known protein by recombinant means it would be rare these days to allow claims to related sequences. Similarly, claims to a new orthologue of an already known gene in a further strain or species are ordinarily regarded as being obvious. However, under these circumstances, it might be possible to allow narrow (probably process) claims restricted to what the applicant had done.

12 *Windsurfing International Inc v Tabur Marine (Great Britain) Ltd* [1985] RPC 59 (Court of Appeal)

13 *Pozzoli SPA v BDMO SA* [2007] EWCA Civ 588 (Court of Appeal)

28. Claims to an antibody raised against a known protein would also lack an inventive step as immunizing an animal with an antigen and/ or preparation of a hybridoma cell line is a routine procedure. Nevertheless some methods for generating new antibodies, such as by certain antibody engineering techniques, may involve a skill that is beyond routine laboratory practice and therefore may involve an inventive step. Likewise, antibodies may be raised against a particular antigenic sequence that is demonstrated to have a particular advantage over the whole protein or other randomly selected sequences, or an antibody may display unexpected properties. Again, these antibodies may be considered to be inventive. Consequently, whilst each case would be considered on its own merits, an antibody that cannot be obtained by standard laboratory procedure may be capable of patent protection. Similarly, an antibody with unexpected properties may also be considered to be capable of patent protection. Such practice is consistent with the practice in other technological areas, such as the patenting of small organic molecules for pharmaceutical purposes.

“In the end the question is simply ‘was the invention obvious?’ This involves taking into account a number of factors, for instance the attributes and common general knowledge of the skilled man, the difference between what is claimed and the prior art and so on. Some factors are more important than others. Sometimes commercial success can demonstrate that an idea was a good one. In others ‘obvious to try’ may come into the assessment. But such a formula cannot itself necessarily provide the answer. Of particular importance is of course the nature of the invention itself”

Generics (UK) Ltd v H. Lundbeck A/S [2007] RPC 32 (at page 20) (Patents Ct)

Assessing inventive step: Person skilled in the art/ Common general knowledge

29. The skilled person should be taken to be a worker who is aware of everything in the state of the art and who has the skill to make routine developments but not to exercise inventive ingenuity. On the other hand, if the individual needed to perform scientific research rather than routine work in that area of technology then inventive step may be acknowledged¹⁴. The “person skilled in the art” may be a multi-disciplinary team rather than a single individual^{15, 16, 17}.

14 *Gist Brocades/ Cloning in Kluyveromyces* (not reported) (T 0441/93)

15 *Genentech Inc’s Patent* [1989] RPC 147 (Court of Appeal)

16 *Chiron v Organon Teknika (No. 3)* [1994] FSR 202 (Patents Court)

17 *Harvard / Fusion proteins* OJEPO 1992, 268 (T 0060/89)

“ , the skilled person in this field is well aware of the fact that even a small structural change in a product (e.g. a vector, a protein, a DNA sequence) or in a procedure (eg a purification process) can produce dramatic functional changes. Therefore, the said expert would constantly be conditioned by the prior art and, before taking action, would carefully ponder any possible modification, change or adjustment against the background of the existing knowledge. Under these circumstances, , the skilled person would adopt a conservative attitude. However, this must not be seen in the sense of being reluctant or opposed to modify or adjust a known product or process, but rather in the sense of being cautious. For example, the skilled person in question would neither go against an established prejudice nor try or enter into “sacrosanct” or unpredictable areas nor take incalculable risks. However, with the normal design procedures, the said expert would readily seek appropriate, manifest changes, modifications or adjustments which involve little trouble or work and no risk or only calculable risks, especially for the sake of obtaining a more handy or convenient product or of simplifying procedure. In particular, the skilled person working in one field (e.g. expression in yeast) would regard a means conveniently adopted in a neighbouring field (e.g. the bacterial art) as being readily usable also in that field, if this transfer of technical knowledge involves nothing out of the ordinary.

Genentech et al / Expression in yeast OJEPO 1995, 684 (T 0455/91)

30. The common general knowledge was considered in *Angiotech*¹⁸, and was deemed to be what the skilled person would know and take for granted. It also extends to that which the skilled person considers might work, and not just that which had been proven to work.

“‘Common general knowledge’ was not formulaic but was merely a term used in patent law to describe that the notional skilled person would know and take for granted. If the evidence showed that people were looking at a certain technique as a way forward, then even if it had not been proved to work, it was nonetheless part of his mental equipment, not on the basis that he knew it would work but on the basis that it might”

Angiotech Pharmaceuticals Inc v Conor Medsystems Inc [2007] RPC 20 (Court of Appeal)

Assessing inventive step: The goal is known

31. It is generally agreed, and it is particularly relevant in the field of biotechnology, that a patent should not be granted merely because the applicant had been involved in labourious and costly effort. If the goal is known and sufficient of the theory and practice is known for the applicant to predict where he is going, without there being an original step, then an obviousness objection would be well founded^{15, 19}. For example claims to a knockout animal where the knocked out gene is already known are likely to be considered to relate to an obvious goal.

18 *Angiotech Pharmaceuticals Inc v Conor Medsystems Inc* [2007] RPC 20 (Court of Appeal)

19 *DSM NV's Patent* [2001] RPC 35 (Patents Court)

32. The rejection by the Court of Appeal in 1989 of Genentech's claim to recombinant-PA⁷ is interesting because it was the first biotechnology case to be heard by the Court of Appeal but has limited value because although all three judges decided the patent was invalid, they did so for different reasons. It is however useful in casting some insight into how the courts look at the issues which arise frequently in biotechnology cases. The t-PA case also firmly established that the validity of a patent is not secured simply because the inventor thought the steps he had taken were inventive.
33. However, a subsequent Office decision²⁰ in 1994 and decisions of the EPO Boards of Appeal confirmed that a specific recombinant DNA is obvious if there is evidence to show that all the techniques needed to produce the sequence were well known.

"In the light of all the information available, it would have readily occurred to the skilled person to try to complete the work described in document (1) by identifying and characterising the primary structure of the DNA sequences encoding HbsAg and HbcAg within the said fragments of the genome of HBV subtype adyw and to express them in a recombinant DNA system such as, for example, that described in document (1) so as to produce antigenically active products. This would have involved nothing out of the ordinary for a skilled person in the field of molecular biology at that time as all the necessary methods and means (eg antisera specific for HbcAg and HbsAg) as well as techniques for the location and DNA sequence analysis were known in the art The skilled person merely needed to proceed experimentally as done by previous authors in documents (2), (3), or (6), knowing from document (1) that the expression of antigenically active products was to some extent feasible in a recombinant DNA system. In this respect, it must be kept in mind that the expression of HBV antigen in general, not the efficiency of expression is at issue here."

Biogen Inc / Hepatitis B virus [1999] EPOR 361 (T 0886/91)

34. The more there is known about various genomes and the function of the constituent genes, the more difficult it will be to establish an inventive step for any isolated gene.

"..... the existence of additional 7TM receptors was predicted in the prior art and the procedure for the identification of said additional member of 7TM receptor family has been well established. Consequently, the disclosure of the primary structure of an additional 7TM protein which is arrived at by following the well established methods disclosed in the prior art is not considered inventive"

ICOS Corporation / Seven transmembrane receptor OJEPO 2002, 293 (EP-B-0630405)

The development of bioinformatics has also changed the way invention in the context of polynucleotide and polypeptide sequences must be viewed.

35. Following the sequencing of various genomes, there is unlikely to be an inventive step in identifying from within a sequenced genome any new gene, even those without known homologues. It is obvious to trawl the genome for previously unidentified genes, and any skilled worker would have some expectation of success. In Genentech an idea was considered obvious if “the materials in question were lying in the road and ready for a research worker to use”, even if the skilled man faced a number of obstacles in proceeding to his goal. However, if overcoming these obstacles required “a spark of imagination....beyond the imagination properly attributable to him as a man skilled in the art” then there may be some element of inventive step. In Genentech/PF4A receptors²¹, the EPO Technical Board of Appeal considered that the use of a non-standard method for the isolation of receptors interacting with members of the PF4A family of cytokines was sufficient to provide an inventive step to the claims.
36. The use of bioinformatics tools would not seem to pose obstacles requiring a spark of imagination to overcome, and therefore data mining to identify a polynucleotide or a polypeptide homologous to a polynucleotide or polypeptide, having a known function or activity, will not normally involve an inventive step. Moreover, while a specified degree of homology may serve to distinguish the newly identified sequence from one or more known, homologous sequences, it cannot usually serve to establish an inventive step. It therefore follows that the identification of a human homologue of a previously characterised gene from another species is not inventive, and this is regardless of the methods used to identify the homologue^{22,23,24}. Whilst each case should be taken on its own merits, it is reasonable to presume initially that it is obvious to:-
- identify previously unknown members of a known family by homology
 - identify a gene in a database of known structural information about the corresponding protein
 - assign a function to a gene by homology comparison with gene(s) of known function
37. The identification of the function of a novel gene that has not been identified by any form of homology searching may be inventive; this will depend upon the methods used to determine the function and by what is known in the prior art. Thus, claims to uses or applications of genes, where the invention lies in the function of the gene, may be allowable, provided that the function has been demonstrated, and is inventive.

21 *Genentech/PF4A receptors* (not reported) (T 0604/04)

22 *Aeomica, Inc.* (not reported) BL O/286/05

23 *Aeomica, Inc.* (not reported) BL O/197/05

24 *Aeomica, Inc.* (not reported) BL O/170/05

38. Similarly, the identification of a new single nucleotide polymorphism(s) within a known gene may be inventive provided that a novel and non-obvious function can be assigned to it, for example a relationship between a particular polymorphism(s) and the predisposition towards a certain disease. However, any prior art disclosure of any polymorphisms within the same gene and their association with the same disease will usually render obvious the discovery of further polymorphisms. Likewise, new haplotypes of a known gene may also be inventive provided a new and non-obvious function can be assigned to them.
39. Genes that have been mutated artificially might be inventive if it is demonstrated that the mutated gene has an unexpected advantage over the naturally occurring gene. Such artificially mutated genes are considered to be a selection invention. The previous criteria for determining selection inventions were set out in *I G Farbenindustrie AG's Application*²⁵. This has been superseded by the Court of Appeal in *Dr Reddy's Laboratories (UK) Ltd v Eli Lilly & Co Ltd* [2010] RPC 8²⁶. In such cases, the question to be asked is whether the invention makes a technical contribution or is merely an arbitrary selection. If it is merely an arbitrary selection then the invention is obvious. In order for there to be a technical contribution, and thus for the selection to be inventive, the criteria derived from the EPO Board of Appeal decision in T 939/92 *AGREVO/Triazoles* 6 OJ/EPO 309 should be satisfied (see the Manual of Patent Practice, paragraphs 3.88-3.93). Therefore, the advantage of the mutated gene over the naturally occurring gene must be common to all of the mutations proposed for that particular gene. Furthermore, the advantage provided by the mutation(s) must be in respect of a specific feature of that particular gene, for example a particular sequence involved in a particular function of the corresponding protein.
40. The "selection invention" criteria can also be applied to the specific combination of probes on a microarray. For example if the exact combination of probes on a microarray meant a more accurate detection and / or a more precise diagnosis than the use of the probes individually, then the particular selection of probes may provide a surprising effect and inventive step. Moreover, this surprising effect may confer a unity of invention to the probe combination (see paragraphs 52-54 below). Again, in order for the combination of probes to be considered as a selection invention they would need to meet the requirements of *Dr Reddy's Laboratories (UK) Ltd v Eli Lilly & Co Ltd*²⁶.

25 *I G Farbenindustrie AG's Patent* 47 RPC 289 (at pages 322-323) (Patents Court)

26 *Dr Reddy's Laboratories (UK) Ltd v Eli Lilly & Co Ltd* [2010] RPC 8 (Court of Appeal)

Assessing inventive step: Fulfilling a need

41. The fact that other workers were attempting to find recombinant methods of preparing t-PA at the same time as Genentech, was another reason for the Court finding the patent invalid. However, in *Chiron v Organon Teknika*¹⁶ which related to polypeptide sequences of a hepatitis C virus, the invention was found to be inventive because the agent responsible for “non-A non-B hepatitis” had been sought by researchers for 10 years or so.

Assessing inventive step: Obvious to try

42. An invention is obvious if the skilled worker (see paragraph 29) would assess there to be a reasonable expectation of success to warrant a trial.

“..... to render an invention obvious it was not necessary that the materials in question should have been the first choice of the notional research worker; it was enough that the materials were ‘lying in the road’ and there for the research worker to use.”

Genentech Inc’s Patent [1989] RPC 147 (at page 243) (Court of Appeal)

43. On the other hand, the invention would not be obvious if the skilled worker required skills beyond common general knowledge and the amount of trial and error which could be expected of the skilled worker was excessive¹⁷. Also where there is some prejudice against following a particular course or something which negatively influences the degree of confidence of the skilled person in a successful outcome of an experiment, the invention may not be obvious^{27, 28}. In *Schering Corp*²⁹, the lack of significant homology between the IL-174 gene and other known IL-17 family members meant that a reasonable expectation of success of retrieving that gene could not be assumed when screening DNA libraries. In other words, it would not be obvious to look for the IL-174 gene, nor would routine screening techniques have been sufficient to identify the gene.

“The fact that the process as claimed appears to be simple does not necessarily mean that it is obvious. In the Board’s opinion, the prior art disclosures as analysed above would lead a person of ordinary skill to a process according to which PHA and serum, each playing apparently sensitive roles in the process of inducing IL-2, could not be applied at the same time and furthermore should not be removed from the growth media completely without the process being terminated or at least disturbed. In the light of this, the simplicity of the claimed method comprises an elegant feature which is considered by the Board to go beyond ordinary skill.”

Hooper Trading Co. N.V. / T-cell growth factor [1993] EPOR 6 (T 0877/90)

27 *Hooper Trading Co. N.V. / T-cell growth factor* [1993] EPOR 6 (T 0877/90)

28 *Mycogen Plant Science, Inc / Modifying plant cells* OJEPO 1997, 408 (T 0694/92)

29 *Schering/ IL-17 related polypeptide* (not reported) (T 1165/06)

44. In a case³⁰ where the expression of a cloned DNA in a chosen foreign host was the invention, a reasonable expectation of success was evaluated by taking account of the real difficulties related to that step. In order to be considered, any allegation of features putting reasonable expectation of success in jeopardy must be based upon technical facts.

“....., it has to be borne in mind that “the hope to succeed” should not be misconstrued as “a reasonable expectation of success” (see T 296/93, OJEPO 1995, 627). In the boards judgment, the former is the mere expression of a wish whereas the latter requires a scientific evaluation of the facts at hand. In the case of gene expression, this evaluation necessitates that the properties of the “expression partners” (the gene to be expression and its protein product on the one hand, and the recombinant host on the other) be compared.”

Biogen, Inc / Human beta-interferon OJEPO 1999, 273 (T 0207/94)

45. However, in a relatively new technical area where there is a lack of a well established general level of knowledge and so uncertainty about the likelihood of success of an attempted technique, the successful application of the technique could involve an inventive step³¹. For example, even if an earlier document speculates in the direction of a later invention, the question that arises is what basis is given in the document to contemplate the necessary modifications for the invention to work, and where such modifications would come from, according to the relevant knowledge at the time of the priority date³².

“The Board therefore concludes that, having regard to the fact that the area of genetic engineering here under consideration was relatively new at the relevant date, having further regard to the uncertainty at that date about the facts influencing the success of the attempted recombinant-DNA techniques, and to the absence of a well-established general level of knowledge in this particular technical area, the present successful technical application of recombinant-DNA techniques, according to Claims 1 and 2 under consideration, involves an inventive step.”

Biogen N.V. / Alpha interferon II [1993] EPOR 69 (T 0500/91)

Assessing inventive step: Obvious replacement

46. Biotechnology has seen technical breakthroughs that can be applied generally to existing techniques to improve them. Where the advantages of a new technology are common general knowledge, there may not be an inventive step in modifying an existing process by applying the new technology. One such breakthrough was the advent of monoclonal antibodies in 1975 and this provided an opportunity to address disadvantages associated with the previous use of monospecific polyclonal antibodies. As a consequence, it often did not require any inventive step to use monoclonal antibodies in processes that previously used monospecific polyclonal antibodies^{33, 34}.

30 *Biogen, Inc / Human-beta interferon OJEPO 1999, 273 (T 0207/94)*

31 *Biogen N.V. / Alpha interferon II [1993] EPOR 69 (T 0500/91)*

32 *Genentech 1 / Polypeptide expression OJEPO 1989, 275 (T 0292/85)*

33 *Unilever PLC / Immunoglobulins [1996] EPOR 235 (T 0499/88)*

34 *Akzo Nobel N.V. (not reported) (T 0063/94)*

47. Similarly, the generation of humanised antibodies against a known target is not likely to involve an inventive step if non-humanised antibodies against the same target are already known as such modifications are well known in the art and so it would be obvious to replace them. Likewise, characterisation of an antibody by its CDRs is unlikely to involve an inventive step if antibodies against the same target are already known. However, if the applicant can demonstrate a particularly useful property of their antibody that is not realised by those disclosed in the prior art then it may be possible to demonstrate an inventive step.
48. Obvious replacement can also involve the use of a technique which is less commonly used than another for a particular purpose¹⁹. This principle has been established in the context of a number of biotechnology cases ^{2,3,4}.

“I do not consider that, because chromatofocusing was the more normal method of purifying proteins (save if the sole purpose of obtaining a sample was for sequencing), to think of another method of purification (normally used for a slightly different purpose) represented an addition to common general knowledge, if that technique is already well known for that purpose.”

DSM NV’s Patent [2001] RPC 35 (paragraph 109) (Patents Court)

Assessing inventive step: No contribution to the art

“The definition of an invention as being a contribution to the art, i.e. solving a technical problem and not merely putting forward one, requires that it is at least made plausible by the disclosure in the application that its teaching solves indeed the problem it purports to solve.”

Johns Hopkins /Factor-9 (not reported) (T 1329/04)

49. When assessing inventive step, the EPO uses the “problem-solution” approach, whereby the problem to be solved is considered. In such cases, application has to teach the person skilled in the art how to solve a technical problem. In *Johns Hopkins*³⁵, the EPO Technical Board of Appeal found that the protein GDF-9 could not be “clearly and unambiguously identified as a member of the TGF- β superfamily by only using a structural approach” as there was no experimental data to support this assertion. This lack of experimental evidence coupled with a lack of homology between GDF-9 and other TGF- β family members meant that there was not enough evidence in the application to make it plausible that a solution was found to the problem which was supposedly solved.

35 *Johns Hopkins/ Factor-9* (not reported) (T 1329/04)

50. Whilst the “problem/ solution” approach is not used to assess inventive step in the Intellectual Property Office, recent case law has suggested that the issue of the problem to be solved should be considered in those cases where there is a lack of industrial application³⁶. In *Eli-Lilly v HGS*, in the Patents Court, Kitchin found that the application did not “teach the person skilled in the art how to solve any technical problem, and its teaching as to the range of applications of Neutrokine- α is implausible”. As this left the reader with a research programme to put the invention to use, he found that the invention itself was obvious. This clearly is a detraction from the *Windsurfer/Pozzoli* test used by the Intellectual Property Office and the UK Courts alike, but in applications in the biotech area, where there is an inherent lack of industrial application, an objection under inventive step can be made on the grounds that there is no technical contribution to be solved, in line with the judgement of Kitchin.
51. Industrial application per se will be considered in paragraphs 55-61 below.

Multi-component inventions

“...before you can apply section 3 and ask whether the invention involves an inventive step, you first have to decide whether you are dealing with one invention or two or more inventions. Two inventions do not become one invention because they are included in the same hardware. A compact motor car may contain many inventions, each operating independently of each other but all designed to contribute to the overall goal of having a compact car. This does not make the car a single invention.”

Sabaf SpA v MFI Furniture Centres Ltd [2005] RPC 10 (House of Lords)

52. As mentioned in paragraph 40 above, an inventive step might be provided by a specific combination of elements of an invention, such as a specific combination of probes on a microarray. The judgement of the House of Lords in *Sabaf*³⁷ considered the inventive step of an invention that had a number of different components. In his judgement, Lord Hoffman stated that before applying inventive step you had to first consider whether you were dealing with one or more than one invention, and referred to the EPO Examination Guidelines³⁸ and the issue of combination versus juxtaposition or aggregation when considering inventive step. The EPO Guidelines state that “... where the claim is merely an aggregation or juxtaposition of features and not a true combination, it is enough to show that the individual features are obvious to prove that the aggregation of features does not involve an inventive step. A set of technical features is regarded as a combination of features if the functional interaction between the features achieves a combined technical effect which is different from, e.g. greater than, the sum of technical effects of the individual features.” In other words, if each component of the invention interacts upon each other, so that the combination has a greater or different effect than the sum of its parts (ie there is synergy between them), then they relate to a single inventive concept having a combined effect. But, if each component forms its own function independently of any of the others then there is no inventive step in merely aggregating these features. Each component is considered to relate to a separate inventive concept, and the obviousness test is applied to each one separately.

³⁶ *Eli Lilly & Co v Human Genome Sciences Inc* [2008] EWHC 1903 (Pat) (Patents Court)

³⁷ *Sabaf SpA v MFI Furniture Centres Ltd* [2005] RPC 10 (House of Lords)

³⁸ Available at www.european-patent-office.org/legal/gui_lines/e/index.htm

53. For some inventions, the synergistic effect may not be clear cut. For example, with microarrays, some synergy will need to exist between each probe in order for them to relate to the same inventive concept, and furthermore this concept itself must be inventive in order for the microarray as a whole to be inventive. Usually each probe in a microarray acts independently and so it is unlikely that there would be any chemical synergy between the probes. However, if the foundation of the invention is in the discovery of a synergistic effect in nature, and the claimed probes can reveal this synergistic effect, then a functional synergy may exist. In such a situation the synergy is not in the probes but in what the probes detect; if there is also no synergy in what the probes detect then Sabaf can be applied. For example, if gene X and gene Y were found to have an important synergistic effect in the development of cancer, then probes for the detection of these genes would relate to a single inventive concept according to Sabaf and can therefore be assessed for inventive step as one invention.
54. Plurality of invention is considered in more detail in paragraphs 82-85 below.

Industrial application

55. The wording of section 1(1)(c) requires that an invention must be “capable of” industrial application. Section 4(1) further states that an invention is capable of industrial application if it “can be made or used in any kind of industry”. In *Chiron Corp*, the Court of Appeal observed that section 4(1) is not satisfied if the product made is useless³⁹.

“...the sections require that the invention can be made or used “in any kind of industry” so as to be “capable” or “susceptible of industrial application”.....But industry does not exist in that sense to make or use that which is useless for any known purpose.”

Chiron Corp v Murex Diagnostics Ltd [1996] RPC 535 (Court of Appeal)

It is therefore necessary to consider whether the invention claimed has a useful purpose, and whether the specification identifies any practical way of exploiting it. It is not the purpose of a patent to reserve an unexplored field of research for an applicant⁴⁰. Where the invention resides in a sequence or partial sequence of a gene, paragraph 6 of Schedule A2 to the Act additionally requires disclosure in the application as filed of the industrial application of that gene. The absence of this disclosure in an application when filed would seem to be fatal to that application. (It should be noted that this requirement for disclosure of an industrial application in the application as filed does not extend to inventions which reside in the sequence or partial sequence of proteins. Nevertheless protein sequences must still be capable of industrial application).

39 *Chiron Corp v Murex Diagnostics Ltd* [1996] RPC 535 (Court of Appeal)

40 *Max-Planck/BDP1 phosphatase* (not reported) (T 0870/04)

Assessing industrial application

56. Determining if a biotechnology invention is capable of industrial application (i.e. has a useful purpose) can be difficult because unlike inventions in many other areas of technology, the industrial application of a biotechnological invention, such as a gene or protein sequence, is very often not apparent from the invention itself. On the other hand it is well known to use short DNA sequences or ESTs (which are partially sequenced cDNA clones) as probes. Thus, the question arises what needs to be shown to establish that a biotechnological invention is capable of industrial application; a recent ruling by the UK Supreme Court has clarified the law in this area.
57. In *HGS v. Eli Lilly* [2011] UKSC 51⁴¹, the first patent case to be considered by the Supreme Court sitting as the UK's highest appellate court, the question of industrial application (Art. 57 EPC) and its application to biotechnology patents was considered in some detail. Previously, *Eli Lilly v Human Genome Sciences*^{36, 42} was the first case to be heard before the UK Courts where a gene, neutrokin- β , had been found by data mining techniques, and a function assigned to it based upon its homology to other members of the TNF ligand superfamily, but without any data obtained from *in vivo or in vitro* studies. In the Patents Court, Kitchin J applied nine principles for industrial application and rejected the patent application on the grounds that it lacked industrial applicability. In contrast, and after detailed consideration of UK case law and European jurisprudence together the submissions from the BioIndustry Association ("the BIA") relating to the policy issues surrounding Industrial Applicability in the area of biotechnology, the UK Supreme Court overturned the decision of the Patents Court (previously upheld at appeal), thus coming to the same decision of the European Board of Appeal in T 0018/09. Lord Neuberger summarized his ruling using what he referred to as 'the essence of the Board's approach in relation to the requirements of Article 57 in relation to biological material' in the following points:
- (i) The patent must disclose "a practical application" and "some profitable use" for the claimed substance, so that the ensuing monopoly "can be expected [to lead to] some ... commercial benefit" (T 0870/04, para 4, T 0898/05, paras 2 and 4);
 - (ii) A "concrete benefit", namely the invention's "use ... in industrial practice" must be "derivable directly from the description", coupled with common general knowledge (T 0898/05, para 6, T 0604/04, para 15);
 - (iii) A merely "speculative" use will not suffice, so "a vague and speculative indication of possible objectives that might or might not be achievable" will not do (T 0870/04, para 21 and T 0898/05, paras 6 and 21);
 - (iv) The patent and common general knowledge must enable the skilled person "to reproduce" or "exploit" the claimed invention without "undue burden", or having to carry out "a research programme" (T 0604/04, para 22, T 0898/05, para 6);

41 *Human Genome Sciences v. Eli Lilly* [2011] UKSC 51, [2012] RPC 6 (UK Supreme Court).

42 *Eli Lilly and Company v. Human Genome Sciences Inc* [2010] EWCA Civ 33 (Court of Appeal)

Where a patent discloses a new protein and its encoding gene:

- (v) The patent, when taken with common general knowledge, must demonstrate “a real as opposed to a purely theoretical possibility of exploitation” (T 0604/04, para 15, T 0898/05, paras 6, 22 and 31);
- (vi) Merely identifying the structure of a protein, without attributing to it a “clear role”, or “suggest[ing]” any “practical use” for it, or suggesting “a vague and speculative indication of possible objectives that might be achieved”, is not enough (T 0870/04, paras 6-7, 11, and 21; T 0898/05, paras 7, 10 and 31);
- (vii) The absence of any experimental or wet lab evidence of activity of the claimed protein is not fatal (T 0898/05, paras 21 and 31, T 1452/06, para 5);
- (viii) A “plausible” or “reasonably credible” claimed use, or an “educated guess”, can suffice (T 1329/04, paras 6 and 11, T 0640/04, para 6, T 0898/05, paras 8, 21, 27 and 31, T 1452/06, para 6, T 1165/06 para 25);
- (ix) Such plausibility can be assisted by being confirmed by “later evidence”, although later evidence on its own will not do (T 1329/04, para 12, T 0898/05, para 24, T 1452/06, para 6, T 1165/06, para 25);
- (x) The requirements of a plausible and specific possibility of exploitation can be at the biochemical, the cellular or the biological level (T 0898/05, paras 29-30);

Where the protein is said to be a family or superfamily member:

- (xi) If all known members have a “role in the proliferation, differentiation and/or activation of immune cells” or “function in controlling physiology, development and differentiation of mammalian cells”, assigning a similar role to the protein may suffice (T 1329/04, para 13, T 0898/05, para 21, T 1165/06, paras 14 and 16, and T 0870/04, para 12);
 - (xii) So “the problem to be solved” in such a case can be “isolating a further member of the [family]” (T 1329/04, para 4, T 0604/04, para 22, T 1165/06, paras 14 and 16);
 - (xiii) If the disclosure is “important to the pharmaceutical industry”, the disclosure of the sequences of the protein and its gene may suffice, even though its role has not “been clearly defined” (T 0604/04, para 18);
 - (xiv) The position may be different if there is evidence, either in the patent or elsewhere, which calls the claimed role or membership of the family into question (T 0898/05 para 24, T 1452/06, para 5);
 - (xv) The position may also be different if the known members have different activities, although they need not always be “precisely interchangeable in terms of their biological action”, and it may be acceptable if “most” of them have a common role (T 0870/04, para 12, T 0604/04, para 16, T 0898/05, para 27).
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58. The *Eli-Lilly* decision gives us guidance on how to deal with applications that apparently lack industrial application, and therefore these principles should be taken into consideration when assessing an invention for industrial application.

Proposed industrial application based upon homology

59. Patent applications where the industrial application of gene and peptide sequences has been based upon a proposed function, wherein the proposed function has been identified by homology to sequences of known function are not uncommon. In the light of *HGS v. Eli Lilly* [2011] UKSC 51, it would appear that the assessment of industrial application should be based on principles xi to xv. It would thus appear that there should be a presumption that a “nature identical” polynucleotide or polypeptide sequence, which has no assigned function, or a “nature identical” polynucleotide or polypeptide should be considered capable of industrial application when the function or application of one or more orthologues is indeed known (note however, the potential for Inventive Step objections arising). Note, however, that it remains a requirement, for polynucleotides, that the industrial application must be fully established in the application as filed.
60. The lack of any industrial application for one aspect of an invention can have implications for other aspects of that invention. For example, if the one aspect of the invention is a receptor, the absence of any industrial application for the receptor would mean that an agonist to the receptor would also not be capable of industrial application. Similarly, a method of identifying agonists to the receptor would not be industrial applicable. On the other hand, if the specification established, for example by *in vivo* or *in vitro* data, that the receptor had some relevance to e.g. the treatment of obesity, the receptor, agonists and method of identifying agonists would all be capable of industrial application.
61. Whilst a crystalline form of a protein may be novel (see paragraph 21), it must have a specific, substantial and credible industrial application. The EPO, USPTO and JPO issued their trilateral report on protein 3D structure and related claims at the end of 2002. The practice of the Intellectual Property Office in this area is largely consistent with the conclusions of this trilateral study (see Annex C).
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Methods of treatment, etc

62. It is common to find biotechnological inventions claimed in terms of methods of treatment of the human or animal body by surgery or therapy or methods of diagnosis practised on the human or animal body. However, by virtue of section 4A(1) of the Act such methods are not patentable. This is discussed further in the Examination Guidelines for Medical Inventions.

Sufficiency/support

63. Paragraphs 14.58 - 14.61 and 14.142 - 14.156 of the Manual of Patent Practice provide general guidance on sufficiency and support. As indicated there, the requirement that the disclosure should be sufficient often overlaps with the requirement that the claims be supported by the description since both are concerned with the relationship between the extent of the disclosure and the scope of the claims. Thus, if a claim is unduly broad and speculative having regard to what has been disclosed, it might be difficult to decide whether the objection should be that the disclosure is incomplete, or that the claim is not supported by the description. Objection in these circumstances before grant should, as a matter of general practice, be made on the ground of lack of support. However, there will be instances where it will be appropriate to object on the grounds of insufficiency rather than support where the description is clearly insufficient. It is important to remember this because much of the case law addressing the breadth of claims relies on sufficiency since support is not one of the grounds specified in section 72 of the Act, which can be used to revoke a patent.
64. It has been recognised⁴³ that it is inevitable in a young science that dramatically new things would be done for the first time. Those who followed, even by different routes, could have greater confidence by reason of the initial success, but this was not enough to justify a monopoly for the whole field. Care is needed not to stifle further research and healthy competition by allowing the first person who had found a way of achieving an obviously desirable goal to monopolise every other way of doing so.

Enabling disclosure

65. At least one embodiment of the invention or at least one method for performing the invention must be described so that it can be reproduced without the need for inventive ingenuity. If a skilled person following the directions given in the specification has to find out something that is new in order to reproduce the invention, the disclosure is insufficient. However, this does not mean that the disclosure of an invention is incomplete merely because a reasonable degree of difficulty was experienced in its reproduction. Similarly, it is not necessary that a specific example of a process must be exactly repeatable. For example, variations in the constitution of an agent used in a process are immaterial to the sufficiency of the disclosure provided the claimed process reliably leads to the desired product⁴⁴.

43 *Biogen Inc v Medeva plc* [1997] RPC 1 (House of Lords)

44 *Unilever / Preprothauartin* OJEPO 1989, 202 (T 0281/86)

66. Moreover, the non-availability of some unspecified variants of a functionally defined component feature of the invention is immaterial to sufficiency so long as there are suitable variants known to the skilled person as common general knowledge which provide the same effect for the invention.

“Thus it is the view of the Board that an invention is sufficiently disclosed if at least one way is clearly indicated enabling the skilled person to carry out the invention. Consequently, any non-availability of some particular variants of a functionally defined component feature of the invention is immaterial to sufficiency as long as there are suitable variants known to the skilled person through the disclosure or common general knowledge, which provide the same effect for the invention. The disclosure need not include specific instructions as to how all possible component variants within the functional definition should be obtained.”

Genentech 1 / Polypeptide OJEPO 1989, 275 (T 0292/85)

67. An insufficient application could not become sufficient because of general developments in the state of the art after the filing date. The relevant date for complying with the requirement for sufficiency is the filing date of the application and not eg the date of publication of the specification⁴³.

Scope of claims

68. The disclosure must also enable the whole width of the claimed invention to be performed.

“..... the specification must enable the invention to be performed to the full extent of the monopoly claimed. If the invention discloses a principle of general application, the claims may be in correspondingly general terms. The patentee need not show that he has proved its application in every individual instance. On the other hand, if the claims include a number of discrete methods or products, the patentee must enable the invention to be performed in respect of each of them”

Biogen Inc v Medeva plc [1997] RPC 1 (House of Lords)

In other words an application should provide enough information to allow a person skilled in the art to carry out substantially all that which falls within the ambit of what is claimed. This principle of UK patent law has also been applied by the Technical Board of Appeal of the EPO^{32, 45, 46}. The decision by the Board in *Genentech 1 / Polypeptide* expression came to be misinterpreted by some who read “at least one way” as meaning “only one way”. While there may be cases where the disclosure of only one way of putting the invention into practice may be adequate for sufficiency purposes, frequently only the disclosure of several ways will justify a broad claim⁴⁷.

45 *Exxon / Fuel oils* OJEPO 1994, 653 (T 0409/91)

46 *Unilever / Detergents* OJEPO 1995, 188 (T 0435/91)

47 *Mycogen / Modifying plant cells* OJEPO 1997, 408 (T 0694/92)

“In certain cases a description of one way of performing the claimed invention may be sufficient to support broad claims with functionally defined features, for example where the disclosure of a new technique constitutes the essence of the invention and the description of one way of carrying it out enables the skilled person to obtain without undue burden the same effect of the invention in a broad area by use of suitable variants of the component features In other cases, more technical details and more than one example may be necessary in order to support claims of broad scope, for example where the achievement of a given technical effect by known techniques in different areas of application constitutes the essence of the invention and serious doubts exist as to whether said effect can readily be obtained for the whole range of applications claimed However, in all these cases the guiding principle is always that the skilled person should, after reading the description, be able to readily perform the invention over the whole area claimed, without undue burden and without needing inventive skill”

Mycogen / Modifying plant cells OJEPO 1997, 408 (T 0694/92)

69. The House of Lords in *Generics v Lundbeck*⁴⁸ considered the issue of sufficiency for a claim defining a product per se. The appellants argued that the claims were insufficient as Lundbeck only disclosed one method of making a (+) enantiomer of citalopram (escitalopram), and therefore the claims should be limited to the compound when made by that process, even though the compound itself was novel and inventive. They also argued that if the per se claim to escitalopram was allowed then the patentee would be given a monopoly that exceeded their technical contribution to the art. In considering this, Lord Neuberger stated that *“Although it is an extra-statutory concept, I accept that, at least as a general rule, the monopoly granted to the patentee is to be assessed by reference to the ‘technical contribution’ made by the teaching of the patent”*. In this case the patentee had made the (+) enantiomer for the first time, and therefore was entitled to claim the (+) enantiomer per se.
70. In reaching the decision in *Generics v Lundbeck*, the facts of the case were compared with those of *Biogen v Medeva*⁴³. In *Biogen*, the claims were to a product that was characterised partly in how it was made and partly by what it does (ie partly a product-by process claim). The technical contribution therefore was in how the product was made, and consequently, for sufficiency purposes, the process of making the product is important and so the patentee was only entitled to claim one way of making it. However, in *Generics v Lundbeck*, the House of Lords found that the technical contribution lay in what had been invented and not how it was done, and therefore the patentee was entitled to claim any method of making it.
71. Claims of the type “Recombinant DNA coding for protein X” where the protein is known should be rejected on the ground that they merely define a problem, not the technical means for solving it, although as such a claim would inherently be obvious an objection is likely to be raised under inventive step in the first instance rather than sufficiency or support.

48 *Generics (UK) Ltd and others v H Lundbeck AS* [2009] UKHL 12

72. The fact that a claim might embrace the use of unknown or not yet envisaged possibilities, such as specific variants which might be provided or invented in the future does not necessarily mean that the claim lacks support. Unless the claims also embrace variants, which are, now or later on, equally suitable to achieve the same effect in a manner which could not have been envisaged without the invention, the protection provided by the patent would be ineffectual³². Thus, functional terminology may be used in the claims if the relevant features cannot otherwise be defined more precisely without restricting the scope of the invention and their reduction to practice was not an undue burden.
73. Analogues or variants of polynucleotides or polypeptide sequences, in the form of additions, substitutions or deletions, could extend to an almost infinite number of variants. However, the Court of Appeal (in *Kirin Amgen*) agreed with the Patents Court that this does not provide a basis for an objection that a claim seeking to protect all these variants lacks support, so long as the claim is restricted to variants sharing a common, specific activity with eg a nature identical material⁸. Whilst the House of Lords considered that the invention lay in the process of making the polypeptide and its variants rather than the polypeptide per se, it still concluded that a claim would be supported if the person skilled in the art could make variants which shared the activity of the polypeptide with without any undue burden⁷.

“In our view the judge was right to conclude that the specification disclosed a principle capable of general application. It follows that Amgen were entitled to a claim in correspondingly general terms. To obtain the grant of the patent Amgen did not need to show that they had proved its application in every individual instance. In any case the question of support for a claim was for the European Patent Office not this Court. To establish this ground of insufficiency TKT needed to prove that at least one DNA sequence of groups (a), (b) and (c) of claim 1 would not be suitable for expressing EPO. As there was no such evidence TKT have not established this ground of insufficiency.”

Kirin-Amgen Inc. and others v. Transkaryotic Therapies Inc. and others [2003] RPC3 (Court of Appeal)

74. In essence what is required is the specific disclosure of a principle of general application. Thus, for example in the case of analogues of a nature identical protein, the number of possible amino acid substitutions could lead to a virtually infinite number of analogues to be tested to identify those with the activity of the nature identical protein. However, it would be a routine exercise to the skilled person to see whether the substitutions produced a polypeptide having the activity of the protein.. This is very different from the situation⁴⁹ which arises in the field of chemical compounds, which are not proteins, and in respect of which there is no general knowledge and experience as to the types of variants which might retain the effective characteristics of the compound specifically identified by the inventor.

49 *American Home Products Corporation v Novartis Pharmaceuticals UK Ltd* [2001] RPC 8 (Court of Appeal)

75. If a claim seeks to unify analogues and variants by a specified degree of homology rather than a specific activity, lack of support and indeed lack of industrial application, will arise if the homologues cannot be shown to share the same activity. In *Millennium/ Human Delta3-Notch*⁵⁰ the EPO Technical Board of Appeal concluded that a limitation by specific activity was not necessary as the polypeptide of the claims required a close structural identity (of at least 95%), and the molecules in question displayed a low degree of identity to the closest structurally related molecules (a maximum of 54% identity). In this case, the Board reasoned that there would be no doubt that the polypeptides claimed could be used in at least one of the several biological activities contemplated in the description.
76. On the other hand where eg DNA sequences are claimed on the basis that they hybridise with a specifically identified probe and that they possess a certain activity, the claim will not be supported if the hybridisation conditions result in a large number of false drops and if the skilled worker needs to depart from the express teaching of the patent and to experiment over what may be a long passage of time to achieve the desired result¹⁹.
77. The specific binding of antibodies was considered by the Technical Board of Appeal in *Millennium/ Human Delta3-Notch*⁵⁰, where they concluded that there is no difference in the terms “specifically reactive with” and “selectively binds to”, as both meant that the antibodies in question were limited to those that only bind epitopes specific to the polypeptide of the invention. They reasoned that although it cannot be excluded with absolute certainty that epitopes that discriminate the claimed protein from structurally related proteins are present in other unrelated proteins, antibodies raised against these epitopes would not be “specifically reactive” with the protein of the invention and therefore would not be within the scope of the claims.
78. For inventions relating to the three-dimensional or crystal structure of a polypeptide, the crystal structure must be characterised in the claim, for example by the specification of the cell unit dimensions, and methods of manufacture and use of the claimed crystals must be disclosed in order for the specification to meet support and sufficiency requirements.
79. The question of support also arises when considering the claimed use of a polypeptide or polynucleotide. It is not uncommon to see a listing of a wide range of unrelated diseases as potential therapeutic or diagnostic targets of a claimed gene or the protein that it encodes. Whilst it is possible that the gene may play an important role in the treatment of one or more of the listed diseases, it is unlikely that gene or its product will have a role in all of the diseases. Such claims are generally made when the activity of the protein has not been fully characterised, and therefore any potential uses of the protein are speculative. Even if the function of the polypeptide has been characterised, and its association with one type of disease has been ascertained, this is not enough to support the use of the polypeptide in the diagnosis or treatment of numerous other unrelated diseases. Therefore, if there is no evidence in the application as filed that the gene or polypeptide is of therapeutic or diagnostic use in each different disease listed, then there is no support for the range of stated uses.

50 *Millennium/ Human Delta3-Notch* (not reported) (T2101/09)

“... the Patent Office ought to have very clearly in mind that it is undesirable to allow claims the object of which is to cover a wide and unexplored field or where there is no disclosure in the specification which is in any way coterminous with the monopoly indicated in the claims”

Genentech Inc’s Patent [1989] RPC 147 (at page 236-237) (Court of Appeal)

Reach through claims

80. Reach through claims seek to protect things which may not have been identified by the applicant at the time of filing but which may be identified in the future by carrying out the applicant’s process. Thus the claims “reach through” to things which the applicant has not yet identified. Such speculative claims differ from “product by process” claims because the product of a process requires repetition of the process to obtain more product, whereas the subject of a “reach through” claim does not. It follows that “reach through” claims may even extend to known materials which are not modified in any way by the process used to identify them. Examples of such claims are those directed towards candidate compounds that are identified by the use of screening methods. Such compounds are generally only defined by their function eg as modulators of receptor X, and no relationship between this function and the structural features of the compounds is described. In the absence of any knowledge of any relationship, either from the specification or from common general knowledge, the skilled person would not know how to produce and use the compounds. Moreover, the skilled person would not know before undertaking the labourious task of performing the screening assay if any given compound would fall within the scope of the claim. It would require an undue burden of experimentation to screen undefined compounds for the desired activity. There will also be a lack of support where the function of the compounds identified is not specified.
81. There is currently no European or UK case law relating specifically to reach through claims. However, a recent US Federal Court of Appeal case considered the validity of reach through claims⁵¹. Claims to compounds identified in a screening assay, with no disclosure of what the compounds might be were found to be invalid on the basis that they did not meet the written description requirements of a patent application, i.e. the claims were attempting to encompass subject matter that is not described within the specification. Whilst US case law has no bearing upon the application of UK patent law, the basis for objection to reach through claims by the Intellectual Property Office would be the same, i.e. the scope of the claims extends beyond what has been disclosed in the description.

51 *University of Rochester v G.D. Searle & Co., Inc* 358 F. 3d 916 (Federal circuit 2004)

Plurality of invention

82. The process of gene sequencing is so efficient that it is not uncommon for a patent application to contain, and even claim, a large number of polynucleotide and polypeptide sequences. Not only does an extensive sequence listing lead to practical problems at the printing and publication stage, but the claiming of a large number of sequences can lead to problems during the search stage. In particular, it is not always clear that a plurality of claimed sequences relate to the same invention. The problem of identifying a single inventive concept is in addition to other patentability issues, such as industrial application and inventive step that commonly arise with polynucleotide and polypeptide sequences. Claims to microarrays and combinations of probes also need to be considered for plurality, although consideration should also be given to the precise selection of probes (i.e. a “selection invention”), and to any possible synergistic effect (See paragraphs 40 and 52-54 above).
 83. The problem of plurality also arises in an application where a number of single nucleotide polymorphisms are claimed within a single gene. If the gene itself was previously unknown then there will be unity of invention when claiming a number of SNPs, regardless of their function within the gene. Similarly, if the polymorphisms are associated with a single disease within a known gene then they will relate to the same inventive concept (although any prior art disclosure of the association of this gene with the same disease may render the invention obvious- see paragraph 38). There may also be unity of invention if the polymorphisms are associated with a number of related diseases, such as a number of different neurological disorders. However, if the polymorphisms are related to several distinct diseases, such as a neurological disorder and a cardiovascular disorder, then each group of polymorphisms related to each distinct disease will relate to a separate inventive concept. This is in line with Trilateral report WM4 on SNPs and Haplotypes (see Annex D).
 84. Where a number of sequences are claimed and no unifying inventive concept can be identified, then each sequence should be regarded as relating to separate inventions and just the first sequence searched.
 85. Where a claim to a number of sequences has met the synergy and / or the surprising effect requirement (see paragraphs 40 and 52-54), then this use can form the basis of a search. As probes are generally based upon a known gene sequence, a keyword search for the gene and the utility of the invention will suffice for inventive step purposes. However, for novelty purposes the probe sequences *per se* will need to be searched. It is not practical to search a large number of sequences, and therefore the examiner will need to use his or her judgement in determining what sequences should be searched. This should be determined on a case by case basis, and the applicant should be informed of the restricted scope of the search. There may be instances when the examiner may consider that it is useful to contact the agent before the search in order to ensure that the sequences of most importance are searched.
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Publication of sequence listings

86. It is not uncommon for biotechnology patent applications to contain sequence listings that run into hundreds if not thousands of pages in length. Sequence listings should only be included in the published specification where they are short enough to be reasonably accommodated. However, the omitted sequence listing remains part of the published specification and becomes open to public inspection on the publication date. A notice referring to the omission should be included on the front page (see Manual of Patent Practice, paragraphs 16.27-16.28).

Patents for plants

87. As confirmed by the Biotech Directive plant and animal varieties are not patentable. Plant varieties are currently protected under the Plant Varieties Act 1997. Both the 1997 Act and a separate European Community regime (Council Regulation (EC) No. 2100/94) are based on the 1991 UPOV Convention. In the UK the system for granting plant variety rights is administered by the Plant Variety Rights Office (PVRO) at Cambridge. This system differs substantially from the patent system and to gain protection a variety must be tested for distinctness from other varieties, uniformity and stability.
88. Plant variety rights are confined to individual varieties. Patents may claim plant genera or species but they cannot claim individual varieties.

“Inventions which concern plants or animals may be patentable if the technical feasibility of the invention is not confined to a particular plant or animal variety.”

Paragraph 4, Schedule A2 to the Patents Act 1977

89. In the early days of granting plant patents neither the EPO nor the Intellectual Property Office had a problem with granting claims to plants in general even though it could be argued that such claims could be regarded as covering, in reality, a number of plant varieties. The EPO's Enlarged Board of Appeal was eventually called on to consider this issue⁵². The Enlarged Board found:
- (i) A claim wherein specific plant varieties are not individually claimed is not excluded from patentability under Article 53(b) EPC even though it may embrace plant varieties;
 - (ii) When a claim to a process for the production of a plant variety is examined, Article 64(2) EPC is not to be taken into consideration;

52 *Novartis/ Transgenic plant* OJEPO 2000, 111 (G 0001/98)

- (iii) The exception to patentability applies to plant varieties irrespective of the way in which they were produced. Therefore, plant varieties containing genes introduced into an ancestral plant by recombinant gene technology are excluded from patentability
90. Thus, claims to transgenic plants are perfectly acceptable, unless expressed in plant variety terms or the invention is confined to modifying a particular plant variety. It may be, therefore, that if all the examples in an application are directed towards modifying a single variety, there could be a presumption that the invention is specifically for a plant variety.

Patents for animals

91. Schedule A2 to the Patents Act 1977 excludes the patenting of animal varieties but not of animals in general and therefore the same reasoning is applied to patents for animals as is applied to patents for plants.
92. There is no separate system for the protection of animal varieties so there is no established view on what constitutes an animal variety. It has been held⁵³ that animal varieties rank below species and so claims to non-human mammals are not excluded.
93. Claims in animal patent applications are often extremely broad and it is sometimes questionable whether a description based on, for example, transgenic mice is sufficient to support a claim to non-human mammals in general.
94. Patents on human beings are not allowable as confirmed by Paragraph 3 (a) of Schedule A2 to the Patents Act 1977.

53 *Harvard /Onco-mouse* OJEPO 1990, 476 & OJEPO 1992, 588 (T 0019/90)

Essentially biological processes

95. Essentially biological processes for the production of plants and animals, which are not micro-biological or other technical processes are excluded from patentability by virtue of Paragraph 3(f) of Schedule A2 to the Patents Act 1977.
96. Whether or not a (non-microbiological) process is to be considered as “essentially biological” has to be judged on the basis of the essence of the invention taking into account the totality of human intervention and its impact on the result achieved. However, the necessity for human intervention alone is not a sufficient criterion for an invention not being “essentially biological”. Human intervention may only mean that the process is not a purely biological process, without contributing anything beyond the trivial level. Moreover, it is simply not a matter of whether such intervention is of a quantitative or qualitative character. In one decided case⁵⁴ the claimed process was not considered to be “essentially biological” because it involved multiplying parent plants by cloning before repeated crossing of the cloned parent lines on a large scale to provide the desired resulting hybrid population.
97. Recently the Enlarged Board of Appeal of the EPO has issued two decisions^{55, 56} concerning whether claims relating to plant breeding were excluded under Art. 53(b) EPC 2000 (corresponding to Paragraph 3(f) of Schedule A2 to the Patents Act). The EBoA considered the definition of an “essentially biological process” as per Rule 26(5) EPC, which corresponds to paragraph 11 of Schedule A2.
98. The EBoA found that claims to any non-microbiological processes for the sexual crossing of the whole genomes of plants are to be considered as being excluded as being “essentially biological” Furthermore, claims to a breeding process do not escape the exclusion merely by the addition of a further step of a technical nature which serves to enable or assist the performance of the steps of sexually crossing or subsequently selecting the offspring. This is because such steps do not move the process beyond what is considered to be an “essentially biological process”. Therefore, in order to be patentable at least one additional technical step must be performed within the steps of sexually crossing and selection, which, for instance *‘by itself introduces a trait into the genome or modifies a trait in the genome of the plant produced, so that the introduction or modification of that trait is not the result of the mixing of the genes of the plants chosen for sexual crossing’*, although each case will be assessed on its own merits.

54 *Lubrizol / Hybrid plants* OJEPO 1990, 71 (T 0320/87)

55 *State of Israel/Tomatoes* [2008] EPOR 26 (G 1/08)

56 *State of Israel/Broccoli* [2011] EPOR 27 (G 2/07)

Exclusions under section 1(2) of the Act

99. Patent applications in the Biotechnology area can comprise subject matter that is excluded under section 1(2) of the Act, such as computer programs, mathematical methods, and methods for performing a mental act. In order to determine whether an application relates to excluded matter, the *Aerotel/Macrossan* test is now used⁵⁷. This is a four-step test comprising:

- I. Properly construe the claim
- II. Identify the actual contribution
- III. Ask whether it falls solely within excluded subject matter
- IV. Check whether the actual or alleged contribution is actually technical in nature

100. An example of an invention that could be assessed using this test is a program for protein alignment. The contribution of such an invention would lie in the alignment algorithm, and as this is merely a mathematical method it is excluded from patentability by section 1(2)(a) of the Act.

101. Mr Justice Warren found, in *Population Diagnostics*⁵⁸, that if there was no inventive step then there was no technical contribution. Therefore, if the only technical (i.e. non-excluded) contribution was obvious then this was not enough to take the invention outside of section 1(2).

“A novel or non-obvious contribution in a non-excluded field is a technical contribution so that the invention will not fall within excluded matter under the technical effect approach. Again, that flows through to the Aerotel test at stage 3 with a check at stage 4. But what is the position where the actual contribution has two elements, one which falls within excluded matter and one which, although not falling within excluded matter, is obvious? Is the obvious contribution which is not within excluded matter a technical contribution for the purposes of the “technical effect approach” and, applying the Aerotel test, does the obvious contribution take the case out of section 1(2)? In my judgment, the obvious contribution is not a technical contribution: a contribution which does not fall within an excluded field will only be a “technical contribution” if it is either novel or non-obvious. Further, the obvious contribution does not take the case out of section 1(2)”

Population Diagnostics Inc v Comptroller General of Patents [2012] EWHC 3541 (Ch) (at Paragraph 124) (Patents Court)

57 *Aerotel Ltd v Telco Holdings Ltd (and others) and Macrossan’s Application* [2006] EWCA Civ 1371

58 *Population Diagnostics Inc v Comptroller General of Patents* [2012] EWHC 3541 (Ch) (Patents Court)

Discoveries

“An instance of a ‘soft exclusion’ is a discovery. It is well-settled law that, although you cannot patent a discovery, you can patent a useful artefact or process that you were able to devise once you had made your discovery. This is so even where it was perfectly obvious how to devise the artefact or process, once you had made the discovery.”

CFPH LLC’s Applications [2006] RPC 5 (at Paragraph 34) (Patents Court)

102. There is a difference between the patentability of discoveries and the other exclusions of section 1(2), which is of importance as a number of inventions in the area of biotechnology are based upon discoveries, with the discovery itself being the new and inventive feature and the technical aspects of the invention being based upon routine applications. The Court of Appeal in *Genentech* established that the practical application of a discovery does not relate to a discovery as such even if the practical application might be obvious once the discovery had been made¹⁵. Consequently, the discovery itself can form part of the assessment for novelty and inventive step.
103. Paragraph 2 of Schedule A2 to the Patents Act 1977 permits biological material which is isolated from its natural environment or produced by means of a technical process to be the subject of an invention even if it previously occurred in nature. Paragraph 5 of Schedule A2 similarly states that an element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may also constitute a patentable invention, even if the structure of that element is identical to that of a natural element.
104. However, in line with section 1(2)(a) of the Patents Act and Paragraph 3(a) of Schedule A2, the simple discovery of biological material, eg a human gene, is not patentable. This is the situation that applies when a gene sequence is known simply as a sequence, possibly as part of the genome or in an isolated state. In that sense it is a discovery; nothing more is known about it other than that it exists as a piece of information.

3D structure of proteins and computer models

105. It is becoming increasingly possible to elucidate the 3D structure of chemical compounds, such as proteins, mainly through the use of computer programs. As a result of this claims to the 3D structure of proteins are becoming increasingly common. However, claims to the 3D structure of a known protein are not patentable, not the least because such structures are merely representations of the atomic coordinates of a peptide in space, do not have any technical character, and do not solve any technical problem. Computer models of the 3D structure of proteins would seem to amount to no more than a discovery, and as such are excluded by virtue of section 1(2)(a). A claim to a computer-readable storage medium encoded with the atomic coordinates of a protein is not patentable, as it amounts to no more than the presentation of information, and is excluded by virtue of section 1(2)(d). Nevertheless, each application should be considered on its own merits and the *Aerotel/Macrossan* test applied (see paragraph 94).

Morality

106. Paragraph 3(b) - 3(e) of Schedule A2 to the Patents Act 1977 identifies types of inventions whose commercial exploitation would be contrary to public policy or morality and should not be granted a patent. These types of invention are listed in the Biotech Directive and are those specific inventions which amongst other things were considered important enough at the time the Directive was adopted to be morally unacceptable for the grant of a patent. With the passage of time there may be other inventions, which although presently not in the list, may be regarded as similarly unacceptable and hence open to objection. Section 1(3) of the Act also prevents the patenting of an invention that would be expected to encourage offensive, immoral or antisocial behaviour.
107. According to Schedule A2, the following inventions are currently not patentable on moral grounds -
- (a) processes for cloning human beings;
 - (b) processes for modifying the germ line genetic identity of human beings;
 - (c) uses of human embryos for industrial or commercial purposes; and
 - (d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.
108. The term 'embryo' should not be restricted to a live human embryo produced by the fertilisation of a female egg, but should be interpreted to include an embryo produced without such fertilisation, such as one created by cell nuclear replacement⁵⁹. In addition, all references to a human being should be interpreted as referring to the human being from the embryonic state⁶⁰.
109. When considering the patenting of transgenic mice that were engineered to develop tumours, the EPO Technical Board of Appeal concluded that it was merely a likelihood of animal suffering that was sufficient to invoke the provisions highlighted in (d) above⁶¹. Therefore, a substantial medical benefit had to be demonstrated if there was any possibility of animal suffering. Furthermore, this substantial medical benefit had to be demonstrated for all of the animals claimed. Consequently, a claim relating to transgenic rodents was rejected under Rule 23d(d) EPC (ie paragraph 3(e) of Schedule A2 to the Patents Act), as the patentee had not demonstrated that a substantial medical benefit could be gained from the use of any rodent. The subsequent limitation of the claims to transgenic mice was allowed.

59 R (Quintavalle) v Sec of State for Health [2003] UKHL 13, [2003] 2 All ER 113, [2003] 1 FCR 577

60 Official Journal C 110, 08/04/1998 p0017 (at para 35)

61 Harvard/ Oncomouse OJEPO 2005, 229 (T 0315/03)

Human embryonic stem cells

110. Paragraph 3(d) of Schedule A2 states that uses of human embryos for industrial or commercial purposes are not patentable inventions. On this basis, an objection should be raised against any process for obtaining stem cells from human embryos. Claims to methods and processes where stem cells are obtained from an embryo yet the embryo remains intact are also excluded as even though the embryos are not destroyed, it is still considered to be used for an industrial or commercial purpose.
111. Human totipotent cells have the potential to develop into the entire human body. In view of this potential, such cells are not patentable because the human body at various stages of its formation and development is excluded from patentability by Paragraph 3(a) of Schedule A2. Similarly, a method of culturing or propagating human totipotent cells are also excluded from patentability as a claim to a method also provides protection for the product of such a method.
112. Following the recent decision of the Court of Justice of the European Union (CJEU) in the case *Oliver Brüstle v Greenpeace eV C-34/10*⁶² (“Brüstle”), the Office issued a Practice Notice on 17 May 2012 on the patentability of inventions involving human embryonic stem cells. This Practice Notice partially supersedes the Practice Notice of February 2009 which followed the EPO Enlarged Board of Appeal Judgment in the “WARF” case (G 02/06 WARF/Use of embryos [2009] 5 OJEP 306^{63,64}). The May 2012 Practice Notice sets out that the Office will now recognise that where the implementation of an invention requires the use of cells that originate from a process which requires the destruction of a human embryo, the invention is not patentable, even if the claims of the patent do not refer to the use of human embryos and irrespective of when the destruction necessarily took place. This replaces part (iii) of the 2009 Practice Notice which set out that inventions involving embryonic stem cells would not be patentable if at the filing or priority date the invention could only be obtained by the destruction of human embryos. In *Brüstle* the CJEU also ruled that the term “human embryo” **in the Biotech Directive** must be interpreted broadly to include any organism that is “capable of commencing the process of development of a human being”. This includes any non-fertilised human ovum into which a cell nucleus from a mature human cell has been transplanted, and an ovum whose division has been stimulated by parthenogenesis. A recent IPO decision⁶⁵ applied this restriction in *International Stem Cell Corporation*, which was subsequently appealed to the Patents Court. Uncertain of the limitations imposed by the wording of the CJEU in *Brüstle*, Henry Carr QC, sitting as deputy judge, referred the case to the CJEU to ask whether parthenotes that contain only pluripotent cells and are not capable of developing into human being, are included in the term “human embryos”

62 *Oliver Brüstle v Greenpeace eV C-34/10*

63 *WARF/ Use of embryos* [2009] EPOR 15 (G 0002/06)

64 The UK submitted an *amicus curiae* brief before the EPO Enlarged Board of Appeal on WARF, following invitation for submissions from third parties on how the questions should be answered. The UK’s *amicus curiae* brief argued that the EPO should not refuse to grant patents on moral grounds where there is no consensus among its contracting states on the morality of stem cell research and patenting. This would deny patent protection in those member states where such technology is morally acceptable and allowable (See Annex G).

65 *International Stem Cell Corporation* BL O/316/12

in Article 6(2)(c) of the Biotech Directive^{66,67}. The IPO will therefore await the outcome of this referral before examining any further applications relating to cell lines derived from human parthenotes.

113. The EPO revoked patent EP1040185 held by Oliver Brüstle on the grounds that amendments filed in order to overcome the exclusion of commercial and industrial uses of human embryos added matter. During opposition proceedings, the disclaimer *“with the proviso that the method does not include the destruction of human embryos”* was inserted into the independent claims. The opposition division took account of the decision of the Enlarged Board of Appeal in G 1/03⁶⁸, which stated that a disclaimer may be allowable to disclaim subject matter which is excluded from patentability for non-technical reasons. However, in reaching its decision in G1/03, the Enlarged Board reasoned that a disclaimer which becomes relevant for the assessment of inventive step or sufficiency of disclosure adds subject matter. The opposition division also referred to the decision of the Enlarged Board in G 2/10⁶⁹, which makes it clear that the restriction using a disclaimer is only allowable if the subject matter remaining in the claim was originally disclosed in the application or could be directly and unambiguously derived from the application as filed.
114. Brüstle’s EP patent as filed did not disclose any methods for obtaining hESCs other than by destroying human embryos. Moreover, such methods were not known at the time of filing. Whilst the patentee argued that such methods for deriving embryonic germ cells were known, and that these cells were synonymous with hESCs, the opposition division disagreed and considered that a skilled person would not understand the term “embryonic stem cells” to encompass other types of pluripotent stem cells such as embryonic germ cells or induced pluripotent stem (iPS) cells. Therefore, the subject matter remaining in the claims after the disclaimer could not be carried out according to the state of the art at the time of filing. Consequently, as there was no means to obtain cells without destroying a human embryo, the patent was found to be insufficient.
115. Furthermore, the scope of the patent encompassed hESCs that could not be produced at the date of filing, and the subject matter remaining in the claims after the introduction of the disclaimer was not disclosed to the skilled person in the application as filed. As a result, the disclaimer was considered to add matter.
116. Whilst disclaimers are allowable in the UK in order to disclaim subject matter that is excluded, when considering such a disclaimer the same approach should be followed as was taken by the opposition division in Brüstle’s patent for inventions relating to hESCs. It therefore needs to be evident that methods of obtaining hESCs without the destruction of an embryo were available at the filing date of the application in question. Furthermore, if the cell lines exemplified in the method of the invention were not derived by non-destructive uses of an embryo, it must be clear that they can be substituted with hESCs obtained without the destruction of a human embryo. For example, if an invention relies upon a specific property of a cell line then it is unlikely that it could be substituted with an alternative line. Therefore, each case will be considered on its own merits and the evidence provided.

66 *International Stem Cell Corporation v Comptroller General of Patents* [2013] EWHC 807 (Ch)

67 <http://curia.europa.eu/juris/liste.jsf?language=en&jur=C,T,F&num=c-364/13&td=ALL>

68 PPG/ Disclaimer OJEPO 2004, 413 (G 1/03)

69 Scripps/ Disclaimer OJEPO 2012, 376 (G 2/10)

117. The CJEU judgment also confirmed that inventions that are for therapeutic or diagnostic purposes that are applied to and useful to the human embryo are not excluded from patentability. The Office will continue to grant patents for such inventions provided they meet the other legal requirements.
118. Induced pluripotent cells, which are obtained from the de-differentiation of an adult cell by the forced expression of certain genes are clearly not obtained from human embryos and cannot go on to form a human being. Therefore these cells are not subject the exclusions of Paragraph 3(a) or Paragraph 3(d) of Schedule A2.
119. The Intellectual Property Office's position on the patentability of human embryonic stem cells was addressed in the Practice Notices issued in February 2009 and May 2012 (See Annex F).

Deposit of Biological material

120. The Patents (Amendment) Rules 2001 relate to the deposit, access and re-deposit of biological material. Where in the past the Patents Act 1977 and Rules have focussed on “micro-organisms”, the Biotech Directive uses the term “biological material”. As a consequence the Act now refers to “biological material” which is defined in Section 130 as “any material containing genetic information and capable of reproducing itself or being reproduced in a biological system”.
121. The disclosure requirements for patent protection are satisfied if, in the case where biological material is not available to the public at the date of filing, a sample of the material is deposited in a culture collection on or before the date of filing, the application as filed gives such information on the characteristics of the biological material as is available to the applicant and the specification gives the name of the culture collection and the accession number of the deposit. The information about the two latter requirements may be added to the application within a period of 16 months from the earliest date. Giving the necessary information in the specification signifies consent to the availability of the biological material to the public, unless a request is made that the material should only be made available to an expert. It should be noted that where a priority date for the subject matter, made sufficient by the deposition of biological material, is relied upon, it is necessary that the material must have been deposited on or before that priority date⁷⁰.
122. The rules for deposit of microorganisms can vary between jurisdictions, for example it is not a requirement to have made a deposit at the date of filing of a US patent application. However, the EPO Technical Board of Appeal confirmed that an application cannot claim priority from an earlier application if that invention relies upon a deposit for sufficiency purposes, and that deposit had not been made at the date of filing of that earlier application. This is the case even if a deposit in relation to the filing of the earlier application is not necessary in its country of filing⁷¹.

70 *Cellartis AB* (unreported) BL O/050/11

71 *BMS/ CD40 counter receptor* T 0107/09 (not reported)

123. Section 14(3) of the Act lays down the requirement that the description in an application should be sufficient for the invention to be performed by the person skilled in the art. The deposit system might be only one way in which the requirement may be met when biological material is used or made in any invention and it is up to the applicant to determine whether a deposit is necessary or not. Likewise the choice of a suitable depositary institution is up to the applicant. The depositary institution does not have to be one recognised under the Budapest Treaty but may be unacceptable if it is not clearly independent of the applicant and/or does not seem capable of furnishing samples of the biological material when a valid request under the Comptroller's certificate is made.
124. In cases where the biological material used in a process is well known and the process proceeds in a repeatable manner by steps which are adequately described by written description, then there is probably no need for a deposit to be made. Even if the final product is a new biological material, as long as it can be prepared by following the written description without undue burden being placed on a third party, the making of a deposit is not necessary.

Claims to micro-organisms

125. Claims to micro-organisms *per se* have been allowed on the grounds that they are products of microbiological processes. This applies even when they are merely isolated from their natural surroundings, their isolation, culture, characterisation and the finding of a utility turning what would be a discovery into an invention.
126. *Per se* claims for micro-organisms which have been isolated or obtained by artificially induced random mutation, are allowed but generalisations from such specific micro-organisms to a novel species would not normally be permitted. On the other hand, claims to genetically modified micro-organisms derived from readily available known micro-organisms where the invention resides in the gene introduced, may be claimed more generally. Also claims to mutants and variants of a specified deposited micro-organism are allowed provided they possess the same inventive property as the deposited micro-organism⁷². Thus, claims of the type "micro-organism Y and X-producing mutants and variants thereof" would be allowed where the inventive feature of Y is the production of X. A mutant of Y would be regarded as limited to one derived from Y by a single mutation i.e. a direct mutant. The term "variant" although usually allowed is less clearly defined and consideration is always given as to how it should be qualified so that the claim does not end up being totally open-ended.
127. The width of a claim using a micro-organism to produce an end product e.g. an antibiotic depends on where the invention lies. When the invention is in the discovery of a new end product a wide process claim of the type "A process for the manufacture of antibiotic X by culturing an X-producing strain of *Streptococcus pilosus* in a nutrient medium" would be allowed but even here regard is had to whether the description demonstrates that more than one strain had been used. If however the invention resides in the discovery that a known end product can be made using a different micro-organism

72 *Chinoi's Application* [1986] RPC 39 (Patents Court)

not previously known to make it, then the process claim must be limited to the use of the actual micro-organism discovered.

Intellectual Property Office

November 2013

ANNEX A

CLAIM CONSTRUCTION AND GENERAL CONSIDERATIONS

It is important that claims are interpreted properly and consistently. The following examples of some common forms of claim along with the accompanying explanations should assist with this.

Example 1

- (a) “An **isolated** polynucleotide
- (b) “A **purified** polynucleotide
- (c) “cDNA

Claims of this form are often drafted to protect natural polynucleotides or their equivalents. However, the words “isolated” and “purified” used in (a) and (b) distinguish the claimed polynucleotide from the polynucleotide as it exists in nature, ie unisolated or unpurified. cDNA is by its very nature distinguished from the corresponding DNA found in nature.

Example 2

- (a) “An isolated polynucleotide **of** SEQ ID No. 1”
- (b) “An isolated polynucleotide consisting of SEQ ID No.1”

Claims of this form are for the isolated polynucleotide exactly as listed in SEQ ID No.1. These polynucleotides would be distinguished from a polynucleotide having missing or additional nucleotides when compared to the one listed.

Example 3

- (a) “An isolated polynucleotide **including** a polynucleotide of SEQ ID No.1”

A claim of this form protects the polynucleotide as listed in SEQ ID No. 1 when it is combined with additional nucleotides at the head and/or tail of the listed sequence. The claim would not protect a polynucleotide having additions and/or deletions within the body of the listed sequence.

Example 4

- (a) “An isolated polynucleotide **comprising** SEQ ID No. 1”

This claim protects not only the polynucleotide exactly as listed in SEQ ID No. 1 but also the listed polynucleotide with additional nucleotides at its head and/or its tail. Thus this claim would provide the protection offered by the claims of both Examples 2 and 3.

Example 5

- (a) “An isolated polynucleotide having a sequence **homologous** to SEQ ID No. 1, or a **portion / fragment** thereof”
- (b) “An isolated polynucleotide which **hybridises to** SEQ ID No.1, or a **portion / fragment** thereof”
- (c) “A protein / polypeptide having the sequence SEQ ID No. 1 or a variant, homologue, or portion / fragment thereof”

Terms such as “homologous”, “portion”, “fragment”, “hybridizes”, “variant”@, and “homologue” should be considered with care.

- A **homologous** sequence, whether a nucleic acid sequence or an amino acid sequence, should be limited to one having the same properties as the parent sequence (although these may be more difficult to define in respect of nucleic acid sequences);
 - A **portion / fragment** of a sequence may obviously be something very small and simple and, apart from anything else, may be readily anticipated;
 - **Hybridisation** sequences cause certain problems because of the degree of homology required. Many applications define a minimum of agreement, for example 60%, with higher homology being “preferred” (70%), “most preferred” (80%), “particularly preferred” (90%) and “especially preferred” (95%). There is no general rule for determination of the required agreement, which depends on context, most significantly the stringency conditions. As an example, a low homology sequence may “pick out” a newly sequenced DNA/RNA, whereas to separate sequences encoding isoenzymes (which have closely related structures), homology of over 95% may be required. Thus the scope of the claim needs to be considered in the context of the specification as a
-

whole. Claims should be limited by reference to the activity of the reference sequence where there is doubt about the identity of a homologue in relation to the reference sequence

With mutants and variants the claims should be limited to those having at least one specified biological property of the parent protein polypeptide.

Example 6

- a) "An isolated polynucleotide having the sequence of one of SEQ ID No 1, 3, 5, 7, 9, 11, 13, 15, 17...."
- b) "An isolated polypeptide having the sequence of one of SEQ ID No 2, 4, 6, 8, 10, 12, 14, 16, 18...."
- c) "An isolated polynucleotide encoding the polypeptide of one of SEQ ID No 2, 4, 6, 8, 10, 12, 14, 16, 18...."

These claims seek to protect a number of polynucleotide and polypeptide sequences. In many cases it is not clear whether these sequences share a common inventive concept, and therefore we have adopted the practice of writing to the applicants inviting them to identify this concept before commencing a search. For example, if the applicant can identify a common activity then it is this activity that will form the basis of the search. If no common inventive concept exists, then we consider that each polynucleotide sequence (and corresponding polypeptide sequence) relate to a separate inventive concept.

Example 7

- a) "A polypeptide/ compound which is the product of the method according to claim X"
- (b) "A polypeptide/ compound (when) obtained by the method of claim X"
- (c) "A polypeptide/ compound (when) produced by the method of claim X"
- (d) "A polypeptide/compound obtainable by the method of claim X"

These are a "product by process" claims which seek to protect eg the polypeptide product of a specific method. However, these claims are interpreted as claims to the product (e.g. the polypeptide or compound) *per se* and therefore any prior disclosure of the polypeptide or compound would anticipate the claim. In addition, these claims are not allowed if another means (such as chemical or physical means) of defining the product is available. Therefore such claims when relating to e.g. polypeptide products are unlikely to be acceptable as polypeptides can generally be defined in terms of their sequence/ Mw/ pI/ biological function etc. However, these claims when relating to a novel and inventive compound require further consideration as they may be allowable in the absence of any other way to distinguish the novel compound from similar compounds in the prior art.

Example 8

- (a) “An isolated polypeptide identified by the method of claim X”
- (b) “A polypeptide identifiable by the method of claim X”
- (c) “A polynucleotide obtained by the screening method of claim X”

This form of claim seeks to protect any polypeptide / polynucleotide which has been identified using a claimed method. Such claims are commonly called reach through claims and generally lack support. They should not be confused with product by process claims where something is produced and not simply identified from amongst pre-existing material.

- (d) A method comprising
 - (i) contacting polypeptide X with a compound to be screened and determining whether the compound affects the activity of the polypeptide
 - (ii) formulating any active compound into a pharmaceutical composition
- (e) A process for the production of a pharmaceutical composition comprising the process of claim X and further formulating the active compound identified in the last step of said method into a pharmaceutically acceptable formulation

These are also examples of reach through claims, but are worded such that they can be easily confused with product by process claims. It is important to remember that any method that merely screens existing materials does not give rise to products and therefore claims resulting from such methods ‘reach through’ to as yet unidentified materials.

Example 9

- (a) “An antibody specific for the polypeptide of claim 2”

This claim seeks to protect an antibody to the identified polypeptide but no others. If the specification identifies the antibody, its specificity should be accepted unless there is evidence that this antibody acts against another, different polypeptide.

Example 10

- (a) “A computer model of protein X”
 - (b) “An isolated protein having a tertiary structure as defined by....”
 - (c) “A crystalline form of protein X....”
-

The above claims are becoming more common as the tertiary structures of proteins are being elucidated, and seek to protect proteins based upon their tertiary structure. A computer model of a protein, as in (a), is not considered to be a patentable invention as it is merely a representation of the atomic coordinates of the protein in space, and has no technical effect in itself. As such, it merely relates to a method of presentation of information, and is excluded from patentability by section 1(2)(d). The definition of a protein by its tertiary structure, as in (b) is a patentable invention, however any prior disclosure of the same peptide isolated from the same source having the same molecular weight may destroy the novelty of such a claim as the isolated protein would inherently possess the same tertiary structure. A crystalline form of a protein, as in (c), is patentable and would be considered to be novel if the protein is known but not in its crystalline form.

ANNEX B

RELEVANT UK CASE LAW

Aeomica, Inc. (not reported) BL O/170/05

Aeomica, Inc. (not reported) BL O/197/05

Aeomica, Inc. (not reported) BL O/286/05

Aerotel Ltd v Telco Holdings Ltd (and others) and Macrossan's Application [2006] EWCA Civ 1371

American Home Products Corporation v Novartis Pharmaceuticals UK Ltd [2001] RPC 159 (CoA)

Angiotech Pharmaceuticals Inc v Conor Medsystems Inc [2007] RPC 20 (CoA)

Asahi's Application [1991] RPC 485 (HoL)

Biogen Inc v Medeva plc [1997] RPC 1 (HoL)

Cellartis AB (unreported) BL O/050/11

Chiron Corp v Murex Diagnostics Ltd [1996] RPC 535 (CoA)

Chiron v Organon Teknika (No. 3) [1994] FSR 202 (PatCt)

Dr Reddy's Laboratories (UK) Ltd v Eli Lilly & Co Ltd [2010] RPC 8 (Court of Appeal)

DSM NV's Patent [2001] RPC 35 (PatCt)

Eli Lilly & Co v Human Genome Sciences Inc [2008] EWHC 1903 (Pat) (PatCt)

Eli Lilly and Company v. Human Genome Sciences Inc, [2010] EWCA Civ 33 (Court of Appeal)

Evans Medical Ltd's Patent [1998] RPC 517 (PatCt)

Genentech Inc's Patent [1989] RPC 147 (CoA)

Genentech's (Human Growth Hormone) Patent [1989] RPC 613 (PatCt)

Generics (UK) Ltd and others v H Lundbeck AS [2009] UKHL 12

Human Genome Sciences v. Eli Lilly [2011] UKSC 51, [2012] RPC 6.

I G Farbenindustrie AG's Patent 47 RPC 289 (at pages 322-323) (PatCt)

International Stem Cell Corporation BL O/316/12

International Stem Cell Corporation v Comptroller General of Patents [2013] EWHC 807 (Ch)

Kirin-Amgen Inc. and others v Hoechst Marion Roussel Ltd and others [2005] RPC 9 (HoL)

Kirin-Amgen Inc. and others v. Transkaryotic Therapies Inc and others [2003] RPC 3 (CoA)

Population Diagnostics Inc v Comptroller General of Patents [2012] EWHC 3541 (Ch) (Patents Court)

Pozzoli SPA v BDMO SA [2007] EWCA Civ 588 (CoA)

R (Quintavalle) v Sec of State for Health [2003] UKHL 13, [2003] 2 All ER 113, [2003] 1 FCR 577 *Chinoin's Application* [1986] RPC 39 (PatCt)

Sabaf SpA v MFI Furniture Centres Ltd [2005] RPC 10 (HoL)

SmithKline Beecham Plc's (Paroxetine methanesulfonate) Patent [2006] RPC 10 (HoL)

Windsurfing International Inc v Tabur Marine (Great Britain) Ltd [1985] RPC 59 (CoA)

ANNEX C

RELEVANT DECISIONS UNDER THE EPC

(available at: www.europeanpatentoffice.org/dg3)

G 0001/98	OJEPO 2000, 111	<i>Novartis/ Transgenic plant</i>
G 0001/03	OJEPO 2004, 413	<i>PPG/ Disclaimer</i>
G 0002/06	[2009] EPOR 15	WARF/ Use of embryos
G 0002/07	[2011] EPOR 27	<i>State of Israel/Broccoli</i>
G 0001/08	[2008] EPOR 26	<i>State of Israel/Tomatoes</i>
G 0002/10	OJEPO 2012, 376	<i>Scripps/ Disclaimer</i>
T 0150/82	OJEPO 1984, 309	<i>International Flavours & Fragrances, Inc</i>
T 0292/85	OJEPO 1989, 275	<i>Genentech / Polypeptide expression-I</i>
T 0281/86	OJEPO 1989, 202	<i>Unilever / Preprothaumatin</i>
T 0081/87	OJEPO 1990, 250	<i>Collaborative / Preprorennin</i>
T 0301/87	OJEPO 1990, 335	<i>Biogen/ Alpha interferon</i>
T 0320/87	OJEPO 1990, 71	<i>Lubrizol / Hybrid plants</i>
T 0499/88	[1996] EPOR 235	<i>Unilever PLC / Immunoglobulins</i>
T 0060/89	OJEPO 1992, 268	<i>Harvard / Fusion proteins</i>
T 0019/90	OJEPO 1990, 476	<i>Harvard /Onco-mouse</i>
T 0877/90	[1993] EPOR 6	<i>Hooper Trading Co. N.V. / T-cell growth factor</i>
T 0409/91	OJEPO 1994, 653	<i>Exxon / Fuel oils</i>

T 0435/91	OJEPO 1995, 188	<i>Unilever / Detergents</i>
T 0455/91	OJEPO 1995, 684	<i>Genentech et al / Expression in yeast</i>
T 0500/91	[1995] EPOR 69	<i>Biogen N.V. / Alpha interferon II</i>
T 0886/91	[1999] EPOR 361	<i>Biogen Inc / Hepatitis B virus</i>
T 0694/92	OJEPO 1997, 408	<i>Mycogen Plant Science, Inc / Modifying plant cells</i>
T 0296/93	OJEPO 1995, 627	<i>Biogen, Inc/ HBV antigen production</i>
T 0441/93		<i>Gist Brocades/ Cloning in Kluyveromyces</i>
T 0020/94		<i>Amorphous TPM/Enichem (not reported)</i>
T 0063/94		<i>Akzo Nobel N.V. (not reported)</i>
T 0207/94	OJEPO 1999, 273	<i>Biogen, Inc / Human-beta interferon</i>
T 0272/95	OJEPO 1999, 590	<i>Howard Florey Institute</i>
T 0315/03	OJEPO 2006, 229	<i>Harvard/ Oncomouse</i>
T 0604/04		<i>Genentech/PF4A receptors (not reported)</i>
T 0870/04		<i>Max-Planck/BDP1 phosphatase (not reported)</i>
T 1329/04		<i>Johns Hopkins/ Factor-9 (not reported)</i>
T 0641/05		<i>Pharmacia/GPCR-like receptor</i>
T 1165/06		<i>Schering/ IL-17 related polypeptide (not reported)</i>
T1452/06		<i>Bayer/Serine protease (not reported)</i>
T0107/06		<i>BMS/ CD40 counter receptor (not reported)</i>
T2101/09		<i>Millennium/ Human Delta3-Notch (not reported)</i>
T2352/09		<i>Ajinomoto/ Amino acid production (not reported)</i>
V 0008/94	OJEPO 1995, 388	<i>Howard Florey Institutes Application</i>

RELEVANT DECISIONS OF THE CJEU

C-34/10

Oliver Brüstle v Greenpeace Ev

(available at <http://curia.europa.eu/juris/celex jsf?celex=62010CJ0034&lang1=en&type=NOT&ancre=>)

ANNEX D

EPO, JPO & USPTO: TRILATERAL STUDIES

- 1. Trilateral Project 24.1** Biotechnology Comparative Study on Biotechnology Patent Practices

Available at: http://www.trilateral.net/projects/biotechnology/patent_practices/

- 2. Trilateral Project B3b(ex-24.1)** Comparative Study on Biotechnology Patent Practices (Theme: Patentability of DNA fragments)

Available at: http://www.trilateral.net/projects/biotechnology/patentability_of_dna_fragments/

- 3. Trilateral Project B3b** Mutual understanding in search and examination Comparative study on biotechnology patent practices (Theme: Nucleic acid molecule-related inventions whose functions are inferred based on homology search)

Available at: http://www.trilateral.net/projects/biotechnology/mutual_understanding/

- 4. Report on Comparative Study on Biotechnology Patent Practices Carried Out Under Trilateral Project B3b** Biotechnology patent practices: reach through claims

Available at: http://www.trilateral.net/projects/biotechnology/reach_through_claims/

- 5. Report on Comparative Study in New Technologies Carried Out Under Trilateral Project WM4** Theme: Comparative study on “protein 3-dimensional (3-D) structure related claims”

Available at: http://www.trilateral.net/projects/biotechnology/protein_3d/

- 6. Report on Comparative Study in New Technologies Carried Out Under Trilateral Project WM4** Theme: Comparative study on examination practice relating to single nucleotide polymorphisms (SNPs) and haplotypes

Available at: http://www.trilateral.net/projects/biotechnology/examination_snp/

ANNEX E

***USPTO:
REVISED UTILITY GUIDELINES
TRAINING MATERIAL***

Available at: <http://www.uspto.gov/web/menu/utility.pdf>

ANNEX F

Intellectual Property Office: STEM CELL PRACTICE NOTICES

Available at:

[http://www.ipo.gov.uk/pro-types/
pro-patent/p-law/p-pn/p-pn-stemcells-20090203.htm](http://www.ipo.gov.uk/pro-types/pro-patent/p-law/p-pn/p-pn-stemcells-20090203.htm)

[http://www.ipo.gov.uk/pro-types/
pro-patent/p-law/p-pn/p-pn-stemcells-20120517.htm](http://www.ipo.gov.uk/pro-types/pro-patent/p-law/p-pn/p-pn-stemcells-20120517.htm)

ANNEX G

***Intellectual Property Office:
AMICUS CURIAE BRIEF FOR G02/06***

Available at: <http://www.ipo.gov.uk/warf.pdf>



Concept House
Cardiff Road
Newport
NP10 8QQ

Tel: 0300 300 2000
Minicom: 0300 0200 015
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