UK Supreme Court, 2 November 2011, Human Genome Sciences v Eli Lilly

PATENT LAW

Supremacy principles laid down by the Board's jurisprudence

- **the question which needs to be decided is whether, as the Court of Appeal held, Kitchin J followed the principles laid down by the Board's jurisprudence. If he did, then it seems to me that it would be inappropriate to interfere with his conclusion that the Patent did not satisfy the requirements of Article 57, unless the conclusion was one which he could not reasonably have reached. If he did not, then things would stand on a very different footing.**

Sufficient disclosure to satisfy requirements of article 57 EPC regarding "a practical application" and "some profitable use"

- **In those circumstances, it seems to me that, subject to dealing with a number of specific arguments to the contrary, the disclosure of the existence and structure of Neutrokine-α and its gene sequence, and its membership of the TNF ligand superfamily should have been sufficient, taking into account the common general knowledge, to satisfy the requirements of Article 57, in the light of the principles which I have attempted to summarise in para 107 above.**

Points (viii), (ix) and (x) appear to apply so far as the plausibility of at least some of the claims are concerned, and points (xi), (xii) and (xiii) all appear to be satisfied, given the evidence in relation to the TNF ligand superfamily (and point (xiv) cannot be invoked by Eli Lilly).

- **As Lord Hope says at para 152 below, the Board's conclusion was effectively this, that the disclosure of what was accepted to be a new member of the TNF ligand superfamily (coupled with details of its tissue distribution) satisfied Article 57, because all known members were expressed on T-cells and were able to co-stimulate T-cell proliferation, and therefore Neutrokine-α would be expected to have a similar function.**

This conclusion was supported, or reinforced, by the statement that Neutrokine-α was expressed in B-cell and T-cell lymphomas (referred to in T 0018/09, para 30), and indeed by the interest and effort in the pharmaceutical industry in finding a new member of the superfamily (as explained by Kitchin J at [2008] RPC 29, paras 72-74).

No different assessment of evidence if one concludes that the disclosure satisfies article 57 in line with Board's jurisprudence

- **Once one concludes that the effect of the Board's jurisprudence is that, in the light of the common general knowledge, the disclosure of Neutrokine-α as a member of the TNF ligand superfamily (coupled with its amino acid and encoding gene sequences and the tissues in which it is expressed), the claims in relation to the invention's potential satisfy Article 57.**

As a result, the relevance of the degree of effort needed in relation to any subsequent work falls away. (The same point undermines Eli Lilly's reliance on a number of other small differences between the findings of the Judge and the Board on the expert evidence).

Sufficient disclosure to satisfy article 57 goes hand in hand with sufficiently enabling disclosure

- **133. Although the Court of Appeal did not consider this point, Jacob LJ did say at the end of his judgment, that he "rather suspect[ed]" that the insufficiency argument "would go hand-in-hand with Article 57" – [2010] RPC 29, para 159. Subject to one point, which turns on the meaning of Claim 1 (as well as some of the other claims), it seems to me that that must be correct. If Claim 1 is simply to the encoding gene of Neutrokine-α, then, subject to any other points which have yet to be decided by the Court of Appeal, the reason why I consider the Judge and the Court of Appeal were wrong to hold that Article 57 is not satisfied is the same reason for holding the claim to be sufficient.**

General principles Board's approach in relation to article 57 in relation to biological materials

- **The general principles are:**

(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";
(ii) A "concrete benefit", namely the invention's "use … in industrial practice" must be "derivable directly from the description", coupled with common general knowledge;
(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;
(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";

- **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";

(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;
(vii) The absence of any experimental or wet lab evidence of activity of the claimed protein is not fatal;
(viii) A "plausible" or "reasonably credible" claimed use, or an "educated guess", can suffice;
(ix) Such plausibility can be assisted by being confirmed by "later evidence", although later evidence on its own will not do;
(x) The requirements of a plausible and specific possibility of exploitation can be at the biochemical, the cellular or the biological level;

- **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;
(xii) So "the problem to be solved" in such a case can be "isolating a further member of the [family]";
(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";
(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;
(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.

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UK Supreme Court, 2 November 2011
(Lord Hope, Lord Walker, Lord Neuberger, Lord Clarke, Lord Collins)
Michaelmas Term
[2011] UKSC 51
On appeal from: ***[2010] EWCA Civ 33***
JUDGMENT
Human Genome Sciences Inc (Appellant) v Eli Lilly and Company (Respondent)
before
[...]
JUDGMENT GIVEN ON
2 November 2011
Heard on 18, 19 and 20 July 2011
Appellant , Simon Thorley QC, Michael Tappin QC, (Instructed by Powell Gilbert LLP)
Respondent, Andrew Waugh QC, Thomas Mitcheson (Instructed by Field Fisher Waterhouse LLP)
LORD NEUBERGER
Introduction
1. This appeal is concerned with the validity of a patent which claims the nucleotide sequence of the gene which encodes for a novel protein (and which has further associated claims). Although there is an insufficiency issue, which I will consider at the end of this judgment, the primary issue on this appeal raises a difficult question, namely the way in which the requirement of industrial applicability in Articles 52 and 57 of the European Patent Convention ("the EPC") extends to a patent for biological material.
2. While this issue can be said to raise an important question of principle, its resolution is inevitably fact-sensitive, and therefore any answer may be of limited value in other cases. Further, the issue arises in the context of a fast-developing field, which requires a court to approach it with caution. The need for caution is reinforced by the fact that the answer may give rise to potentially far-reaching consequences for scientific research, the biotech industry, and human health. On the other hand, for those very reasons, it is particularly important that the law in this area is as clear, consistent and certain as possible.
The patent in suit
3. The patent in suit ("the Patent") is European Patent (UK) 0,939,804. It describes the encoding nucleotide, the amino acid sequence, and certain antibodies, of a novel human protein, which it calls Neutrokine-α, and includes contentions as to its biological properties and therapeutic activities, as well as those of its antibodies. These contentions are predictions, which are substantially based on the proposition that Neutrokine-α is a member of the TNF ligand superfamily.
4. The application for the Patent was filed by Human Genome Sciences Ltd ("HGS") on 25 October 1996, and it was granted by the Examining Division of the European Patent Office ("the EPO") to HGS on 17 August 2005. Accordingly, the Patent's validity is to be judged as at October 1996.
5. For present purposes, it is unnecessary to go into the claims or the description of the Patent in much detail. The claims, although not in their final form as allowed by the Technical Board of Appeal of the European Patent Office, are set out in an appendix to the judgment of Kitchin J at first instance, [2008] EWHC 1903 (Pat), [2008] RPC 29. The centrally important claim for present purposes is Claim 1, which essentially extends to the encoding nucleotides of the gene of Neutrokine-α.
6. The specification, or description, of the Patent is well summarised by Kitchin J at [2008] RPC 29, paras 100-133. It is confusingly long, diffuse, and widely expressed, running to over 25 closely typed pages, and nearly 200 paragraphs of descriptive text, and a further twelve pages of sequences of polypeptide amino acids and DNA nucleotides. Also, as Kitchin J said, the specification "contains extravagant and sometimes contradictory claims" - [2008] RPC 29, para 134. Perhaps rather more tolerantly, the Technical Board of Appeal of the European Patent Office ("the Board") referred to the Patent as having been drafted on a "boiler-plate" basis, which it described as "a practice used by patentees"- T 0018/09 Neutrokine/Human Genome Sciences, para 27.

7. The specification begins by explaining that Neutrokine-α is a new protein, and a member of the TNF ligand superfamily of cytokines, which are proteins which act as inter-cellular mediators in inflammation and other immune responses. It states that all the known members of that superfamily "are involved in regulation of cell proliferation, activation and differentiation, including control of cell survival or death by apoptosis or cytotoxicity...". The specification also explains that the first identified member of the superfamily is known as TNF-α, which was isolated in 1975 and whose encoding gene was sequenced in 1985. By 1996, it was clear that TNF-α had a variety of effects on different cell types, which the specification describes as including "immunoregulatory actions including activation of T-cells, B-cells, monocytes, [and] thymocytes …". Accordingly, it is claimed, "there is a need to provide cytokines similar to [TNF-α] that are involved in pathological conditions".

8. The specification goes on to reveal the existence and structure of Neutrokine-α, to claim it as a member of the superfamily, and to explain that it is "expressed … in neutrophils … in kidney, lung, peripheral leukocyte, bone marrow, T-cell lymphoma, B-cell lymphoma, activated T-cells, stomach cancer, smooth muscle, macrophages and cord blood tissue." The specification then describes the claimed invention as potentially useful for the diagnosis, prevention, or treatment of an extraordinarily large and disparate number of, sometimes widely expressed, categories of disorders of the immune system, and other conditions and actions, either through Neutrokine-α itself or through its antagonists. However, nowhere in the Patent is there any data or any suggestion of in vitro or in vivo studies, so there is no experimental evidence to support any of those suggestions.

9. Among its many contentions, the specification states that, "[l]ike other members of TNF family, Neutrokine-α exhibits activity on leukocytes including for example monocytes, lymphocytes and neutrophils", and so "is active in directing the proliferation, differentiation and migration of these cell types". These activities are said to be "useful for immune enhancement or suppression, myeloprotection, stem cell mobilization … and treatment of leukemia". The specification also discusses the tissues in which Neutrokine-α is expressed, and goes on to state that, because Neutrokine-α belongs to the TNF superfamily, "it will have a wide range of anti-inflammatory activities" and "may be suitable to be employed as an anti-neovascularizing agent to treat solid tumors by stimulating the invasion and activation of host defense cells, e.g., cytotoxic T-cells …". It is also said that Neutrokine-α may be "suitable to be employed to enhance host defenses against resistant chronic and acute infections" and also "to inhibit T-cell proliferation" or "for the treatment of T-cell mediated auto-immune diseases and lymphocytic leukemias".

10. In very summary terms, the disclosure of the Patent thus includes the following features:

(i) the existence and amino acid sequence of Neutrokine-α,
(ii) the nucleotide sequence of the gene encoding for Neutrokine-α,
(iii) the tissue distribution of Neutrokine-α,
(iv) the expression of Neutrokine-α by its mRNA (the encoding gene) in T-cell and B-cell lymphomas, and
(v) the information that Neutrokine-α is a member of the TNF ligand superfamily.

Technical background to the Patent

11. The teaching in the specification must, of course, be read through the eyes of the notional addressee (or "the person skilled in the art"), an appropriately skilled person or group of persons, as at October 1996. In that connection, the Judge said this at [2008] RPC 29, paras 30 and 32:

"30. The Patent is directed to a team of people with about two years of post doctoral experience. It would include a molecular biologist familiar with routine techniques of cloning, expression and sequencing of genes and proteins; a biochemist to make and purify recombinant proteins; and a biologist or immunologist with experience of the TNF superfamily and with the skills necessary to generate and test antibodies. I am also satisfied that any team interested in identifying a new member of the TNF superfamily would carry out a literature search to gather as much knowledge as possible about the existing members.

32. … [T]he skilled team looking for a new member of the TNF superfamily would have been aware that the science of bioinformatics could provide assistance in the search and, if a bioinformaticist was not already a member of the team, would have considered it worthwhile to consult such a person."

12. Accordingly, particularly in the light of the last sentence of the first of those two paragraphs, recourse must be had not only to the common general knowledge as at October 1996, but also to the results of any research into the literature which such notional addressees could be expected to carry out as at that time.

13. While a fuller explanation of the background and technique of bioinformatics, referred to in the passage quoted in para 11 above, was provided by the Judge at [2008] RPC 29, paras 78-99, I shall attempt a very brief explanation in the ensuing five paragraphs.

14. DNA molecules are found in virtually every human and mammalian cell. They consist of a long chain of units called nucleotides, many of which encode, via a related molecule called RNA, for proteins through specific regions known as genes. A gene is a stretch of DNA, which normally includes non-coding regions as well as protein-encoding regions. RNA is made from DNA, and the non-coding regions are removed as the RNA is processed into mature messenger RNA (mRNA). mRNA thus contains the protein encoding regions of a gene. mRNA is unstable outside the cell so it is copied in the laboratory to produce the more stable cDNA.

15. Proteins consist of a chain (or sometimes linked chains) of amino acids, and, in mammals, they perform

many essential functions in the body; they include, for instance, insulin and erythropoietin. There are four different nucleotides, and contiguous groups of three specific nucleotides in DNA encode either for a specific amino acid or to indicate the end of a particular encoding exercise (known as protein translation). The result of the translation process is often a linear strand of amino acids, which is called a polypeptide, and which folds up to form a functional protein. The sequence of nucleotides in DNA which encodes the amino acid sequence of a particular protein is the encoding gene of that protein.

16. Part of the relevant art is to identify the gene of a particular protein, and to discover in which body tissues that gene is "switched on" so as to "express" the protein. Traditional "wet lab" experiments as at 1996 included the use of Expressed Sequence Tags ("ESTs"), which are usually relatively small pieces of cDNA, in attempts to identify novel protein encoding genes. However, EST cDNAs normally do not encompass the entire sequence of the original mRNA, and consequently do not give complete DNA sequence information. Therefore, it was often very difficult to derive the correct or complete protein amino acid sequence (and hence to the identity of the protein) from such experimental strategies.

17. In the early 1990s, a new technique, known as bioinformatics, was developed. It relies upon what Kitchin J described as "the considerable increase in the amount of DNA and amino acid sequence data created and stored in publicly accessible databases and a parallel increase in the power of computers" – [2008] RPC 29, para 6. Bioinformatics enables researchers to identify genes (and the proteins for which they encode) by comparing their sequences with previously identified and characterised genes.

18. However, it is not possible to determine, at least conclusively, the actual activity of any gene or protein identified by this technique until after the gene has been cloned and the resultant protein has been subjected to in vitro and in vivo assays. As the Judge explained at [2008] RPC 29, para 75, "Assays are essential to determine the activities and functions of a cytokine. They are also necessary to determine whether any putative therapeutic is effective."

19. The immune system is the body's defence mechanism against infection, which, in technical terms, involves the body being attacked by foreign bodies known as pathogens (bacteria, viruses, fungi, parasites). The system is based on white blood cells (or leukocytes), of which there are various types, including lymphocytes. Lymphocytes recognise and interact with structures on, or derived from, pathogens known as antigens. Two types of lymphocyte-based mechanism are relevant for present purposes; they are:

(i) The development (in the bone marrow, in the case of adults) of type B lymphocytes ("B-cells"), which produce antibodies, which are molecules which bind to specific antigen sites (or epitopes) on the surface of specific pathogens, in order to clear those pathogens from the body, and

(ii) The development (in the thymus) of type T lymphocytes ("T-cells"), which directly react with epitopes derived from specific pathogens, again in order to clear those pathogens from the body.

20. Once a new protein is found and identified, it is relatively easy for those skilled in the art to generate antibodies (or antagonists, which for present purposes can be treated as being the same thing), but it can be much more difficult to produce useful pharmaceuticals as a result. The production of a useful pharmaceutical from an antibody can be seen as initially involving three steps, namely (i) finding a murine antibody which is derived from a single B-cell and which neutralises a particular antigen, (ii) ensuring that that antibody does not bind to other antigens, (iii) conversion of the murine antibody so that it can be effective in humans. This often involves engineering it so that it is not recognised and eliminated by the human immune system. Further to this, extensive clinical trials are required to confirm its efficacy in human disease.

21. A more detailed explanation of the immunology may be found in Kitchin J's judgment, [2008] RPC 29, paras 34-50.

22. A family or superfamily of proteins is a group of proteins, all of which enjoy a significant degree of homology, i.e. they all have certain specified structural characteristics. Although the distinction is not always observed, members of a particular family will normally have close structural similarity and similar functions, whereas members of a particular superfamily, while retaining related structural characteristics, will often be more distantly related and will include members which have similar functions but also may include members with different functions. However, even that is an over-simplification, as, in some cases, proteins will have pleiotropic functions, "that is to say a multitude of different effects on different cell types, driving multiple biological processes" – per Kitchin J at [2008] RPC 29, para 71. Accordingly, there will be cases where members of a family or superfamily have some functions which are common to all (or a majority) of the members, and other characteristics which are unique to one member (or a few members).

23. The TNF superfamily is sufficiently described for present purposes as consisting of certain cytokines with common structural molecular characteristics. The nature of those characteristics need not be particularised for present purposes (they are described by Kitchin J at [2008] RPC 29, paras 53-56). As the Patent records, the founding member of the superfamily was TNF-α, which, by 1996, had long been known as a cytokine with a significant role in regulating immune cells; at least eight other members of the family had been found, including one called TNF-ß.

24. At [2008] RPC 29, para 71, Kitchin J stated that the following features would have been appreciated by the notional addressee of the Patent about members of the TNF ligand superfamily as at October 1996:

"i) They were all expressed by activated T-cells and some by other [types of cell].

ii) Their activities were mediated by binding to receptors, of which a number had been identified.
iii) They were known to have pleiotropic actions …. Some of those activities were understood to be unique to particular TNF ligands and others were understood to be shared by some or all the other TNF ligands.
iv) They all played a role in the regulation of T-cell proliferation and T-cell mediated immune responses [and they all co-stimulated T-cell proliferation – [2008] RPC 29, para 65].
v) Some of the ligands played a role in the regulation of B-cell proliferation and antibody secretion and some took part in T-celldependent regulation of B-cells.
vi) Some of the ligands had an ability to induce cell death by necrosis or apoptosis.
vii) TNF-α and TNF-ß were functionally linked as primary mediators of immune regulation and inflammatory response.
viii) It had been suggested that various ligands were associated with a very wide range of particular disease states …. But no disease had been identified in which all the ligands were involved.
ix) TNF-α was the only ligand shown to have a therapeutic application; that being for the treatment of rheumatoid arthritis through the use of a specific monoclonal antibody. …"

25. Earlier in his judgment, at [2008] RPC 29, paras 62-68, the Judge had described what a person skilled in the art would have been expected of a new member of the TNF ligand superfamily as at October 1996. Such a person would have "anticipated that one of the activities of any new member [of the TNF ligand family] would relate to T-cells". Such a new member would also have been expected to "have the same roles, to some degree, as" existing members, roles which included "involve[ment] during lymphoid or thymic development, T-cell mediated immune responses, T-cell dependent help for B-cells or humoral B-cell activity", and being a "co-stimul[ant] of T-cell proliferation". It was also clear that an effect on B-cell proliferation and "involve[ment] with distinct human diseases" would also have been anticipated as a "possible property" of a new member of the TNF ligand superfamily.

26. The Judge also said this:

"72. [I]t was appreciated that further studies were both needed and desirable to identify further ligands in the TNF superfamily and, in relation to each ligand, to seek to identify its unique and redundant biological functions. There was undoubtedly an incentive to do so, because of their apparent roles in the regulation of the immune system and inflammatory response, their possible involvement in various different diseases and so also, in due course, their potential as therapeutic agents. The rewards were potentially very great. …
74 … [T]he reality [was] that pharmaceutical companies and academic institutions were indeed looking for further members of the TNF ligand and receptor superfamilies and seeking to elucidate their various biological functions and roles in disease states, ultimately with a view to developing a therapeutic or diagnostic product, if possible."

The proceedings in the EPO and in the English courts

27. The central issue both in the High Court proceedings before Kitchin J and in the opposition proceedings before the EPO was whether, in the light of the common general knowledge at October 1996, by disclosing the facts summarised in para 10 above (namely the existence and structure of Neutrokine-α, the sequence of its encoding DNA, its tissue distribution, its expression, and its membership of the TNF ligand superfamily), the Patent satisfied Articles 52 and 57 of the EPC so as to enable HGS to claim the encoding gene for Neutrokine-α.

28. Article 52 of the EPC provides that an invention cannot be patented unless it is "susceptible of industrial application". Article 57 of the EPC ("Article 57") goes on to state that an invention is susceptible of industrial application "if it can be made or used in any kind of industry, including agriculture." In its various decisions discussed below, the Board always refers to Article 57 alone, and I will adopt the same approach.

29. After the grant of the Patent to HGS, it was the subject of opposition proceedings brought in the EPO by Eli Lilly and Company ("Eli Lilly"). Following an oral hearing before the Opposition Division of the EPO ("the OD") in June 2008, the Patent was revoked on the basis that the claimed invention constituted, as the Judge put it, a claim to an arbitrary member of the TNF ligand superfamily without a known function.

30. HGS appealed against the OD's decision to the Board, which, after a hearing lasting around a day and a half, in a decision given on 21 October 2009, allowed the appeal. The Board's decision was, in very summary terms, based on the ground that the notional addressee of the Patent would have appreciated that, "in the light of the common general knowledge of the TNF ligand superfamily and its properties", Neutrokine-α would, as the Patent states, be "active in directing the proliferation, differentiation, and migration of [T-cells]", and that was a sufficient function to vindicate the Patent under Article 57 – see T 0018/09, paras 23-24. Accordingly, the Board referred the case back to the OD with a direction that the Patent be maintained.

31. Meanwhile, Eli Lilly brought parallel proceedings in the High Court for revocation of the Patent in this jurisdiction. The proceedings came before Kitchin J, who, after a hearing held over some thirteen days, decided to revoke the Patent. His decision was, again in very summary terms, based on the conclusion that, in the light of the common general knowledge, the notional addressee of the Patent would have concluded that the "functions" of Neutrokine-α "were, at best, a matter of expectation and then at far too high a level of generality to constitute a sound or concrete basis for anything except a research project" - see [2008] RPC 29, para 234.

32. Kitchin J's decision was given on 31 July 2008, after the decision of the OD, but before HGS had appealed to the Board. HGS appealed against Kitchin

J's decision to the Court of Appeal, who, on 9 February 2010, dismissed the appeal - [2010] EWCA Civ 33, [2010] RPC 14. The Court of Appeal's reasoning effectively followed and approved that of Kitchin J, although it was given after the ruling of the Board. In his judgment, with which Hallett LJ and Lewison J agreed, Jacob LJ discussed the reasoning of the Board in T0018/09. It is, of course, against the decision of the Court of Appeal which HGS now appeal.

33. HGS's case on this appeal is that, notwithstanding Kitchin J's impressively full and careful analysis of the law, the relevant technology, the Patent and the expert evidence, and its affirmation by the Court of Appeal, his decision that the Patent failed to satisfy Article 57 was wrong. That case effectively mirrors the reasoning of the Board in T0018/09. In summary, HGS contends that the reasoning of the Board was correct, and that it shows that Kitchin J and the Court of Appeal set too high a standard for industrial applicability in the context of a patent for biological material.

34. HGS and Eli Lilly each rely on the jurisprudence of the Board prior to the decision in T 0018/09 as to the way in which the requirement of industrial applicability extends to biological material patents, as did both Kitchin J, and the Board itself in T 0018/09. Kitchin J also referred to some domestic jurisprudence and to decisions of courts in the United States. It was also suggested below that the Biotech Directive (99/44EC) ("the Directive") was of some assistance.

The Directive, and domestic and US jurisprudence

35. Article 5 of the Directive confirms that a naturally occurring gene is patentable, but states that "[its] industrial application … must be disclosed in the patent application". As Jacob LJ put it, "*However clever and inventive you may have been in discovering a gene sequence, you cannot have a patent for it or for the protein for which it encodes if you do not disclose how it can be used"* – [2010] RPC 14, para 57.

36. It was common ground that the Directive cannot alter the meaning of Article 57 (both because it came into force after 1996, and because the EPC extends to countries outside the EU). While that may not prevent the Directive being of some assistance in a case where Article 57 is in play in relation to a patent for biological material, it seems to me that it is not helpful in the present case, as it begs the central question, namely how far an applicant for a patent for biological material has to go in disclosing industrial application. Jacob LJ's pithy formulation at [2010] RPC 14, para 57, cited in para 35 above, applies equally to Article 57 before the Directive came into force as it does afterwards.

37. So far as the cases in this jurisdiction are concerned, as Kitchin J said at [2008] RPC 29, para 186 "[t]here is very little authority" on the topic of industrial applicability: only a brief and very general comment from the Court of Appeal in Chiron Corp v Murex Diagnostics Ltd [1996] RPC 535, 607-608, and a decision in 2005 of a Divisional Director acting for the Comptroller of UK Patents, Aeomica's Application BL O/286/05, which analysed the issue more fully. In my view, neither case provides any assistance to the problem raised on this appeal. The conclusions in both Chiron [1996] RPC 535 and Aeomica BL O/286/05 appear equally consistent with HGS's and Eli Lilly's contentions, the observations in the former case are at a high level of generality, and the reasoning in the latter case rests on the US jurisprudence.

38. As for the US courts, their approach to the question of what constitutes "any new and useful … composition of matter" under section 101 of 35 USC was considered by the US Supreme Court in Brenner v Manson 383 US 519 (1966) 534-536, and by the US Court of Appeals for the Federal Circuit in Fisher v Lalgudi 421 F 3d 1365 (2005) (and both decisions are discussed and quoted from by the Judge at [2008] RPC 29, paras 218-224).

39. The analyses in the US cases deserve great respect, and it is interesting to note that, in Fisher 421 F 3d 1365, the US Court of Appeals referred to a requirement that "an invention is useful to the public as disclosed in its current form" as opposed to "prov[ing] useful at some future date after further research", and that the invention "can be used to provide a well-defined and particular benefit to the public."

40. However, there are obvious risks in relying on US jurisprudence when considering the precise nature of the requirements of Article 57 in relation to a claim for a patent for biological material under the EPC. There have been moves over the past fifty years (and more) to harmonise patent law across jurisdictions (the EPC and TRIPS - the Trade-Related Aspects of Intellectual Property Protection - being two important examples), and it is a laudable aim to seek to ensure that all aspects of the law of patents are identical throughout the world. However, the achievement of such an aim is plainly not currently practicable, and, although they have a great deal in common, there are significant and fairly fundamental differences (over and above the different words used in Articles 52 and 57 of the EPC and section 101 of 35 USC) between US patent law and the EPC (two notorious examples being the first to file rule in Europe, and file wrapper estoppel in the US).

41. Accordingly, particularly when it comes to a nice question such as the precise delineation of boundaries between patentability and unpatentability on the ground of industrial application, it would be unsurprising if the law was not identical under the two jurisdictions.

42. In the event, as both parties to this appeal acknowledge, it is in the jurisprudence of the EPO, and in particular that of the Board, that the applicable principles are really to be found. So I now turn to that jurisprudence.

The Board's jurisprudence on Article 57 and biological material

43. There are a number of decisions of the Board prior to its decision in relation to the Patent, which are of importance to the present appeal. In their oral arguments, the parties concentrated on two of them, T 0870/04 BDP1 Phosphatase/ Max-Planck, on which Eli Lilly placed reliance, and T 0898/05 Hematopoietic receptor/ZymoGenetics, from which HGS sought to derive assistance. However, because it is important to

establish the nature and ambit of the approach which the Board has adopted to the application of Article 57 to patents for proteins and their encoding genes, it is, in my view, necessary to consider all the decisions to which we were referred. I also consider that it is necessary to quote a number of passages from the decisions. As both parties accept, the reasoning of the Board in those decisions contains the principles applicable to this appeal, but they disagree as to the precise nature of those principles.

44. In T 0870/04, decided on 11 May 2005, the Board upheld the rejection by the Examining Division of the EPO ("the ED") of an application which disclosed BDP-1, a new polypeptide, said to be a member of the so-called PTP-PEST family. The application suggested that PTP-PESTs played an important role in certain specified cellular functions, and were possible "candidate anti-cancer proteins". It also disclosed that BDP-1 was expressed in most tissues and cell lines, particularly in epithelium origin cell lines and in cancer cell lines.

45. The Board began its reasoning by giving some general guidance. At T0870/04, para 3, it said that the concept of "industry" in Article 57 was very broad, extending to all activities carried out for "for financial (commercial) gains". In the following paragraph, it explained that "a 'practical' application of the invention has to be disclosed" so that there is "some profitable use for which the [claimed] substance can be employed."

46. Turning to the disclosure in the particular application, the Board pointed out at T 0870/04, paras 11-12 (and in the light of the subsequent jurisprudence, I draw particular attention to para 12):

"11. … [T]he application does not explicitly disclose the specific nature and the possible significance of [the] suggested roles for BDP1. … [T]he application stops short of suggesting, let alone identifying, an anti-cancer activity for BDP1 or a therapeutic use of BDP1 as a tumour-suppressor agent. There is no evidence as to whether BDP1 plays a passive role … or an active role in cancer. ...

12. Nor can the identification of BDP1 as a PTP-PEST be taken as any clear indication of its function or use, as the prior art does not attribute clear functions to PTP-PESTS as a class. …"

47. At T 0870/04, paras 21-22, the Board concluded:

"21. … [A]lthough the present application describes a product (a polypeptide), means and methods for making it, and its prospective use thereof for basic science activities, it identifies no practical way of exploiting it in at least one field of industrial activity. In this respect, it is considered that a vague and speculative indication of possible objectives that might or might not be achievable by carrying out further research with the tool as described is not sufficient for fulfilment of the requirement of industrial applicability. The purpose of granting a patent is not to reserve an unexplored field of research for an applicant. …

22. The present case is already on the [wrong] side of the borderline. … [T]he only practicable use suggested is to use what is claimed to find out more about the natural functions of what is claimed itself. This is not in itself an industrial application, but rather research undertaken either for its own sake or with the mere hope that some useful application will be identified."

48. Shortly after this, on 28 June 2005, the Board decided T 1329/04 Factor- 9/John Hopkins, in which it again upheld the ED's refusal of a patent application. At T 1329/04, para 4, the Board embarked on its familiar problem/solution approach, and described "the problem to be solved … as isolating a further member of the TGF-β superfamily", whose established members it described as "[having] influence on a wide variety of differentiation processes such as adipogenesis, myogenesis etc". The Board went on to say that the patent's claimed solution was the nucleotide sequence encoding for the claimed polypeptide, and described the issue as being "[w]hether or not the problem … has been plausibly solved".

49. The Board concluded on this issue at T 1329/04, para 11, in a passage which illuminatingly indicates what was lacking in the application:

"[A]s a significant structural feature fails to be identical in TGF-9 and the members of the TGF-β superfamily, and no functional characterisation of TGF-9 is forthcoming in the application, it is concluded that the application does not sufficiently identify this factor as a member of this family i.e. that there is not enough evidence in the application to make at least plausible that a solution was found to the problem which was purportedly solved."

50. The Board added at T 1329/04, para 12, that "even if supplementary postpublished evidence may in the proper circumstances also be taken into consideration, it may not serve as the sole basis to establish that the application solves indeed the problem it purports to solve."

51. In T 0604/04 PF4A receptors/Genentech, decided on 16 March 2006, the Board allowed an appeal from the OD where the claim was to certain polypeptides on the ground that they were members of the PF4AR family of chemokine receptors. At T 0604/04, para 6, dealing with the issue of inventive step, and having accepted that "there is no absolute certainty that the [claimed] polypeptides … are receptors for members of the PF4A family of cytokines to which IL-8 belongs", the Board said that "[certain] structural features make it plausible that this is indeed the case." In the following paragraph, the Board expressly distinguished T 1329/04, "where it was not accepted that the polypeptide … then claimed was a member of the TGF-β superfamily".

52. Dealing with Article 57, the Board said this at T 0604/04, para 13: *"In summary, the patent in suit identifies applications for the claimed polypeptides which may ultimately lead to some profitable use. It provides a structural characterisation which enables their assignment to the category of receptors which bind members of the PF4A family of chemokines and, insofar, indicates what their function might be. Yet, in*

the absence of any characterisation of their ligands, this function remains at best incompletely understood".

53. After referring to T 0870/04, the Board said at T 0604/04, para 15:

"[T]he technical data provided in respect of the [claimed] polypeptides ... fall somewhat short of fulfilling them insofar as, as already above mentioned, there is no evidence available as to which ligands these polypeptides bind to. Yet, of course, each case has to be considered on its own merit ...and it is important here to take into account the common general knowledge at the priority date as well as the then prevalent attitude of the person skilled in the art as it may be inferred from the documents illustrating this common general knowledge."

54. At T 0604/04, para 16, the Board said that, as at the priority date:

"*chemokines were already known as mediators of the inflammatory response, a role which most of them were thought to play, in particular, through ... a biological interaction of the chemokines with the cells which they attract which involves binding to the receptors present on the cell surface. Thus, the skilled person would understand that any role of a given chemokine was reflected in its receptor."*

55. At T 0604/04, para 18, the Board concluded that:

"It is clear ... that chemokines as a family were considered not only to be interesting in fundamental research but also as important for the pharmaceutical industry irrespective of whether or not their role had been clearly defined. It follows that their receptors must have been considered equally important since the mode of action of chemokines is through their receptors. It is, thus, reasonable to conclude that the [claimed polypeptides] which exhibit the characteristics of receptors of members of the PF4A family of cytokines would have been regarded as important to the pharmaceutical industry, i.e. that industrial applicability may be acknowledged."

56. The Board also said at T 0604/04, para 22 that in its "judgment, and in the absence of any evidence to the contrary, the patent specification provides adequate experimental instructions for the skilled person to be able to reproduce without undue burden the [claimed] polypeptides ...".

57. I turn now to the Board's decision on 7 July 2006 in T 0898/05. This was an appeal against the ED's refusal of a patent application, which disclosed the nucleotide sequence and the encoded amino acid sequence of a polypeptide and receptor, Zcytor1, and claimed inter alia the encoding nucleotide and the polypeptide.

58. As in T 0870/04, the Board made some general observations at the outset. Thus, at T 0898/05, para 4, after referring to the reasoning in T 0870/04, the Board said that "a patent application [must describe] its subject invention in sufficiently meaningful technical terms that it can be expected that the exclusive rights resulting from the grant of a patent will lead to some financial or other commercial benefit." And in the next paragraph, the Board said that "the invention claimed must have such a sound and concrete technical basis that the skilled person can recognise that its contribution to the art could lead to practical exploitation in industry."

59. The Board then elaborated its approach in these terms:

"6. .. [T]he expression 'profitable use' should be understood more in the sense of 'immediate concrete benefit'. This conveys, in the words 'concrete benefit', the need to disclose in definite technical terms the purpose of the invention and how it can be used in industrial practice to solve a given technical problem, this being the actual benefit or advantage of exploiting the invention. The essence of the requirement is that there must be at least a prospect of a real as opposed to a purely theoretical possibility of exploitation. Further, the use of the word 'immediate' conveys the need for this to be derivable directly from the description, if it is not already obvious from the nature of the invention or from the background art. It should not be left to the skilled reader to find out how to exploit the invention by carrying out a research programme. ....

7. Accordingly, a product whose structure is given (e.g. a nucleic acid sequence) but whose function is undetermined or obscure or only vaguely indicated might not fulfil the above criteria, in spite of the fact that the structure of the product per se can be reproduced. If a patent is granted therefor, it might prevent further research in that area, and/or give the patentee unjustified control over others who are actively investigating in that area and who might eventually find actual ways to exploit it.

8. On the other hand, a product which is definitely described and plausibly shown to be usable, e.g. to cure a rare or orphan disease, might be considered to have a profitable use or concrete benefit, irrespective of whether it is actually intended for the pursuit of any trade at all. Thus, although no particular economic profit might be expected in the development of such products, nevertheless there is no doubt that it might be considered to display immediate concrete benefits."

60. The claimed disclosure is described at T 0898/05, paras 13-16. In summary terms, it disclosed the nucleotide sequence and the encoded amino acid sequence of the cytokine, Zcytor1, its tissue distribution, including in "both B- and T-cells", and claims that Zcytor1 accordingly had various roles such as "in proliferation, differentiation, and/or activation of immune cells" and that it could therefore be "useful in different therapeutic conditions", of which a fair number of different possibilities were given. No experimental evidence was provided to support these claimed roles or uses.

61. At T 0898/05, para 19, the Board identified the two reasons the ED had refused the patent application. They were "(i) the use of a computer-assisted alignment … did not allow any concrete conclusions to be made as to the actual specific function of the protein, because such studies provided only speculation of a vague nature and no specific therapeutic or diagnostic use could be ascertained therefrom"; and (ii) Zcytor1 "was only a

research tool … whose disclosure was only the first step in the quest for industrially applicable matter".

62. The Board then started its consideration of the ED's two reasons for refusing ZymoGenetics' application in these terms:

"21. In the present case, based on computer-assisted sequence homology studies and on tissue distribution studies, the Zcytor1 receptor was identified in the application as a putative member of the hematopoietin receptor family and it was assigned a role in proliferation, differentiation and/or activation of immune cells and thus a possible role for its ligands in therapeutic conditions associated with the functioning of the immune system. Admittedly, no experimental evidence for the suggested role of the receptor and/or its ligands is made available in the application. Later evidence, however, confirmed this sort of 'educated guess', which the examining division considered to be - in its own words - 'reasonably credible'.

22. The fact that the putative function of the Zcytor1 receptor was assigned in the examples based on computer-assisted methods, rather than on the basis of traditional wet-lab techniques, does not mean that it has to be automatically disregarded or excluded from a careful and critical examination. ... [The] probative value [of such examples] has to be examined on a case-by-case basis regarding the nature of the invention and the prior art relating thereto. Such methods of analysis are increasingly becoming an integral part of scientific investigations and can often allow plausible conclusions to be made regarding the function of a product before it is actually tested."

63. The Board then explained at T 0898/05, para 24, that the identification of "the Zcytor1 receptor … as a putative member of [the] hematopoietin receptor family" of cytokines was "based on [its] general structure", and was not called into question by anything in the Patent or by any other evidence. The Board also said that "post-published evidence, which confirms the preliminary finding and actually supports the conclusion, cannot be ignored."

64. After quoting the ED's view that the "suggested role" of the Zcytor1 receptor was too "vaguely defined", not least because "the members of the family all obviously have different functions", the Board said this at T 0898/05, para 27:

"It might well be possible that members of a structurally related family have, notwithstanding their related structure, a different activity and function. However, there is no reference to the prior art in the decision under appeal which supports such a case in the hematopoietin receptor family. In fact, from the prior art cited in the application and concerned with this family of receptors ..., it may be derived that, although none of these members are precisely interchangeable in terms of their biological action, there is considerable redundancy of action as well as an ability to elicit, under certain conditions, similar biological responses. Even more important is the fact that this prior art does not cast significant or serious doubts on the suggested role of the Zcytor1 receptor. Thus, the assumption (or 'educated guess') made in the patent application is plausible."

65. At T 0898/05, paras 29-31, the Board concluded as follows:

"29. ... The function of a protein (and thus of the nucleic acid encoding it) can be seen at different levels. These include: (i) the biochemical activity of the protein ..., i.e. its molecular function; (ii) the function of the protein in cellular processes ..., i.e. its cellular function; and (iii) the influence of those cellular processes within a multicellular organism, ... this being its biological function in a broad sense. ...

30. The elucidation of one of these particular levels of function might result, under certain conditions, in a straightforward industrial application, even though the other levels of activity remain completely unknown or only partially characterized. ... For the purpose of Article 57 ..., none of these levels is more fundamental ... than the other ones ... .

31. In the present case, the suggested role of [Zcytor1] corresponds to the level of the biological function and the practical applications or the concrete technical benefits derived therefrom are clearly disclosed in the present application, namely the stimulation of cellmediated immunity and of lymphocyte proliferation by agonist ligands of Zcytor1 and the suppression of the immune system by antagonists of the Zcytor1 receptor ... . Although the details of the biochemical activity and the cellular function of the Zcytor1 receptor have not been elucidated in the application, the (therapeutic) treatments directly derivable from the biological function identified by the computer-assisted method cannot be considered to be so 'vaguely defined' that they do not suggest any therapeutic or diagnostic use. On the contrary, the treatments referred to in the application are specifically in relation to the function plausibly attributed to the molecule, and are in the areas of rheumatoid arthritis, multiple sclerosis, diabetes mellitus, etc."

66. In T 1452/06 Serine protease/Bayer (10 May 2007) the Board considered and applied its reasoning in T 0870/04 and T 0898/05, when upholding a decision of the ED refusing an application claiming a patent for a polypeptide and its encoding gene. Having said that there was "no experimental evidence whatsoever … in support of [the claimed] serine protease activity" of the claimed polypeptide, the Board then said at T 1452/06, para 4, that such support "might be provided by a (computer-assisted) comparison of [the disclosed] sequence with sequences of known serine proteases and, more particularly, with the allegedly closely related sequence of [the already known] epithin". The Board accepted, at para 6, that such support "might be obtained by a straight (computer-assisted) comparison of the [disclosed] sequence with the sequence of [epithin]". However, the Board pointed out that "epithin is defined as a putative serine protease" (original emphasis) and there was no "experimental evidence in support of [its] serine protease activity nor of any other activity at all." (para 7)

67. In T 1165/06 IL-17 related polypeptide/Schering, decided 19 July 2007, the main issue was obviousness, but the Board also addressed the question whether the requirements of Article 57 had been satisfied, and concluded that they had. At T 1165/06, para 14, the Board, adopting its problem/solution approach, said "the technical problem to be solved can be defined as the isolation of a further polypeptide of the IL-17 cytokine family, and a nucleotide sequence encoding the polypeptide". The appellant's case was that the claimed polypeptide exhibited "significant sequence similarity to the [IL-17 cytokine family which had four established members, all of] which functioned in controlling physiology, development and differentiation of mammalian cells"

68. At T 1165/06, para 25, the Board concluded: *"The sequence information provided in the application with respect to the presence in IL-174 of the characteristic cysteine spacing of the IL-17 cytokine family makes it plausible that [the claimed] polypeptide may belong to this family and have biological activities similar to those of the other family members known at the filing date, in particular CTLA-8. This is confirmed by post-published evidence filed by the appellant."*

The reasoning and conclusions of Kitchin J and of the Board

69. As I have mentioned, in their respective decisions, both Kitchin J and the Board referred to and relied on the Board's jurisprudence, but they came to different conclusions. It is therefore appropriate to turn to the reasoning in the two decisions in a little more detail, and in particular the identification of what the notional addressee would get from the Patent, and why the Patent did or did not satisfy Article 57.

70. As to the overall effect of the teaching of the Patent, it is convenient to refer to what Kitchin J said at [2008] RPC 29, paras 231-233, as the view which he expressed was very similar to that of the Board, and was not challenged in this court by HGS. In those paragraphs, he summarised his view as to what the Patent disclosed thus:

"231. In this case I am quite satisfied that the skilled person would consider the Patent does not of itself identify any industrial application other than by way of speculation. ... [I]t contains an astonishing range of diseases and conditions which Neutrokine-α and antibodies to Neutrokine-α may be used to diagnose and treat and there is no data of any kind to support the claims made. The skilled person would consider it totally far-fetched that Neutrokine-α could be used in relation to them all and ... would be driven to the conclusion that the authors had no clear idea what the activities of the protein were and so included every possibility. To have included such a range of applications was no better than to have included none at all.

232. But that is not the end of the matter because the disclosure must be considered in the light of the common general knowledge .... The skilled person would have known that TNF was involved as a primary mediator in immune regulation and the inflammatory response and had an involvement in a wide range of diseases as septic shock, rheumatoid arthritis, inflammatory bowel disease, tissue rejection, HIV infection, and some adverse drug reactions. He would have known that all the members of the TNF ligand superfamily identified hitherto were expressed by T-cells and played a role in the regulation of T-cell proliferation and T-cell mediated responses. Further, ... the skilled person would anticipate that the activities of Neutrokine-α might relate to T-cells and, in particular, be expressed on T-cells and be a co-stimulant of B-cell production; that it might play a role in the immune response and in the control of tumours and malignant disease; that it might have an effect on B-cell proliferation ... .

233. On the other hand, the skilled person would have also known that the members of the family had pleiotropic actions; that some of those activities were unique to particular TNF ligands and others were shared by some or all the other TNF ligands and that no disease had been identified in which they were all involved. Moreover, ...

the therapeutic application of TNF-α monoclonal antibody for the treatment of rheumatoid arthritis was believed to operate by interrupting the cytokine cascade and by controlling the recruitment and trafficking of blood cells to the joint – a rather specific activity."

71. Eli Lilly's case to the effect that the teaching of the Patent fell short of the requirements of Article 57 was accepted by Kitchin J at [2008] RPC 29, paras 230 and 234-5 (which were effectively approved by the Court of Appeal). But before quoting them, it is appropriate to refer to three earlier passages in his judgment.

72. At [2008] RPC 29, para 118, the Judge accepted that the claims of the Patent in relation to Neutrokine-α were "significant" because:

"[T]hey reveal the importance of the identification of the tissues where [it] is expressed, the tissues where it acts, the nature of its biological activity and how that profile varies in any particular disease state. However, no data is provided to support these claims. Further, ... the variety of conditions for which the described method is said to be useful [is] puzzlingly wide and ... the method itself impossible to operate in the absence of any information as to the standard level of Neutrokine-α expressed in each of these tissues in normal conditions."

73. Having considered the description of the Patent, the Judge concluded at [2008] RPC 29, para 134, that there was "nothing by way of experimental evidence to support the claims made and … the idea that Neutrokine-α and [its antagonists] could be used to treat the extraordinary range of diseases identified was fanciful." He then said that, in his view, "the skilled person would come to the conclusion that the inventors had no idea as to the activity of Neutrokine-α when drafting the Patent" and that it taught "the skilled person nothing useful about its activity other than that Neutrokine-α is another member of the TNF ligand superfamily".

74. The Judge also considered in some detail the work carried out since October 1996, and concluded at [2008] RPC 29, para 176, that this work established Neutrokine-α's functions more clearly, and in particular that it "plays a significant and particular role in the proliferation and differentiation of B-cells … [and] in the regulation of T-cell proliferation and activation". He went on:

"Neutrokine-α has now been shown to have an important role in the development of autoimmune disease and B-cell cancers; but, at the same time, much of its biology remains unclear and is the subject of continuing study by many different research centres. In my judgment the nature and extent of all this research work, the limited conclusions ultimately drawn and the amount of work that remains to be done point strongly to the conclusion that the therapeutic and diagnostic applications suggested in the Patent were indeed speculative."

75. Turning then to the passage in which he expressed his conclusions, [2008] RPC 29, paras 230 and 234-5, Kitchin J said this:

"230. I accept that the contribution made by HGS was to find Neutrokine-α and to identify it as a member of the TNF ligand superfamily. However it is clear from the cases to which I have referred that simply identifying a protein is not necessarily sufficient to confer industrial utility upon it. … It may be sufficient if the identification of the protein will immediately suggest a practical application, such as was the case with insulin, human growth hormone and erythropoietin. But if the function of the protein is not known or is incompletely understood and if no disease has been attributed to a deficiency or excess of it, then the position may well be different. In these cases the industrial utility must be identified in some other way. …

234. Does [the] common general knowledge, taken as a whole, disclose a practical way of exploiting Neutrokine-α? Or does it provide a sound and concrete basis for recognising that Neutrokine-α could lead to practical application in industry? In my judgment it does not. The fact that Neutrokine-α might be expected to play a role in regulating the activities of B-cells and T-cells and play an unspecified role in regulating the immune and inflammatory response did not reveal how it could be used to solve any particular problem. Neither the Patent nor the common general knowledge identified any disease or condition which Neutrokine-α could be used to diagnose or treat. Its functions were, at best, a matter of expectation and then at far too high a level of generality to constitute a sound or concrete basis for anything except a research project.

235. I believe this conclusion is confirmed by the activities of those in the pharmaceutical industry in the years following the filing of the application. HGS, Lilly and Biogen (and possibly others too) carried out research programmes to try and find out where Neutrokine-α was expressed, where its receptors were expressed and what its activities appeared to be. They carried out in vitro assays and animal studies and determined that it appeared to have an activity in relation to B lymphocytes with a particular biological profile. On the basis of this work they recognised that it was an important therapeutic target – some two to three years after the application for the Patent had been filed. It is significant that in so doing they considered that its utility might lie in the treatment of B-cell disorders of particular kinds."

76. The passage I have just quoted from Kitchin J's judgment encapsulates Eli Lilly's case, and HGS's case is well summarised in the Board's reasoning at T0018/09, paras 22-26. The first of those paragraphs sets the scene in terms of the general approach:

"22. As pointed out in T 870/04, [paras 5 and 6], in many cases the allocation of a newly found protein to a known protein family with known activities suffices to assign a specific function to the protein because normally the members of the family share a specific function. This may be a well-characterized and perfectly understood function which provides in a straightforward manner enough support for industrial applicability. In such cases, the 'immediate concrete benefit' is manifest. In other cases, where the members of a protein family have different, pleiotropic effects which may even be opposite and neither completely characterized nor understood, no effect can be assigned to a new member without relying on some experimental data. Between these two extreme situations, a variety of other situations may arise for which a detailed examination of all the facts may be required. Indeed, this is the case for the TNF ligand superfamily."

77. In the next two paragraphs, the Board sought to follow that approach in relation to the instant Patent:

"23. As known in the art and acknowledged in the [Patent], all members of the TNF ligand superfamily are known to participate in the regulation of (immune) cell proliferation, activation, and differentiation, and are involved in various medical conditions. They are pleiotropic cytokines which display a wide range of activities and have distinctive, but also overlapping biological functions…. As acknowledged in the art, a feature common to all members (without exception) of the TNF ligand superfamily is the expression on activated T-cells and the ability to co-stimulate T-cell proliferation … In view of the assignment of Neutrokine-α to the family, the skilled person expects it to display this common feature, the relevant question here being whether anything in the Patent specification contradicts this expectation.

24. The Patent specification, besides providing the undisputed structural identification of Neutrokine-α as a member of the TNF ligand superfamily, also provides some further relevant technical data which are fully in line with the expected properties of a member of that superfamily. In particular, it discloses the tissue distribution of Neutrokine-α mRNA expression using the nucleic acid sequence encoding the Neutrokine-α protein, as a cDNA probe and, as expected, reports - although without concrete experimental data – the expression of Neutrokine-α in activated T-cells… . It

further states that '(l)ike other members of TNF family, Neutrokine-α exhibits activity on leukocytes including for example monocytes, lymphocytes and neutrophils. For this reason Neutrokine-α is active in directing the proliferation, differentiation and migration of these cell types' ….
This broad statement, far from contradicting the ability of Neutrokine-α to co-stimulate T-cell proliferation, actually supports it. In the light of the common general knowledge of the TNF ligand superfamily and its properties, no serious doubts can be cast on this explicit additional information. Nor can this information be taken as a mere theoretical or purely hypothetical assumption. First of all, it is plausible and, secondly, there is ample post-published evidence on file confirming both the presence of Neutrokine-α on activated Tcells and its ability to co-stimulate T-cell proliferation."

78. The Board then turned to Eli Lilly's contention that "in view of the numerous contradictory statements and of the broad range of conditions and diseases referred to in the patent-in-suit, the skilled person would have disregarded such information as constituting only hypothetical assumptions or speculations", and said this at T 0018/09, para 26:

"When reading the patent specification, a skilled person would distinguish the positive technical information such as that mentioned above from other allegedly contradictory and broad statements found in the patent-in-suit, such as … the wide range of activities and conditions for which Neutrokine-α could be useful. This is because the skilled person realises that the description of the structure of Neutrokine-α, its structural assignment to the family of TNF ligands, and the reports about its tissue distribution and activity on leucocytes, are the first essential steps at the onset of research work on the newly found TNF ligand superfamily member. In view of the known broad range of possible activities of such a molecule, the skilled person is aware of the fact that the full elucidation of all properties requires further investigations which will gradually reveal them. In this context, the skilled person regards the long listing of possible actions of Neutrokine-α and of medical conditions in which it might take part as the enumeration or generalisation of the properties of the TNF ligand superfamily. This is seen as the frame in which the newly found molecule has to be placed as one could prima facie have a reasonable expectation that most of them could in fact be present."

79. The Board accordingly concluded at T 0018/09, para 27 that "the description of the patent delivers sufficient technical information, namely the effect of Neutrokine-α on T-cells and the tissue distribution of Neutrokine-α mRNA, to satisfy the requirement of disclosing the nature and purpose of the invention and how it can be used in industrial practice."

80. At T 0018/09, paras 28-30, the Board then considered the arguments that "in view of the technical difficulties involved in measuring the co-stimulation of T-cells by Neutrokine-α", the implementation of the teaching of the Patent would involve an "undue burden", and that, in any event, "no industrial application can be directly derived from a mere co-stimulation of T-cells". Those arguments were also rejected. Although the Board acknowledged that such assays had produced "a few contradictory results", there was "post-published evidence" which showed that Neutrokine-α activity could be reasonably easily measured in relation to both Tcells and B-cells. Further, the Board said that the activities of Neutrokine-α, as taught by the Patent ("in particular, the inhibition of co-stimulation and/or proliferation of lymphocytes") "may represent a valid basis for a possible industrial application".

81. The Board went on to say at T 0018/09, para 30, that the Patent's teaching as to "the expression of Neutrokine-α mRNA in B-cell and T-cell lymphomas provides in itself in the context of the disclosure a valid basis for an industrial application", adding that the "presence of Neutrokine-α in these lymphomas, which is also confirmed by post-published evidence … may be used to develop appropriate means and methods for their diagnosis and treatment based on the disclosure of the [Patent]".

82. In the next four paragraphs, the Board also rejected the contention that "alleged technical problems" meant that "no industrial application could be derived from [the] information [in the Patent]"; this was because Eli Lilly was unable to establish "serious doubts, substantiated by verifiable facts", so that it was relying on mere "unsupported assumptions".

Following the Board's jurisprudence

83. Where the EPO decides that a patent, or a claim in a patent, is invalid, then that is the end of the issue (subject, of course, to the patentee or applicant appealing to the Board) in relation to all countries which are signatories to the EPC. Where, however, the EPO decides that a patent, or a particular claim, is valid, then, as this case shows, it is still open to a national court to decide that the patent, or claim, is invalid within its territorial jurisdiction. In all cases, however, the EPO and each national court are, of course, applying the principles contained in the EPC. It is plainly appropriate in principle, and highly desirable in practice, that all these tribunals interpret the provisions of the EPC in the same way.

84. In a number of recent decisions of the House of Lords, attention has been drawn to "the importance of UK patent law aligning itself, so far as possible, with the jurisprudence of the EPO (and especially decisions of its Enlarged Boards of Appeal)", to quote Lord Walker in Generics (UK) Ltd v H Lundbeck A/S [2009] UKHL 12; [2009] RPC 13, para 35. It is encouraging that the same approach is being adopted in Germany by the Bundesgerichtshof – see Case Xa ZR 130/07 (10 September 2009), para 33.

85. However, as Lord Walker went on to explain in Generics [2009] RPC 13, para 35, "National courts may reach different conclusions as to the evaluation of the evidence in the light of the relevant principles" even though "the principles themselves should be the same,

stemming as they do from the EPC". Thus, the EPO (or another national court) and a national court may come to different conclusions because they have different evidence or arguments, or because they assess the same competing arguments and factual or expert evidence differently, or, particularly in a borderline case, because they form different judgments on the same view of the expert and factual evidence.

86. As Lord Hoffmann said in Conor Medsystems Inc v Angiotech Pharmaceuticals Inc [2008] UKHL 49, [2008] RPC 28, para 3:

"A European patent takes effect as a bundle of national patents over which the national courts have jurisdiction. It is therefore inevitable that they will occasionally give inconsistent decisions about the same patent. Sometimes this is because the evidence is different. In most continental jurisdictions, including the [EPO], cross-examination is limited or unknown. Sometimes one is dealing with questions of degree over which judges may legitimately differ. Obviousness is often in this category. But when the question is one of principle, it is desirable that so far as possible there should be uniformity in the way the national courts and the EPO interpret the [EPC]."

87. Further, while national courts should normally follow the established jurisprudence of the EPO, that does not mean that we should regard the reasoning in each decision of the Board as effectively binding on us. There will no doubt sometimes be a Board decision which a national court considers may take the law in an inappropriate direction, misapplies previous EPO jurisprudence, or fails to take a relevant argument into account. In such cases, the national court may well think it right not to apply the reasoning in the particular decision. While consistency of approach is important, there has to be room for dialogue between a national court and the EPO (as well as between national courts themselves). Nonetheless, where the Board has adopted a consistent approach to an issue in a number of decisions, it would require very unusual facts to justify a national court not following that approach.

88. In the present instance, as discussed above, there has been little helpful domestic guidance as to the application of Article 57 to patents for biological material, but there have been a number of decisions of the Board which have addressed the topic and which at least purport to adopt a consistent approach to the issue. It is true that there is no decision of the Enlarged Board on the instant point, but there was no such decision on the point at issue in Generics [2009] RPC 13. But, again as in that case, there is what may be described, at its lowest, as an intended consistent approach to the issue in a number of carefully considered decisions of the Board. Further, it is not irrelevant to mention that there is unlikely to be a decision of the Enlarged Board on the instant point in the near future, as the Board refused to make a reference in T 0898/05, para 33.

89. Further, while there has been some attack on the reasoning of the Board in its decision on the instant Patent, T 0018/09, both in the judgment of Jacob LJ in the Court of Appeal ([2010] RPC 14, paras 146, 155 and 156) and in the submissions on behalf of Eli Lilly in this court, there has been no attempt either here or below to suggest that the reasoning in the earlier decisions of the Board was wrong, save that Mr Waugh QC, on behalf of Eli Lilly, did make the point that decisions on appeal from the ED, perhaps particularly T 0898/05, should carry less weight as they were unopposed, or ex parte.

90. In relation to the Board's assessment of the factual and expert evidence in a particular ex parte appeal, I can see the force of the point. But I am unimpressed with the point in so far as it is invoked in relation to the applicable principles. In particular, I would reject the implicit suggestion that the Board has been too favourable to patentees in some of the decisions discussed above, as a result of the hearing being ex parte. First, all the decisions discussed above appear to me to demonstrate a consistent approach to the issue raised on this appeal. Secondly, those decisions include an appeal from the OD, namely T 0604/04. Thirdly, the decision of the Board in relation to the instant Patent was from the OD, after strong opposition from Eli Lilly, and, far from resulting in the Board modifying its position, it is Eli Lilly's case in this court that the Board went further in this case in favour of the patentee than in any appeal from the ED.

91. In these circumstances, it seems to me to be right to take the law as being that laid down in the Board's jurisprudence I have discussed. But, of course, as explained by Lord Hoffmann and Lord Walker in the passages quoted above, this does not necessarily mandate the same outcome as the Board arrived at in T 0018/09.

92. It is unlikely that the Board and Kitchin J received very different arguments in the present case, in the light of the reasoning in the two decisions, and the fact that the parties in the two sets of proceedings were the same. It is less clear how similar the evidence before each tribunal was: the witnesses were different, and there was at least one further expert witness statement (on behalf of HGS) before the Board which post-dated Kitchin J's judgment. Further, unlike before Kitchin J, there was no cross-examination of witnesses before the Board.

93. As Jacob LJ said at [2010] RPC 14, paras 25-26, citing the well-known observations of Lord Hoffmann in Biogen Inc v Medeva plc [1997] RPC 1, 45, "appeals are conducted on the evidence and materials before the court of first instance" and "the Court of Appeal gives very considerable deference to the findings of fact of the first instance court. So also to its value-judgments". That is all the more true of appeals to this court from the Court of Appeal, especially where, as here, there are concomitant findings (i.e. where the Court of Appeal has upheld the trial judge's findings of fact and value judgments).

94. In these circumstances, the question which needs to be decided is whether, as the Court of Appeal held, Kitchin J followed the principles laid down by the Board's jurisprudence. If he did, then it seems to me that it would be inappropriate to interfere with his

conclusion that the Patent did not satisfy the requirements of Article 57, unless the conclusion was one which he could not reasonably have reached. If he did not, then things would stand on a very different footing.

95. Before turning to that question, however, it is appropriate to mention another, and rather wider, reason for consistency of approach to patents in the biological field.

Consistency and policy: the wider picture

96. The BioIndustry Association ("the BIA"), which has intervened in these proceedings, describes itself as "a trade association for innovative enterprises in the UK's bioscience sector" and its membership extends to hundreds of companies with an aggregate turnover in 2010 of about £5.5bn, and around 36,000 employees.

97. The requirements of clarity and certainty in this area of law are emphasised by the BIA. As its submissions also explain, after the discovery of a naturally occurring molecule, particularly a protein and its encoding gene, a large amount of research and development is required before there can be any therapeutic benefit. It is therefore important for bioscience companies to be able to decide at what stage to file for patent protection. Thus, *"If the application is filed early, … [t]he company will be left with no patent protection, but would have disclosed its invention in the published patent application to competitors. If the application is filed late, there is a risk in such a competitive environment where several companies may be working on the same type of research projects, that a third party will already have filed a patent application covering the same or a similar invention, in which case the company may not be able to gain any patent protection for its work and by continuing their programme they may risk infringing that third party's patents. In both cases, the company will have lost much of the benefit of its costly research and development."*

98. Similarly, funding for research and development on the potential therapeutic value of a newly discovered and characterised protein or its antibodies is dependent on the funders being reasonably confident that the patent (or patent application) concerned will be reasonably safe from attack (or likely to be granted). It is also relevant that bioscience companies attract investment by reference to their patent portfolios, which gives rise to the same need for certainty.

99. As the BIA suggests, it is worth remembering the purpose of the patent system, namely to provide a temporary monopoly as an incentive to innovation, while at the same time facilitating the early dissemination of any such innovation through an early application for a patent, and its subsequent publication. Although this is true in any sector, it has particular force in the pharmaceutical field, where even many of those who are sceptical about the value of intellectual property rights accept that there is a public interest in, and a commercial need for, patent protection.

100. For obvious reasons, the BIA has not set out to support either of the two parties to this appeal in its trenchant written submissions in these proceedings. However, it does suggest that if we agree with the reasoning of the Court of Appeal there is at least a risk that it will "make it appreciably harder for patentees to satisfy the requirement of industrial applicability in future cases." If that were so, it is suggested that this "would cause UK bioscience companies great difficulty in attracting investment at an early stage in the research and development process".

101. This consequence is said to arise from the reasoning of the Court of Appeal (and hence of Kitchin J), on the basis that there will normally be a need to conduct tests to provide experimental data to establish to the standard they require that a protein (or its antagonists) have therapeutic use. This in turn is said to lead to two problems. First, such tests will or may involve clinical work, which, as I understand it, would be hard to keep confidential, especially in the age of the internet. Secondly, such tests would often be expensive to run, and, as already mentioned, funding would be hard to obtain for a project of this sort which had no protection in the form of a patent application.

102. Having said this, the BIA accepts that it would be wrong in principle to enable applications for patents to be made when the applicant can reveal no more than "a vague indication of possible objectives that might or might not be achievable by carrying out further research". After all, as the BIA also states, the purpose of the patents system is not "to reserve an unexplored field of research for the applicant nor to give the patentee unjustified control over others who are actively investigating in that area and who might eventually find ways actually to exploit it."

Did the courts below follow the Board's jurisprudence?

103. As already mentioned, despite its very wide-ranging and generalised suggestions as to the uses to which Neutrokine-α and its antibodies might be put, over and above revealing the existence and structure of the new protein and its encoding gene, the only relevant teaching of the Patent ultimately arises from its teaching as to the tissue distribution of Neutrokine-α, its expression in T-cell and B-cell lymphomas, and the fact that it is a member of the TNF ligand superfamily. Accordingly, the question is whether the Judge was right, or at least entitled, to conclude that the inferences which would have been drawn from this in 1996 would not have been enough to satisfy Article 57.

104. The determination of that issue, as I see it, ultimately involves focussing on the Judge's conclusion at [2008] RPC 29, para 234, quoted at para 75 above. In that passage, he concluded that the fact that the description in the Patent, even taken together with knowledge which should be attributed to its addressee, neither "reveal[ed] how [Neutrokine-α] could be used to solve any particular problem" nor "identified any disease or condition which [it] could be used to diagnose or treat" was fatal to the patent's validity. He considered that the functions of Neutrokine-α "were, at best, a matter of expectation and then at far too high a level of generality to constitute a sound or concrete basis for anything except a research project".

105. My initial reaction, like that of the Court of Appeal, was that this was a conclusion to which Kitchin J, as the trial judge, who had heard a great deal of evidence, which he had impressively and cogently analysed, was entitled to come, and with which it would be inappropriate to interfere. Standing back, it also seemed to be a conclusion which could be said to accord with good sense. As he held in the next paragraph of his judgment (also quoted in para 75 above), it required what may fairly be characterised as a research project to enable the therapeutic qualities of Neutrokine-α to be identified, or, as HGS would put it, to be confirmed.

106. However, on further reflection, like Lord Hope, I have come to the conclusion that the basis upon which the Judge decided the issue was not consistent with the approach adopted by the Board in the decisions which are discussed above.

107. The essence of the Board's approach in relation to the requirements of Article 57 in relation to biological material may, I think, be summarised in the following points:

The general principles are:

(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); 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).

108. As already explained, Kitchin J concluded that (a) the Patent discloses Neutrokine-α as a new member of the TNF ligand superfamily; (b) all known members of the superfamily had pleiotropic effects, (c) there were some features which all those known members shared, such as expression by T-cells and a role in the regulation of T-cell proliferation and T-cell mediated responses; (d) however, there were other features which some family members had, but others did not; (e) it would be anticipated that the activities of Neutrokine-α "might relate to T-cells and, in particular, be expressed on T-cells and be a co-stimulant of B-cell production; that it might play a role in the immune response and in the control of tumours and malignant disease; that it might have an effect on B-cell proliferation"; (f) subsequent research has confirmed that was indeed the case; (g) there was a search for new members of the family as they were of interest to the pharmaceutical industry.

109. In those circumstances, it seems to me that, subject to dealing with a number of specific arguments to the contrary, the disclosure of the existence and structure of Neutrokine-α and its gene sequence, and its membership of the TNF ligand superfamily should have been sufficient, taking into account the common general knowledge, to satisfy the requirements of Article 57, in the light of the principles which I have

attempted to summarise in para 107 above. Points (viii), (ix) and (x) appear to apply so far as the plausibility of at least some of the claims are concerned, and points (xi), (xii) and (xiii) all appear to be satisfied, given the evidence in relation to the TNF ligand superfamily (and point (xiv) cannot be invoked by Eli Lilly).

110. Like Lord Hope, I derive considerable assistance from the approach set out at T 0018/09, para 22, which appears to me to be entirely consistent with the Board's earlier jurisprudence (as summarised in para 107 above), and the application in the ensuing four paragraphs, of that approach to the Board's view of what constituted the centrally relevant facts, which (subject to the arguments considered in the next section of this judgment) do not appear to me to be inconsistent with the findings made by Kitchin J.

111. As Lord Hope says at para 152 below, the Board's conclusion was effectively this, that the disclosure of what was accepted to be a new member of the TNF ligand superfamily (coupled with details of its tissue distribution) satisfied Article 57, because all known members were expressed on T-cells and were able to co-stimulate T-cell proliferation, and therefore Neutrokine-α would be expected to have a similar function. This conclusion was supported, or reinforced, by the statement that Neutrokine-α was expressed in B-cell and T-cell lymphomas (referred to in T 0018/09, para 30), and indeed by the interest and effort in the pharmaceutical industry in finding a new member of the superfamily (as explained by Kitchin J at [2008] RPC 29, paras 72-74).

The arguments in support of the conclusion reached below

112. The first argument to the contrary is based on the fact that the members of the TNF ligand superfamily were known to have pleiotropic effects. On behalf of Eli Lilly, Mr Waugh QC therefore relies on point (xv) i.e. that the claim to a new member of a superfamily is not good enough because the known members of the family have different activities. In my opinion, that point does not apply in a case where all known members of the superfamily also manifest to a significant degree common activities which are, of themselves, enough to bring the patent within the ambit of points (xi), (xii) and (xiii).

113. Given that the fact that all known family members have sufficient common features to satisfy those points can justify a patent for a new member, it would seem somewhat bizarre if the fact that they had additional, but differing, qualities, should preclude the grant of such a patent. The disclosure of a new member would not only be of greater potential value than if the additional qualities did not exist, but the reason for the grant of the patent is the perceived value of a new member because of the common features of all known members, a feature which is unaffected by the additional qualities.

114. I believe that this conclusion is supported not only by the Board's decision in this case, but also by the Board's conclusion in T 0898/05 that the disclosure of Zcytor1 satisfied Article 57, in circumstances where its predicted activity was based on its membership of a family. As already explained, the Board stated that "although none of these members are precisely interchangeable in terms of their biological action, there is considerable redundancy of action as well as an ability to elicit, under certain conditions, similar biological responses" – T 0898/05, para 27.

115. I also derive support from the fact that the Board in T 0604/04 was prepared to uphold a patent granted in respect of a novel molecule on the basis that it was a member of a family, only "most of" whose known members "were thought to play [a role as] mediators of the inflammatory response"; nonetheless, it was held that the evidence established that it was "reasonable to conclude that the [claimed] polypeptides which exhibit the characteristics of receptors of members of the PF4A family of cytokines would have been regarded as important to the pharmaceutical industry, ie that industrial applicability may be acknowledged" (see T 0604/04, paras 16-18).

116. A second argument raised against validity is the unsatisfactory drafting of the Patent (mentioned by the Court of Appeal at [2010] RPC 14, para 148). If the Judge had found that the drafting of the specification of the Patent was so confusing and potentially misleading that the skilled reader would have been put off the scent in relation to what would otherwise have been appreciated from common general knowledge and reading the literature as to the potential and plausible uses to which the disclosure could be put, that may well have been a problem for HGS's case. However, although the Judge was (in my view, rightly) critical about the drafting of the specification, he did not anywhere in his full and careful judgment say, or even suggest, that its wide-ranging prolix contents would have actually diverted the notional addressees, the appropriately skilled persons, from what they would otherwise have understood the Patent to be revealing, in the light of what was appreciated about the properties of the known members of the TNF ligand superfamily. Indeed, Mr Thorley QC, for HGS, identified passages in the evidence of Professor Saklatvala, which would have made such a finding difficult to justify.

117. Mr Waugh's submission that the extravagant and wordy claims of the specification should count against HGS as a matter of policy has some attraction. However, I refer again to the Board's comments at T 0018/09, para 27, cited in para 6 above. The drafting of a patent is a ticklish business, no doubt particularly in some types of case, of which biological patents may well be an example, not least because it is a fast developing field, with substantial commercial and scientific pressures.

118. In the end, the question is whether the drafting of the Patent would actually have diverted the notional addressees from what their search of the literature, coupled with common general knowledge, would otherwise have led them to understand represented the teaching of the Patent. The Board held that it would not

have done so – see at T 0018/09, para 26. Given (a) the fact that the Judge made no express finding that there would have been such a diversion, (b) the evidence of Professor Saklatvala suggested that there would have been no such diversion, and (c) the way in which the Judge expressed himself at [2008] RPC 29, paras 232 and 234 (quoted respectively at paras 70 and 75 above), I would infer that Kitchin J did not think differently. That is unsurprising, given the fact that there was fairly intense interest in the TNF ligand superfamily as the Judge held at [2008] RPC 29, paras 72 and 74 (quoted at para 26 above), and the fact that there is nothing in the description which positively points away from what was known about the family.

119. A third argument is based on the Judge's remarks at [2008] RPC 29, paras 176 and 234, that the disclosure in the Patent as to the uses of Neutrokine-α, even when taken together with common general knowledge, was no more than "speculative" and did not give rise to an "immediate concrete benefit"– i.e. invoking on points (ii) and (iii). This argument (which was also relied on by the Court of Appeal – see at [2010] RPC 14, para 132) proceeds on the implicit assumption that the disclosure of the Patent as summarised in para 108 above is not sufficient in itself to satisfy the requirements of Article 57.

120. However, if, as I consider, the effect of the Board's jurisprudence is that the sort of disclosure summarised in para 108 above does justify patentability, then the fact that the "plausible" predictions for the use of the invention could also be said to involve speculation takes matters no further. If the known activities of the TNF ligand superfamily were enough to justify patentability for the disclosure of a novel molecule (and its encoding gene) which was plausibly identified as a member of that family, the fact that further work was required to see whether the disclosure actually had therapeutic benefits does not, at least without more, undermine the validity of a patent. In other words, in agreement with Lord Hope, I think that the approach of the Board in this case, in particular at T 0018/09, paras 22-30, appears more in line with the previous EPO jurisprudence than the approach of Kitchin J and the Court of Appeal.

121. The Court of Appeal made much of the Board's statement that a patent should yield an "immediate concrete benefit" (see at [2010] RPC 14, paras 146, 149, 155 and 156). I certainly accept that, in some cases, different tribunals can and will legitimately come to different views as to whether a particular claimed invention can satisfy the requirement of providing an "immediate concrete benefit". However, I am not persuaded that such an argument is open to Eli Lilly in this case. In my view, the Court of Appeal's approach, like that of the Judge, was implicitly predicated on the mistaken basis that it was not enough for the Patent to satisfy the requirements of points (xi) to (xiii).

122. Further, at least in the context of the present case, I do not consider that the Courts below gave proper weight to points (viii), (ix) and (x). In particular, in my judgment, the Court of Appeal did not approach the concept of plausibility consistently with the jurisprudence of the Board. That is well demonstrated by Jacob LJ's observation at [2010] RPC 14, para 112, that "[i]t is not good enough to say this protein or any antibody to it probably has a pharmaceutical use. Such a statement is indeed plausible, but is of no real practical use. You are left to find out what that use is." If the statement "is indeed plausible", then, in the absence of any reason to the contrary, it at least prima facie satisfies the requirements of Article 57 according to the Board.

123. I appreciate that the dividing line between "plausibility" and "educated guess", as against "speculation", just like the contrast between "a real as opposed to a purely theoretical possibility of exploitation", can be difficult to discern in terms of language and application, and is a point on which tribunals could often differ. (I might add that the notion that the dividing line is not very satisfactory is illustrated by the fact that, at one point in his evidence, Professor Saklatvala effectively equiparated speculation with an educated guess.) However, as a result of the decisions discussed above, the Board's approach to patents such as that in this case is, I believe, tolerably clear.

124. I also consider that the Judge did not give sufficient weight to point (x), in that he concentrated on the absence of firm evidence of specific therapeutic roles, as opposed to the other roles of Neutrokine-α. This is well demonstrated by his reliance in what is perhaps the crucial paragraph of his judgment, [2008] RPC 29, para 234, on the fact that "[n]either the Patent nor the common general knowledge identified any disease or condition which Neutrokine-α could be used to diagnose or treat". He did not, in this context, take into account the roles at other levels which could be attributed to Neutrokine-α as a result of its membership of the TNF ligand superfamily and their known activities. (The same point may be made about Jacob LJ's judgment at [2010] RPC 14, paras 112 and 119, quoted by Lord Hope at para 150 below).

125. Eli Lilly also relied on the Judge's finding at [2008] RPC 29, para 234 that the precise uses to which Neutrokine-α could be put would, on the basis of the disclosure in the Patent, involve "a research project", effectively raising point (iv). Although the Court of Appeal also relied on this point (see at [2010] RPC 14, para 149), it does not appear to me to be maintainable, essentially for the reason given in the immediately preceding paragraphs of this judgment.

126. I draw support for this conclusion from the Board's third reason for rejecting a similar argument raised by Eli Lilly in the EPO, namely that "the skilled person would not have been able to reproduce [the activities of Neutrokine α as described in the Patent] without the undue burden of undertaking a research programme". The Board said that the disclosure of the Patent "may represent a valid basis for a possible industrial application. In particular, the inhibition of costimulation and/or proliferation of lymphocytes might be prima facie of relevance for certain immune

diseases" - in T 0018/09, para 29. If a patent advances an appropriately plausible function for the claimed protein, then the question of undue burden has to be considered in relation to the making of the protein, as the Board's observation at T 0604/04, para 22 that "the patent specification provides adequate experimental instructions for the skilled person to be able to reproduce without undue burden the [claimed] polypeptides" shows.

127. A further argument, which is really another formulation of the same point, is that, as was emphasised by the Court of Appeal at [2010] RPC 14, para 152, one important reason why Kitchin J reached a different conclusion from the Board was because he concluded that the necessary assays to determine the precise role and potential of the patent's disclosure would be a "complex task", whereas the Board thought it would simply involve "standard assays" – compare [2008] RPC 29, para 77, and T 0018/09, para 29 respectively.

128. As the Court of Appeal rightly observed, such a conflict is entirely legitimate and understandable, in view of the different evidence, the benefit of cross-examination, and/or the room for difference of opinion between two tribunals. In another case, such a difference in assessment of the evidence could well justify a difference in outcome. But not in this case. Once one concludes that the effect of the Board's jurisprudence is that, in the light of the common general knowledge, the disclosure of Neutrokine-α as a member of the TNF ligand superfamily (coupled with its amino acid and encoding gene sequences and the tissues in which it is expressed), the claims in relation to the invention's potential satisfy Article 57. As a result, the relevance of the degree of effort needed in relation to any subsequent work falls away. (The same point undermines Eli Lilly's reliance on a number of other small differences between the findings of the Judge and the Board on the expert evidence).

Conclusion on the main issue, Article 57

129. Accordingly, I would allow HGS's appeal on the issue as to whether the Patent satisfied the requirements of Article 57, and hold that it does. As explained, I have reached this conclusion by applying my understanding of the jurisprudence of the Board to the facts found by Kitchin J. However, particularly as I have stated in para 105 above that there is good sense in the contrary conclusion reached by the Judge and the Court of Appeal, it is right to emphasise that there is also good sense in the result which, at least in my view, is mandated by the Board's approach to the law in this field.

130. Just as it would be undesirable to let someone have a monopoly over a particular biological molecule too early, because it risks closing down competition, so it would be wrong to set the hurdle for patentability too high, essentially for the reasons advanced by the BIA and discussed in paras 97-100 above. Quite where the line should be drawn in the light of commercial reality and the public interest can no doubt be a matter of different opinions and debate. However, in this case, apart from the fairly general submissions of the parties and of the BIA, we have not had any submissions on such wider policy considerations.

131. That is not the end of this appeal, for two reasons. First, there is an argument based on insufficiency: Eli Lilly contends that, even if the Patent satisfies Article 57, it is invalid on the ground of insufficiency, an argument which largely turns on an issue of interpretation, on which the Judge found against Eli Lilly. Secondly, if Eli Lilly's insufficiency argument fails, there remain some points decided by Kitchin J and not determined by the Court of Appeal, which it is agreed should be remitted to the Court of Appeal.

The contention that claim 1 of the Patent is insufficient

132. The Judge held that, in addition to failing to comply with Article 57, the Patent was invalid on the ground of insufficiency, namely that "the specification does not disclose the invention clearly enough and completely enough for it to be performed by a person skilled in the art" – [2008] RPC 29, para 238. The basis for this conclusion was explained in these terms by the Judge at [2008] RPC 29, para 259: "it would have required a research programme and been far from routine for the skilled person to produce a candidate pharmaceutical or diagnostic composition comprising an antibody to Neutrokine-a, that is to say the pharmaceutical or diagnostic equivalent of a workable prototype".

133. Although the Court of Appeal did not consider this point, Jacob LJ did say at the end of his judgment, that he "rather suspect[ed]" that the insufficiency argument "would go hand-in-hand with Article 57" – [2010] RPC 29, para 159. Subject to one point, which turns on the meaning of Claim 1 (as well as some of the other claims), it seems to me that that must be correct. If Claim 1 is simply to the encoding gene of Neutrokine-α, then, subject to any other points which have yet to be decided by the Court of Appeal, the reason why I consider the Judge and the Court of Appeal were wrong to hold that Article 57 is not satisfied is the same reason for holding the claim to be sufficient.

134. In T 0898/05, para 6, the Board explained the close connection, indeed overlap, between Article 57 and sufficiency in a passage, of which the first sentence has already been quoted:

"It should not be left to the skilled reader to find out how to exploit the invention by carrying out a research programme. [This] corresponds to the requirements of Articles ... 57 (the need to indicate how to exploit the invention), and 83 EPC (the need to provide a sufficient disclosure of the claimed invention). All those provisions reflect the basic principle of the patent system that exclusive rights can only be granted in exchange for a full disclosure of the invention."

135. However, Eli Lilly contend that the Judge was wrong to hold, as he did at [2008] RPC 29, para 137, that claim 1 "is now limited to an isolated nucleic acid molecule comprising one of two sequences which are specifically disclosed and are not defined by reference to their activity". They contend that, on its true

construction, the claim requires the claimed protein, or polypeptide to demonstrate what is referred to in the specification as "Neutrokine-α activity", and that such activity is too imprecisely defined and too difficult to establish, following the
teaching of the Patent and any prior art, to be sufficient.
136. Claim 1, which I have not so far set out, is in the following terms:
"An isolated nucleic acid molecule comprising a polynucleotide sequence encoding a Neutrokine-α polypeptide wherein said polynucleotide sequence is selected from the group consisting of:
(a) a polynucleotide sequence encoding the full length Neutrokine-α polypeptide having the amino acid sequence of residues [as defined]; and
(b) a polynucleotide sequence encoding the extracellular domain of the Neutrokine-α polypeptide having the amino acid sequence of residues [as defined]".
137. In my view, the Judge was right to conclude that the reference to a "Neutrokine-α polypeptide" was simply a reference to the polypeptide, and did not incorporate a provision that the polypeptide had certain activities. There is no express reference in the claim to the polypeptide having any specific activities, and I see no grounds for implying into claim 1 such a provision. There is no commercial or technical reason for implying such a provision, and, of course, it is well established that a term is only to be implied into a written document if there are strong reasons in support.
138. It is true that the phrase "Neutrokine-α" before the word "polypeptide" is strictly redundant on this basis, but that is no reason for giving the phrase an unnatural meaning. The fact that the phrase is strictly redundant does not alter the fact that its natural meaning is to describe the polypeptide by the name which the specification has given to it. It is also true that the specification refers to the claimed invention involving "Neutrokine-α activity" in more than one place. However, the very fact that this expression is not included in claim 1, when it is (to some extent) defined and, in more than one place used, in the specification suggests that it is not intended to apply to the claim.
139. Accordingly, I would dismiss Eli Lilly's cross-appeal on the insufficiency issue.

Conclusion

140. It follows from this that, at least in my opinion, HGS's appeal on the Article 57 issue should be allowed, Eli Lilly's cross-appeal on the insufficiency issue should be dismissed, and the case should be remitted to the Court of Appeal to deal with the outstanding issues.

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LORD HOPE

141. This is a difficult and troublesome case. It is well known that modern techniques in the field of biomedical science offer immense benefits in the promotion of human health, particularly in the combating of a wide range of degenerative diseases previously thought to be incurable and in the provision of techniques for the effective treatment of cancers. As the BioIndustry Association has pointed out in its written intervention, patent portfolios are often the most valuable asset of companies in the bioscience industry. So assessments of the value of a bioscience company's patent portfolio are likely to be a key consideration in deciding whether to acquire or invest in such a company. This in turn affects the funding that is made available for research and development, without which effective progress in putting a patented invention to practical use is likely to be very limited. The evaluation of a patent specification for this purpose will depend on whether it discloses an invention that is reasonably capable of industrial application.
142. There is thus much common ground between the aims of those whose funding is essential for the sustained programme of research and development that will almost always have to be carried out before a product can be placed on the market and the tests that the law lays down for patentability.
Article 52(1) of the European Patent Convention provides:
"European patents shall be granted for any inventions, in all fields of technology, provided that they are new, involve an inventive step and are susceptible of industrial application."
Article 57 provides:
"An invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture."
These articles were implemented in domestic law in sections 1(1)(c) and 4 of the Patents Act 1977. As the tests in both articles are the same, it is convenient to refer to the issue which they raise as the article 57 issue. It is plain that the standard to be applied for determining whether this test has been satisfied must in principle be the same for patents in the bioscience industry as for those in other fields.
143. The bioscience industry is particularly dependent, however, on funding for long term research and development. It is commonplace for those who need money for these activities to have to look to other organisations to provide it. The tests that must be applied are necessarily very rigorous, and it may require many years of investment before a product can be declared safe for use in the promotion of health in humans. The gap between the point of initial research and the point where the discovery is ready to be developed by the pharmaceutical industry can be very wide. Various steps along this uncertain road can be identified in the present case. First, there is the inventive step itself. In this case it revealed the existence of Neutrokine-α, a previously unknown member of the TNF ligand superfamily. The characteristics of the newly discovered protein had then to be examined and analysed. In this case the task was to determine whether the Neutrokine-α molecule had characteristics that offered the prospect of influencing biological mechanisms in the same way as other members of the superfamily. If that could be achieved,

there would then have to follow a large amount of research and development before the molecule could be deployed therapeutically. The question that this case raises is how far along that road the process must go before the invention can be held to be susceptible of industrial application and patented.

144. The core of HGS's argument for the industrial application of Neutrokine-α was identified by their expert witness Professor Noelle in his first witness statement. In para 72 he said:

"*In my opinion, the inventive concept of the Patent is the identification of a new member of the TNF ligand superfamily, which the inventors named Neutrokine-α, and elucidation of its nucleic acid and amino acid sequences. Once the nucleic acid sequence of a novel member of the TNF ligand superfamily became available, it opened up the field such that it was possible to use well known techniques to express the protein, analyze the protein, develop antibodies and make therapeutics and diagnostics for diseases associated with under or over expression of the protein."*

In para 75 he said that disclosure of this novel gene and its encoded protein, and the provision of information about its structure and activities enabled the making of products which could be used in studying its role in disease and for the development of potential diagnostic and therapeutic applications. In para 79 he said that, since the activities ascribed to Neutrokine-α in the Patent were consistent with those activities possessed by other TNF superfamily members, the skilled addressee would consider the activities of Neutrokine-α described in the Patent as specific and also credible. His point, in short, was the description of the protein, when taken with common knowledge as to the techniques that could be applied to it, was sufficient to show that it was possible to use it in the respects that he identified. For him the fact that it opened up the field indicated that it was susceptible of industrial application.

145. The significance of his observations can be seen by comparing what Jacob LJ said in the Court of Appeal with the judgment of the Technical Board of Appeal ("TBA") of the European Patent Office ("the EPO") in the present case, which was published on 1 December 2009: Neutrokine-α/Human Gennome Sciences Inc T 0018/09. The Board reached a different conclusion from that which the trial judge, Kitchin J, had reached on 31 July 2008 when he held that the claimed invention was not susceptible of industrial application at the date of the Patent: [2008] RPC 29, para 237. In the Court of Appeal Jacob LJ attributed this to the fact that the Board was working on different evidence and was using a different procedure: [2010] RPC 14, para 157; see also para 154, where he noted that the judge's findings were arrived at following an extensive examination of the evidence. I think that, while both of these things are true, the conclusion ought to have been that tests that the Board applied were materially different from those applied by the judge and by the Court of Appeal.

146. In para 22 of the reasons for its decision that the Patent provided a concrete technical basis for the skilled person to recognise a practical exploitation of the claimed invention in industry, the TBA said:

"22. As pointed out in T 870/04 of 11 May 2005 [Max-Planck] (cf in particular points 5 and 6 of the Reasons), in many cases the allocation of a newly found protein to a known protein family with known activities suffices to assign a specific function to the protein because normally the members of the family share a specific function. This may be a well-characterized and perfectly understood function which provides in a straightforward manner enough support for industrial applicability. In such cases, the 'immediate concrete benefit' is manifest. In other cases, where the members of a protein family have different, pleiotropic effects which may even be opposite and neither completely characterized nor understood, no effect can be assigned to a new member without relying on some experimental data. Between these two extreme situations, a variety of other situations may arise for which a detailed examination of all the facts may be required. Indeed, this is the case for the TNF ligand superfamily."

147. The expression "superfamily" does not appear to have a precise meaning, as Jacob LJ observed in the Court of Appeal: [2010] RPC, para 73. As he explained, the general idea is that it includes not only very closely homologous compounds but also those with rather less homology. The contrast is between a closely knit family with known activities, and a wider family with a variety of different, pleiotropic effects: cousins, second cousins, distant uncles and so on. The same contrast between two extremes is to be found in para 22 of the TBA's judgment. But the important point that emerges from its comment that it was dealing with a superfamily is to be found in the last two sentences. This case is not one where the different, pleiotropic effects are so poorly understood that it is plain that no effect can be assigned to a new member without relying on some experimental data. That is not true of the TNF ligand superfamily as it lies between the two extremes.

148. So a detailed examination of all the facts is needed before it can be determined whether or not an effect can be assigned to this particular new member. As the TBA said in T 0898/05 (7 July 2006) Hematopoietic cytokine receptor/ZymoGenetics, para 22, the probative value of the claimed invention must be examined on a case-by-case basis regarding the nature of the invention and the prior art relating thereto:

"Such methods of analysis are increasingly becoming an integral part of scientific investigations and can often allow plausible conclusions to be made regarding the function of a product before it is actually tested."

In other words, that examination may be enough in itself to show, without further experiments, that what the TBA refers to as "a specific function" can be assigned to the new member of the family. This is because that "well-characterized and perfectly understood function" is shared by other members of the family which it has been shown to belong to.

149. In paras 6-8 of its judgment in ZymoGenetics the TBA contrasted a product whose structure was given but whose function was undetermined or obscure or only vaguely indicated with one which was "definitely described and plausibly shown to be usable". In the former case, the granting of a patent might give the patentee unjustified control over others who were actively investigating in that area and who might eventually find ways to exploit it. In the latter, because it was plausibly shown to be "usable", it might be considered to display concrete benefits. As these benefits are assumed not yet to have been confirmed by research, the exercise that these passages indicate is necessarily one of prediction. That is why the Board used the word "plausibly". I would not quarrel with Jacob LJ's comment, after consulting the Shorter Oxford English Dictionary, that the sense that word conveys is that there must be some real reason for supposing that the statement is true: para 111. The important point, however, is that the standard is not any higher than that. Further experiments are not needed if sufficient information is provided in the description, when common general knowledge is taken into account, to show that a positive answer can be given to the question whether a profitable use can readily be identified: ZymoGenetics, para 20.

150. In para 102 of his judgment in the Court of Appeal, however, having reviewed the EPO case law, Jacob LJ said:

"It is clear from these authorities that discovering a nucleotide sequence encoding for a human protein and being able to show that the protein concerned has some common homology with known proteins (ie is a member of a family) may satisfy article 57. But whether it does or not is case dependent and in particular depends upon how well established the functions of the other members of the family are. To say, 'my new protein is similar to a known family of proteins' is not all that helpful in indicating a possible use if the function of that family is itself poorly understood at best."

In para 112, having said that to be "plausible" a statement must be sufficiently precise, he added:

"It is not good enough to say this protein or any antibody to it probably has a pharmaceutical use. Such a statement is indeed plausible, but is of no real practical use. You are left to find out what that use is."

In para 119, having summarised the findings and conclusions of Kitchin J, he said:

"So the Judge addressed the crucial question: is it enough to make the invention 'susceptible of industrial application' to tell the skilled reader that Neutrokine-α is 'structurally similar to TNF and related cytokines and is believed to have similar biological effects and activities'? That depends on what was known about the biological effects and activities of the known members of the superfamily. Each of the postulated uses of Neutrokine-α or its antagonists was possible in the sense that one could not rule that out as a matter of science based on what was known about other superfamily members. So in one sense each was 'plausible', even though all of them collectively were not and indeed some contradicted others so both could not be true. But that is miles away from being able to say that any particular use was plausible in the sense of being taken, by the reader, to be reasonably so. In reality one was faced with a research programme to see which, if any, of the possible uses of the Neutrokine-α or its antagonists was real."

151. I think that there are indications in these passages that the standard which Jacob LJ was setting for susceptibility to industrial application was a more exacting one than that used by the TBA. He appears to have been looking for a description that showed that a particular use for the product had actually been demonstrated rather than that the product had plausibly been shown to be "usable".

152. In para 23 of the reasons for its decision in the present case the TBA noted that, as known in the art and acknowledged in the Patent, a feature common to all members of this particular superfamily without exception was the expression on activated T cells and the ability to co-stimulate T cell proliferation. It followed, in view of the assignment of Neutrokine-α to the family, that the skilled person would expect it to display that common feature. Asking itself whether there was anything in the patent specification which contradicted that expectation, the Board found that the technical data in the patent specification, far from contradicting the ability of Neutrokine-α to co-stimulate T-cell proliferation, actually supported it. That information could not be taken as a mere theoretical or purely hypothetical assumption.

153. In para 26 the TBA said that a skilled person, when reading the patent specification, would distinguish the positive technical information from the contradictory and broad statements to which Eli Lilly had drawn its attention:

"This is because the skilled person realises that the description of the structure of Neutrokine-α, its structural assignment of the family of TNF ligands, and the reports about its tissue distribution and activity on leucocytes, are the first essential steps at the onset of research work on the newly found TNF ligand superfamily member. In view of the known broad range of possible activities of such a molecule, the skilled person is aware of the fact that the full elucidation of all properties requires further investigations which will gradually reveal them. In this context, the skilled person regards the long listing of possible actions of Neutrokine-α and of medical conditions in which it might take part as the enumeration or generalisation of the properties of the members of the TNF ligand superfamily. This is seen as the frame in which the newly found molecule has to be placed as one could prima facie have a reasonable expectation that most of them could in fact be present."

154. This is in sharp contrast to Jacob LJ's comment in [2010] RPC 14, para 145 that the Patent, even in relation to T-cell activity, was just too speculative to provide anything of practical value other than information upon which a research programme could be based. Referring to the first sentence of the passage

which I have just quoted, he then said that "a first step at the onset of research work" was hardly enough to provide "an immediate and concrete benefit": para 149. The phrase "immediate concrete benefit" – the "and" which Jacob LJ inserted into this phrase is his own word – comes from para 6 of the TBA's reasons for its decision in ZymoGenetics; see also para 21 of its reasons in the present case. Here again there is an indication that Jacob LJ was applying a different test from that applied by the TBA. The immediate concrete benefit that he was looking for was something more than that there was a reasonable expectation that the molecule would be usable for the purposes of research work.

155. In para 27 the TBA said that, despite its long list of conditions and activities, the description of the Patent delivered sufficient technical information (namely the effect of Neutrokine-α on T-cells and the tissue distribution of Neutrokine-α mRNA) to satisfy the requirement of disclosing the nature and purpose of the invention and how it could be used in industrial practice. In para 29 it rejected Eli Lilly's arguments that, in view of the technical difficulties involved in measuring the co-stimulation of T cells by Neutrokine-α and the absence of any detailed experimental information on the activities of Neutrokine-α listed in the Patent, the skilled person would not have been able to reproduce them without the undue burden of undertaking a research programme and that no industrial application could be directly derived from a mere co-stimulation of T-cells. It pointed out that there was a convincing body of post-published evidence showing that, using standard assays, Neutrokine-α activity was indeed present on T-cells, that the reference in the Patent to the presence of Neutrokine-α activity in lymphocytes would prompt the skilled person to look for that activity in all types of lymphocytes, including B lymphocytes as well as T lymphocytes. Contrary to Eli Lilly's view, it held that these activities might represent a valid basis for a possible industrial application. The industrial application that it had in mind was the use of the molecule for research, which it must be taken to have regarded in itself as an industrial activity.

156. Developing this point further, the TBA said in para 30:

"In the board's judgment, the tissue distribution of Neutrokine-α mRNA disclosed in the patent-in suit, in particular the expression of Neutrokine-α mRNA in B-cell and T-cell lymphomas (cf paragraph [0032]), provides in itself in the context of the disclosure a valid basis for an industrial application. The presence of Neutrokine-α in these lymphomas, which is also confirmed by post-published evidence on file (cf inter alia document D126), may be used to develop appropriate means and methods for their diagnosis and treatment based on the disclosure of the patent-in-suit."

157. These passages are important not so much for the assessment of the evidence that was before the TBA, with which the national court may properly disagree if presented with evidence which it accepts to the contrary, as for the clear indication that they give as to the point in the development of an invention in the biosciences field where it may be said that the requirement that the invention shall be considered as susceptible of industrial application can be taken to have been satisfied. The concluding words of the last sentence of para 30 indicate that the test which the Board was applying, as in ZymoGenetics, para 8, was whether Neutrokine-α was plausibly shown to be "usable". I read this as indicating that it was satisfied that the protein was a research tool which could be used to develop appropriate means and methods for the diagnosis and treatment of B-cell and Tcell lymphomas. In the Board's judgment that was enough for it to be susceptible of industrial application within the meaning of article 57 of the Convention.

158. Kitchin J did not have the benefit of seeing the judgment of the TBA in this case, as it was published more than a year after he handed down his judgment on 31 July 2008. He identified the principles that had emerged from the decisions of the EPO in his judgment at [2008] RPC 29, para 226. Among them were the following (case references omitted):

"(vi)…the purpose of granting a patent is not to reserve an unexplored field of research for the applicant nor to give the patentee unjustified control over others who are actively investigating in that area and who might eventually find ways actually to exploit it.

(vii) If a substance is disclosed and its function is essential for human health then the identification of the substance having that function will immediately suggest a practical application. If, on the other hand, the function of that substance is not known or is incompletely understood, and no disease has been identified which is attributable to an excess or a deficiency of it, and no other practical use is suggested for it, then the requirement of industrial applicability is not satisfied. This will be so even though the disclosure may be a scientific achievement of considerable merit.

(viii) Using the claimed invention to find out more about its activities is not in itself an industrial application."

He derived these principles from the reasons that the TBA gave for its decisions in BDP1 Phosphatase/Max-Planck T 0870/04 (11 May 2005) and, in the case of the second part of the principle in para (vi), from para 8 of ZymoGenetics. But he did not pick up the point made in para 8 of ZymoGenetics that a product which is definitely described and plausibly shown to be usable might be considered to have a profitable use or concrete benefit, or the point made in para 22 that computerised methods of analysis are increasingly becoming an integral part of scientific investigations and that they can often allow plausible conclusions to be made regarding the function of a product before it is actually tested. Careful though his analysis was, I think that it tended to divert attention away from points that were likely to produce an appropriately balanced decision in this case.

159. In para 230 the judge said:
"I accept that the contribution made by HGS was to find Neutrokine- α and to identify it as a member of the TNF ligand superfamily. However it is clear from the cases to which I have referred that simply identifying a protein is not necessarily sufficient to confer industrial utility upon it. Multimeric Receptors/Salk Institute is just one example. It may be sufficient if the identification of the protein will immediately suggest a practical application, such as was the case with insulin, human growth hormone and erythropoietin. But if the function of the protein is not known or is incompletely understood and if no disease has been attributed to a deficiency or excess of it, then the position may well be different. In these cases the industrial utility must be identified in some other way.
In paras 231-232 he said that he was quite satisfied that the skilled person would consider that the Patent did not by itself identify any industrial application other than by way of speculation. The range of diseases and conditions which Neutrokine-α and antibodies to Neutrokine-α might be used to diagnose and treat were astonishing and there was no data of any kind to support the claims made. But he recognised that the disclosure had to be considered in the light of the common general knowledge. Thus the skilled person would have known that TNF was involved as a primary mediator in immune regulation and the inflammatory response and had an involvement in a wide range of diseases, that all the members of the TNF ligand superfamily identified hitherto were expressed by T cells and played a role in the regulation of T cell proliferation and T cell mediated responses. Further, as Eli Lilly's expert witness Professor Saklatvala accepted, the skilled person would anticipate that the activities of Neutrokine-α might relate to T cells, be expressed in T cells and be a co-stimulant of B cell production and that it might play a role in the immune response and in the control of tumours and malignant disease and have an effect of B cell proliferation.
160. Thus far, his analysis of the evidence matches that in paras 27-30 of the reasons which the TBA gave for its decision in this case: see paras 155-156, above. But he then went on to say in para 233 that the skilled person would also have known that the members of the family had pleiotropic actions, that some of those activities were unique to particular TNF ligands and others were shared by some or all the other TNF ligands, that no disease had been identified in which they were all involved and that the known therapeutic application of the TNF-α monoclonal antibody was a rather specific activity. In para 234, drawing these conclusions together, he said:
"Does that common general knowledge, taken as a whole, disclose a practical way of exploiting Neutrokine-α? Or does it provide a sound and concrete basis for recognising that Neutrokine-α could lead to practical application in industry? In my judgment it does not. The fact that Neutrokine-α might be expected to play a role in regulating the activities of B cells and T cells and play an unspecified role in regulating the immune and inflammatory response did not reveal how it could be used to solve any particular problem. Neither the Patent nor the common general knowledge identified any disease or condition which Neutrokine-α could be used to diagnose or treat. Its functions were, at best, a matter of expectation and then at far too high a level of generality to constitute a sound or concrete basis for anything except a research project."
In para 237 he said that he was satisfied that this was a case where the claimed inventions were not susceptible of industrial application at the date of the Patent. It was no answer to say that subsequent research had shown that they might be useful to treat diseases associated with particular B cell disorders.
161. I think that there is here a significant drift away from the approach indicated by the TBA's reasons in ZymoGenetics as subsequently confirmed by the reasons for its decision in the present case. This is not just because the Board was working on different evidence and was using a different procedure, as Jacob LJ seems to have thought. There is a very obvious difference of view as to the test that the invention had to satisfy to be susceptible of industrial application. For the TBA, the question was whether, taking the common general knowledge into account, it had been plausibly shown that the molecule was usable. It was not necessary for a skilled person to undertake a research programme to conclude that the presence of Neutrokine-α in B cell and T cell lymphomas might be used to develop appropriate means and methods for their diagnosis and treatment: para 30. For the judge, this did not go far enough. For him the critical point was that neither the Patent nor the common general knowledge identified any disease or condition which Neutrokine- α could be used to diagnose or treat: [2008] RPC 29, para 234.
162. In para 29 of its reasons in ZymoGenetics the TBA said that the function of a protein, and thus of the nucleic acid encoding it, could be seen at different levels: (i) its molecular function, revealed by the biochemical activity of the protein; (ii) its cellular function, in regard to cellular processes; and (iii) the influence of those cellular processes in a general and more complex network within a multicellular organism, this being its biological function in a broad sense. In para 30 it said that the elucidation of one of those particular levels of function might result in a straightforward industrial application, even though the other levels of activity remained completely unknown or only partially characterised. In ZymoGenetics the suggested role for the receptor corresponded to the biological function, and the therapeutical treatments directly derivable from it were not considered to be so vaguely defined that they did not suggest any therapeutic or diagnostic use: para 31. In the present case the role that the TBA saw for Neutrokine-α was in connection with activities at the level of the cellular function, and this in itself was seen to provide a valid basis for an industrial application: paras 29-30.
163. Jacob LJ observed, I think correctly, that the Board thought that standard assays, of the kind

revealed by common general knowledge, would do the job of providing an immediate concrete benefit: [2010] RPC 14, para 152. He then said that the judge's finding on the facts was to the opposite effect. He quoted the following passage from para 77 of Kitchin J's judgment:

"…In my judgment the skilled person would indeed have been able to identify or develop from his common general knowledge some assays with which to begin the study of the new ligand and start to asses at least some of its possible activities. But I am not satisfied that such studies would have produced informative results and I have no doubt that to carry out a comprehensive screening programme so as to identify the role of the ligand in the biology of any particular cell type would be an altogether more complex task, and one properly characterised as a research programme."

In other words, it was necessary for the skilled person to be able to identify the role of the ligand in the biology of a particular cell type before the newly discovered molecule could be said to be susceptible of industrial application. The test which both he and the judge were applying was not that indicated by the TBA.

164. The same approach is to be found in early parts of his judgment. In para 119 he said that the reader was faced with a research programme to see which, if any, of the possible uses of Neutrokine-α or its antagonists "was real". In para 130, in his discussion of Gruss and Dower's assessment of the practical usefulness of the TNF ligand superfamily as a whole he said that their observations were far from saying that any member of the superfamily or its agonists had "real or indeed any potential as a therapeutic or diagnostic agent". In para 142 he referred to the fact that the judge had preferred Professor Saklatvala's evidence that by 1996 only TNF-α "had been shown to be biomedically useful" to Professor Noelle's comment that he would expect Neutrokine-α to be useful in the same way as other members of the TNF ligand superfamily. In para 145 he said that the Patent was just too speculative to provide anything of practical value "other than information upon which a research programme can be based." It is clear from these passages that for him the fact that the skilled addressee would see that the molecule was usable for a programme of research work, which the TBA thought he would, was not sufficient.

165. For these reasons I cannot agree with Jacob LJ that the differences between the conclusions reached by the judge and the TBA are attributable to the fact the Board was working on different evidence and was using a different procedure. It seems to me that they are attributable to differences of principle about the amount of information that was needed to show that the invention was susceptible of industrial application. The test to be applied to determine this issue is a question of law, not one of fact. As Jacob LJ observed, our practice is to follow any principle of law clearly laid down by the TBA: [2010] RPC 14, para 39.

166. It is a strong thing to disagree with the concurrent findings of judges with such experience in this field. But our decision in this appeal does not depend on a re-evaluation of the evidence. It turns on the principle of law which I find clearly set out by the TBA in the passages to which I have referred. In my opinion that principle leads inevitably to the conclusion that HGS's appeal on the article 57 issue must be allowed and the decision of Kitchin J that the claimed inventions were not susceptible of industrial application at the date of the Patent set aside. I would dismiss Eli Lilly's cross-appeal on the issue of insufficiency for the reasons given by Lord Neuberger. I too would remit the case to the Court of Appeal to deal with the outstanding issues.

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LORD WALKER

167. As Lord Hope observes, this is a difficult and troublesome case. It is also an important case: not only for the parties, but also for the bioscience industry generally (as the intervention of the BioIndustry Association makes clear) and, in some measure, for the future course of patent law in the United Kingdom.

168. I have to say that all my instincts, as an appellate judge, are for dismissing this appeal. The issue is one of multi-factorial evaluation of evidence, a task which has already been carried out twice, with the same result, by a very experienced patent judge, and a division of the Court of Appeal presided over by a Lord Justice with even more experience in the field of patents. Their task was to evaluate the evidence against a statutory test expressed in simple terms, whose meaning is not necessarily made much clearer by elaborate judicial exposition (see the quotation in para 170 below).

169. This Court has recently, in Lucasfilm Limited v Ainsworth [2001] UKSC 39, [2011] 3 WLR 487, para 45, reinforced Lord Hoffmann's much cited statement of the importance, in cases of this sort, of deference to the conclusions of the trial judge. What Lord Hoffmann said in Biogen Inc v Medeva Plc [1997] RPC 1, 45 is too well-known to need repetition. It applies even more strongly in the case of concurrent findings. The same thought was expressed (in a dissenting judgment) by Justice Kirby in the High Court of Australia in Aktiebolaget Hassle v Alphapharm Pty Ltd [2002] 212 CLR 411, para 95 (references omitted):

"The conclusions on obviousness in the proceedings below represented the outcome of a judicial evaluation of a mass of evidence. In the assessment of that evidence, and in the conclusion to be derived from it, the primary judge and the Full Court were better placed to perform the function of fact-finding than this Court is. Unless some error is shown in the application of the relevant law, it would be a rare step for this Court to condescend to re-evaluate such a factual conclusion, reached by concurrent decisions at two levels of the judicial hierarchy."

170. Kirby J also quoted from Biogen, observing (para 97):

"Any exposition of judicial reasons explaining such factual findings is 'inherently an incomplete statement of the impression which was made upon [the judge] by

the primary evidence.' Judges having replaced juries in such matters in Australia, and having entangled themselves in a web of horrible verbal formulae, must do their best to explain their conclusions where, in the past, juries simply announced their verdicts."

171. Nevertheless the powerful and sustained analysis and reasoning in the judgments of Lord Hope and Lord Neuberger has persuaded me, against my inclination, that this appeal must be allowed. There is nothing that I can usefully add to their reasoning, except to repeat that there are two strong policy arguments for allowing the appeal. The first is to reduce the risk of a chilling effect on investment in bioscience (though here the arguments are certainly not all one way).

The other is to align this country's interpretation of the European Patent Convention more closely with that of other contracting states. To my mind these considerations justify this Court in taking what would otherwise be a questionable course.

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LORD CLARKE

172. Like Lord Neuberger, I was initially attracted by the submission that, as the Court of Appeal held, Kitchin J was entitled to reach the conclusion he did. Moreover, Lord Walker has expressed with clarity the correct approach of an appellate court in a case such as this. In short, where the judge, especially a judge of great experience in his field has carried out what Lord Walker calls a multifactorial evaluation of the evidence and the Court of Appeal has refused to interfere with that evaluation, it will be the rare case indeed in which this Court will be entitled to interfere.

173. However, like Lord Walker, I have been persuaded by the detailed analysis by Lord Neuberger of the decisions in this and other cases of the Technical Board of Appeal of the European Patent Office that the appeal should be allowed. In all the circumstances I would allow the appeal for the reasons given by Lord Neuberger and Lord Hope.

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LORD COLLINS

174. For the reasons given by Lord Neuberger and Lord Hope, I would allow the appeal.