Court of Appeal, London, 9 February 2010, Eli Lilly v Human Genome Sciences

Appeal allowed and case remitted: IPPT20111102, UKSC, Human Genome Sciences v Eli Lilly

PATENT LAW

Authority of decisions of the Technical Boards of Appeal

- **We follow any principle of law clearly laid down by them, only reserving the right to differ if we are sure that the commodore is steering the fleet on to the rocks**

When it comes to legal principles the position of the TBAs (and even more so of course, the Enlarged Board) stands quite differently from its determination of facts or questions of degree. Decisions of the TBAs on questions of law are of immense importance. We do not yet have a European Patent Court to lay down principles through case law. The TBAs (subject to occasional references to the Enlarged Board), albeit that technical members are in the majority, at present are the only body which can perform that function. They will continue to do so unless and until such a Court, staffed principally by lawyer judges, comes into being. Few would say they have done a bad job. Indeed it would not be exaggerating to say that but for the TBAs, European patent law – especially that concerning validity – would not have the coherence, integrity and predictability which it now has. The users of the system have a lot for which to thank the TBAs.

- **No deference to findings or evaluations of fact by the TBA**

Once one departs from a principle of law and starts trying to consider how a particular TBA applied the legal principles to various sets of facts in different cases, one is inevitably involved in assessing the facts of those cases or what are said to be those facts. The suggested exercise involves comparing the EPO's evaluation of the facts in one or more cases with the facts in the case at hand. I do not see why the English court's intense fact finding and evaluation process should give deference to the findings or evaluations of fact by the TBA in other cases – cases which, as we shall see, the TBA itself regards as fact-sensitive. The English Courts have never, for instance, given deference to the TBAs in the case of the objection of obviousness. I do not see why the position should be different in the case of other fact-evaluation objections such as sufficiency or, here, susceptibility of industrial application.

Industrial Application of gene sequences

- **you can patent an isolated gene sequence but only if you disclose the industrial application of the protein for which it encodes. 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.**

Propositions for industrial application

- **Kitchin J reviewed these and other authorities and drew from them a series of propositions**

(i) The notion of industry must be construed broadly. It includes all manufacturing, extracting and processing activities of enterprises that are carried out continuously, independently and for commercial gain (Max-Planck).

(ii) However, it need not necessarily be conducted for profit (Chiron [1996] RPC 535) and a product which is shown to be useful to cure a rare or orphan disease may be considered capable of industrial application even if it is not intended for use in any trade at all (ZymoGenetics).

(iii) The capability of industrial exploitation must be derivable by the skilled person from the description read with the benefit of the common general knowledge (Genentech).

(iv) The description, so read, must disclose a practical way of exploiting the invention in at least one field of industrial activity (/Max-Planck; Salk Institute T 338/00).

(v) More recently, this has been re-formulated as an enquiry as to whether there is a sound and concrete basis for recognising that the contribution could lead to practical application in industry. Nevertheless, there remains a need to disclose in definite technical terms the purpose of the invention and how it can be used to solve a given technical problem. Moreover, there must be a real prospect of exploitation which is derivable directly from the specification, if not already obvious from the nature of the invention or the background art (ZymoGenetics; Bayer T 1452/06).

(vi) Conversely, the requirement will not be satisfied if what is described is merely an interesting research result that might yield a yet to be identified industrial application (Salk Institute). A speculative indication of possible objectives that might or might not be achievable by carrying out research is not sufficient (Max-Planck). Similarly, it should not be left to the skilled reader to find out how to exploit the invention by carrying out a research programme (/ZymoGenetics).

(vii) It follows that the purpose of granting a patent is not to reserve an unexplored field of research for the applicant (Max-Planck) 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 (ZymoGenetics).

(viii) 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 (Max-Planck).
(xi) Using the claimed invention to find out more about its own activities is not in itself an industrial application (Max-Planck).
(x) Finally, it is no bar to patentability that the invention has been found by homology studies using bioinformatics techniques (ZymoGenetics) although this may have a bearing on how the skilled person would understand the disclosure

Members of TNF-ligand superfamily not "capabale of industrial application".

- **No plausible (at least in the sense of reasonably credible) use for any member of the superfamily.**
- **It is all too speculative to say, on the basis of the information in the patent and common general knowledge that a newly found member of the superfamily is "capable of industrial application."**

Now it is true that it was known that all members of the superfamily were expressed by activated T cells, that they all played a role in the regulation of T cell proliferation and T cell mediated immune responses and that some of the ligands played a role in the regulation of B-cell proliferation and antibody secretion and some took part in T cell dependent regulation of B cells. But it by no means follows that any member of the superfamily has a practical use or that the skilled reader would envisage such a use (other than as a speculation) on being told that a new member of the superfamily had been found. You would have to investigate each of them to find out. It is not impossible they would have such a use of some sort, but no more. It is all too speculative to say, on the basis of the information in the patent and common general knowledge that a newly found member of the superfamily is "capable of industrial application." That view is surely reinforced by the fact that only TNF-α had found any use and that was rather specialised, as I have already noted.

Source: **bailii**

Court of Appeal, London, 9 February 2010
(Jacob, Hallet, Lewison)
Neutral Citation Number: [2010] EWCA Civ 33
Case No: A3/2008/2673
IN THE HIGH COURT OF JUSTICE
COURT OF APPEAL (CIVIL DIVISION)
ON APPEAL FROM THE CHANCERY DIVISION
(PATENTS COURT)
The Hon Mr Justice Kitchin
[...]
B e f o r e :
THE RT HON LORD JUSTICE JACOB
THE RT HON LADY JUSTICE HALLETT
THE HON MR JUSTICE LEWISON

_____

Between:
Eli Lilly and Company
Respondent/Claimant
- and -
Human Genome Sciences Inc
Appellant/ Defendant

_____

Henry Carr QC and Michael Tappin QC (instructed by Messrs Powell Gilbert LLP) for the Appellant/Defendant
Andrew Waugh QC and Colin Birss QC (instructed by Messrs Howrey LLP) for the Respondent/Claimant
Hearing dates: 8, 9, 11 and 14 December 2009
Lord Justice Jacob:
1. Kitchin J held **([2008] EWHC 1903 (Pat)**, 31st July 2008) that HGS's EP (UK) 0,939,804 was invalid and could not be saved by some proffered amendments. HGS appeals. At the time of his decision the Opposition Division ("OD") of the European Patent Office ("EPO") had also held the Patent invalid.
2. Since the Judge's decision things have moved on. In particular on **21st October 2009, the Technical Board of Appeal ("TBA")** of the EPO allowed HGS's appeal based on some more restricted claims. It gave its reasons on 1st December 2009, doing so as part of an accelerated proceeding in co-operative effort with this court (see [1-4] of its reasons).
3. This appeal has accordingly been conducted on the basis of the claims allowed by the TBA. It is not necessary to consider any points about the allowability of the amendments or the associated issue of construction considered by the Judge.
4. Mr Henry Carr QC and Mr Michael Tappin QC argued the case for HGS, Mr Andrew Waugh QC and Mr Colin Birss QC for Lilly.
5. The case is basically about the patentability or otherwise of a protein called by HGS Neutrokine-α, antibodies to it and the polynucleotide sequence encoding for it. HGS were the first to discover its existence, doing so by "bioinformatics" (see more below). Others independently made the same discovery shortly thereafter, each discoverer giving it a different name. That is not very surprising given the very fast accumulation of genetic code information coupled with improvements in computing power and other techniques.
Co-operation between the EPO and National Courts
6. Co-operation between national courts and the EPO of the sort which happened between this court and the TBA in this case is mightily to be welcomed. It should, as far as possible, extend to all the stages of procedure in both national courts and in the OD and Boards of Appeal of the EPO.
7. I should enlarge upon that. Far from all oppositions (and appeals) in the EPO are of immediate commercial concern to the parties. Many, perhaps most (it would be valuable to find out), oppositions are started on a pre-

cautionary basis only: a potential competitor of the patentee takes the view that although the patent is of no immediate concern to him, it might have an impact on his business at some time in the future. If that is so, unless he is to lose all possibility of a central attack, he must start an opposition before the nine month period from grant expires. So he does.

8. Of course there are cases where the patent may have an immediate and obvious important commercial impact. It is in that class of case, and perhaps only that class, that parallel litigation in the EPO and one or more national courts occurs. Such cases are actually rare considering the total number of patents under opposition in the EPO at any one time. And it is in those cases that the sort of co-operation there has been in this case can be most valuable.

9. Actually it would have been better if the co-operation had started earlier. That probably would have happened if either of the parties has asked for it: neither the OD nor the TBA nor a national court can know that a case needs speeding up unless someone tells them and asks for it.

10. The more the overall opposition procedure can be expedited in the relatively small class of cases of immediate commercial concern, the more significant uncertainty (which is inherently damaging) is likely to be reduced for European industry and business. That needs co-operation from the outset not only between the TBA and the national court (as happened here) but co-operation between the national court(s) on the one hand and the EPO (both the OD and the TBA) on the other. And the parties should actively co-operate too. Commercially urgent and important cases need a fast track.

The Issues on the Appeal

11. The Judge held that all the claims of the Patent were invalid on three grounds: they were not susceptible of industrial application, they were insufficient and they were obvious because of a lack of technical contribution. There was also a further distinct finding of insufficiency as regards claims 18 and 19. HGS challenges all these findings.

12. The Judge rejected Lilly's obviousness attack based on two pieces of prior art called "Image clone" and Fujisawa EST. Only obviousness over Image clone was pursued on Lilly's respondent's notice. The point was raised contingently, that is to say Lilly only intended to pursue it if HGS could overcome the Judge's findings of invalidity. On the same contingent basis Lilly challenged the Judge's rejection of its insufficiency attacks on claims 1 and 13 and its claim that the amendment has impermissibly extended the protection of claim 13.

13. After we had heard full argument on HGS's appeal, we concluded that it failed. We accordingly informed the parties it was not necessary to hear argument on the points raised by Lilly – points which, incidentally, we note were decided adversely to Lilly by Kitchin J and the TBA. Of course by so indicating we were also indicating the result of the appeal. So what follows are my reasons for its dismissal.

The nature of a first instance decision in England and Wales

14. Because we are differing from the TBA I should point out some basic matters of procedure and approach which help explain why.

15. A key rule of civil procedure in England and Wales (and indeed in most if not all common law countries as well as some civil law countries) is that each side must marshal all its evidence (expert and factual) and arguments for the trial court – the court of first instance.

16. The process at a trial in England involves an intensive investigation and testing of the evidence. Each party's witness statements and expert reports must be provided in advance of the hearing. The expert witnesses are generally people who have been closely engaged with the very technical subject matter of the case. Each party's internal documents relevant to the issues in the case (and most particularly the documents adverse to its case) have to be disclosed in advance by the process called by most common lawyers "discovery" but now in England "disclosure".

17. At the hearing the evidence, both factual and expert, is severely tested by the process of cross-examination – the asking of questions by a lawyer from the other side who will have been educated deeply in the art by his own party's expert. An expert's opinion, as such, is treated by the court as of little value. His reasons for that opinion are what matter. Those reasons are apt to be probed without remorse before a tribunal which itself will have developed a good understanding of the technical subject-matter. Because that is likely to happen, expert witnesses in English are less apt to "stretch" things in favour of the party relying on them. They know their reputation is "on the line."

18. Moreover the Judge himself will generally not only have an expertise in patent law but also some considerable general technical expertise. Many (but not all) English patent judges have a science degree and many years experience of the practice of patent law. The trial Judge here, Kitchin J, is no exception.

19. Finally in cases of particularly complex subject-matter it is possible for a scientific advisor to be appointed to the court. Sometimes that is done both at first instance and on appeal, sometimes only on appeal. The function of such an advisor is merely to assist the court in its technical understanding. He or she is not there to provide an opinion on the merits. Experience shows that such advisors are well capable of keeping within their proper function.

20. In this very case we have had the benefit of a scientific advisor, Dr John Murphy of Kings College London. He is a Senior Lecturer of the Immunology, Infection and Immunity Research Group within the Division of Life Sciences of that University. His particular experience includes work on autoimmune diseases and immune regulation.

21. Prior to the hearing Dr Murphy gave us some "teach-ins" about the background technology. At the hearing he sat with us and provided valuable further explanation of the technology. At all times he meticulously refrained (as he had been asked) from

commenting on the parties' respective cases and he played no part in our decision making process. I would like to go on record to express the court's thanks to him.

22. The English trial procedure has the very considerable advantage that all parties know that they have to make their best efforts for the first instance decision. Each side has to put its cards on the table. That in itself causes quite a few cases to settle: if the other side has aces and kings and you have only low value cards and you each know broadly what the other has, you had better settle on as best terms as you can get.

23. The system has its problems – particularly in relation to its expense. But in a case of great commercial importance and significance the expense is relatively insignificant to what is at stake. This is such a case.

The Nature of an Appeal in England and Wales

24. In England and Wales appeals lie from first instance decisions to this Court provided they are adjudged (either by the trial Judge or this Court) to have a real prospect of success.

25. But appeals are conducted on the evidence and materials before the court of first instance. There are no new witnesses, expert opinions, or other new evidential matter, save in very exceptional circumstances. The most important of these are where the fresh evidence could not, using due diligence, have been found for use at the trial and even then only when it is likely to have a material effect on the appeal.

26. Further the Court of Appeal gives very considerable deference to the findings of fact of the first instance court. So also to its value-judgments – overall assessments of a question which itself involves a number of factors, such as, for instance, obviousness. Lord Hoffmann said in **Biogen v Medeva [1997] RPC 1** at p.45:

"The need for appellate caution in reversing the judge's evaluation of the facts is based upon much more solid grounds than professional courtesy. It is because specific findings of fact, even by the most meticulous judge, are inherently an incomplete statement of the impression which was made upon him by the primary evidence. His expressed findings are always surrounded by a penumbra of imprecision as to emphasis, relative weight, minor qualification and nuance (as Renan said, la vérité est dans une nuance), of which time and language do not permit exact expression, but which may play an important part in the judge's overall evaluation. .... Where the application of a legal standard such negligence or obviousness involves no question of principle but is simply a matter of degree, an appellate court should be very cautious in differing from the judge's evaluation".

27. The upshot is that an English first instance case is "for real". It is not shadow boxing for a real contest later on an "appeal." Not only must a party put its cards on the table prior to the trial, it must find and play all its best cards at the trial. It is noteworthy that the currently proposed rules of procedure about appeals in a future European Patents Court of Appeal are based on essentially the same principle. And that the recent changes of procedural law in hearing about appeals from the Bundespatentsgericht have moved in the same direction.

The Nature of proceedings in the EPO

28. Inherently the procedure is very different and much less intensive. The very name "opposition", given to what is really and in law an application for revocation, indicates something about it: that it is in some sense regarded as part of the grant process rather than a contest before the ultimate arbiter of validity (though it will be that if the patent is revoked). For the same reason the first instance proceedings in the OD are regarded as "administrative" thus making it legitimate to have on the panel the very examiner who allowed the grant of the patent. The link to the grant process also explains the nine-month rule for entering opposition.

29. The opposition procedure represents a compromise. In theory a true pre-grant opposition would be ideal – any patent which emerged would have finished its patent office processing. But true pre-grant opposition can potentially lead to unacceptable delays in enforceability of the patent in national courts (it certainly did in the UK under the old law). So this form of belated opposition was provided as the compromise.

30. In practice, both before the OD and the Boards of Appeal there is much less room for the testing of evidence (both factual and expert) than there is in the English (and indeed some) other national courts. There is no cross-examination (even of a short and controlled nature) and no compulsory disclosure of documents (particularly those adverse to a party's case).

31. Moreover before the TBAs there is much more latitude for the admission of fresh material on appeal, though wholly fresh grounds of objection may not be considered without the patentee's consent (see Enlarged Board of Appeal decisions G10/91, G 1/95 and G 7/95). Some say this latitude is justified by reason of Art. 114 of the EPC which provides that the EPO is not confined to the arguments and evidence of the parties, implying a general duty not to let any "bad" patent pass or to refuse any "good" one. I am not sure that is so, particularly given the original expectation that the opposition procedure would be one which was so speedy that in general pending national revocation actions would be stayed pending an EPO opposition (see [73] of the Reports on the Second Preliminary Draft of the EPC).

32. Anecdotal evidence from the professions suggests that some Boards are more liberal in their approach to fresh evidence than others. I cannot say whether that is so or not, though it would obviously be unfortunate if it were significantly so. What I can say is that in this case, the TBA permitted further evidence from HGS, amounting to 700 pages, just three weeks before the oral hearing. The material consisted of new technical papers and a declaration of a Dr Kelsoe which the TBA expressly relied upon in two parts of its decision. One is unable to discern whether other parts of the decision were influenced by the new material (though there was express reference to a new paper by Fu), though it is entirely possible - the process of forming a judgment inevitably includes taking into account matters of detail

and impression which do not find their way into express reasoning.

33. It follows from the nature of the procedure that inevitably in some respects – particularly those involving the facts and the testing of expert evidence, the EPO, including its judicial organ, the TBAs, is something of a "coarse filter". It cannot, need not and does not investigate matters affecting validity as profoundly as a national court can. And there will inevitably, even if there is no express acknowledgment to that effect, be something of a benefit of the doubt accorded to the patentee who is in some sense seen still as an applicant for the patent.

34. I wish to make it plain that, by saying this, I in no way intend to disparage the most excellent work done by the TBAs, working as they do under the pressure of an enormous caseload. Far from it. Given what they have to cope with they do as well, perhaps rather better, than could be imagined.

35. It remains the position however, that once a patent has been granted by the EPO and survived any opposition, the ultimate arbiter of its validity in any designated Contracting State is the national court system of that Contracting State deciding the case using its own fact finding procedures. Under the EPC system the national courts are the final judges of validity of a patent which has survived in the EPO.

36. That the national court can differ on the facts from the TBA is illustrated by several English cases. For instance in **Kirin-Amgen v TKT [2004] UKHL 46, [2005] RPC 169** Lord Hoffmann pointed out at [93-96] that the TBA had found that urinary erythropoietin was different from recombinant erythropoietin whereas the trial judge in the UK (Neuberger J) had found otherwise. It was the latter finding which counted. Similarly in **Biogen v Medeva [[1997] RPC 1** the House of Lords held the patent invalid even though it had been upheld by the TBA doing so on a ground of sufficiency not considered by the TBA. And in **Conor v Angiotech [2008] UKHL 49** at [3] Lord Hoffmann said this:

[3] There is still no European Patent Court. 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 European Patent Office ("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 European Patent Convention

37. Of particular significance here is Lord Hoffmann's reference to questions of degree, for as will be seen this case is indeed one involving a question of degree. He clearly indicates that where that is the position, the national court is free to go on its own evaluation rather than give deference to a TBA's assessment.

The status of EPO and especially TBA decisions on questions of law in National (and especially UK) proceedings.

38. When it comes to legal principles the position of the TBAs (and even more so of course, the Enlarged Board) stands quite differently from its determination of facts or questions of degree. Decisions of the TBAs on questions of law are of immense importance. We do not yet have a European Patent Court to lay down principles through case law. The TBAs (subject to occasional references to the Enlarged Board), albeit that technical members are in the majority, at present are the only body which can perform that function. They will continue to do so unless and until such a Court, staffed principally by lawyer judges, comes into being. Few would say they have done a bad job. Indeed it would not be exaggerating to say that but for the TBAs, European patent law – especially that concerning validity – would not have the coherence, integrity and predictability which it now has. The users of the system have a lot for which to thank the TBAs.

39. In the UK the key importance of the TBAs' case law is well settled. We follow any principle of law clearly laid down by them, only reserving the right to differ if we are sure that the commodore is steering the fleet on to the rocks (see **Actavis v Merck [2008] EWCA Civ 444 at [45-48]**, the cases there cited and also the earliest House of Lords case about deference to the EPO on questions of law, Asahi's Appn. [1991] RPC 485 at 540). Other significant national courts follow the same principle, as I understand it. For instance the Bundesgerichtshof has just recently applied TBA jurisprudence in its decision corresponding to (and agreeing with) that of the **House of Lords in Generics v Lundbeck [2009] UKHL 9** (see the BGH decision of 10th September 2009, Case Xa ZR 130/07 at [33]).

40. Mr Carr suggested that our courts should go further: if the TBA has not only laid down a "pure" principle of law but has also set a standard by which it was to be applied in a series of cases, we should follow that standard too. In particular he took us to some other TBA cases which he submitted showed the application of a standard which we should follow.

41. I am not persuaded by this. Once one departs from a principle of law and starts trying to consider how a particular TBA applied the legal principles to various sets of facts in different cases, one is inevitably involved in assessing the facts of those cases or what are said to be those facts. The suggested exercise involves comparing the EPO's evaluation of the facts in one or more cases with the facts in the case at hand. I do not see why the English court's intense fact finding and evaluation process should give deference to the findings or evaluations of fact by the TBA in other cases – cases which, as we shall see, the TBA itself regards as fact-sensitive. The English Courts have never, for instance, given deference to the TBAs in the case of the objection of obviousness. I do not see why the position should be different in the case of other fact-evaluation objections such as sufficiency or, here, susceptibility of industrial application.

The Broad Context of the Invention

42. From the beginning of the genetic engineering revolution (starting around 1980) until the early 90s, scientists created genetically engineered versions of proteins that were already known. The basic, so-called "wet-lab" technique went as follows: the protein of interest was identified and isolated. Some amino-acid sequence data was obtained. The corresponding nucleic acid sequence(s) encoding for the identified sequence could then be deduced. Probes using that sequence or those sequences (generally the latter owing to redundancy) were made and used to clone the actual gene from a library. The cloned gene could then be inserted into a host cell used to express the required protein.

43. Insulin, tissue plasminogen activator, human growth hormone and erythropoietin were amongst the important proteins made using wet-lab techniques. Patents and patent litigation were about details of the techniques, for example the technique used to produce recombinant tissue plasminogen activator was the subject of the first genetic engineering case in England, Genentech's Patent [1987] RPC 553 and [1989] RPC 137 where detailed descriptions of the technique are discussed.

44. By the early to mid-90s another way of doing research became possible – research using "bioinformatics". By then major projects to obtain the full genetic code – the genomes – of living things and particularly the genome of humans were producing results. Large amounts of nucleotide sequence data from the human genome were becoming available as techniques (and computer power) improved.

45. Now just having large amounts of such data tells you nothing in itself. You do not know what the reading frame is. Nor can you tell introns (junk) from sequence data encoding for actual bodily proteins. More has to be done to identify a sequence (excluding introns) encoding for a real protein. It is in that context that expressed sequence tags ("ESTs") started to be identified. ESTs are part of a cDNA clone, but not the full length sequence encoding the entire protein. Knowing the sequence of an EST does not get you all that far. You still do not know what the full-length sequence is, and you do not even know what the reading frame is to deduce the partial amino-acid sequence for which the EST encodes.

46. As techniques improved and amounts of data became more substantial it became possible to do better than ESTs. It was possible to identify from published sequence data full length nucleotide sequences for proteins. Once that is done you can deduce the amino acid sequence of the protein encoded. And you should be able to make it (the details of how do not matter). But, unlike the days of wet-lab techniques (where you knew it at the outset), you do not know what function the protein has.

47. Even at that stage, however, it is more than reasonable to suppose that it has some biological function – after all the body is carrying the gene for it. One can say in general terms that if there is a disease or condition involving a deficiency of the protein then it may be treatable with it. Or if there is a disease or condition caused by overproduction of the protein it may be treatable with an antibody to the protein. So in a very general sense one can say there is probably an application for the protein or its antibodies. As will be seen, however, that is not good enough to make the protein or its antibodies patentable. You have to say something more about their proposed use than they will probably be useful in medicine, though that is very likely to be so. The question in general is how much more you need to say and how reliable what you say needs to be.

48. Without in vitro and ultimately in vivo assays, you cannot definitely know what the protein you have discovered actually does. However even before that stage it may, in the case of some proteins, be possible to make an informed guess. This can be done by seeing how closely the amino-acid sequence of your newly identified protein resembles the amino-acid sequence of a known protein or "family" of proteins. You look for homology between your protein and the known protein or family of proteins. If there is some degree of homology and you know or can predict reasonably well what the known family member(s) do then you can hazard a guess that your unknown one does something like it or them.

49. Of course how likely it is that your guess will turn out to be true depends on a host of factors, for instance how homologous your protein sequence is to the other protein sequence(s), how specific the action of the known protein or family of proteins is known to be and how specific your surmise as to its function is. No doubt other factors also come into play. Depending on all the circumstances the "guess" can range from that which is no more than a "shot in the dark" - something which can be fairly described as wholly speculative - to a firm prediction which is almost surely right.

Susceptible of Industrial Application?

50. This was by far the most important point. Beside it the others pale into insignificance. Apart from the specific obviousness attacks over cited prior art (which we did not get to) it was always this point which was going to be determinative. Mr Waugh persisted in arguing some others without thereby advancing matters. In the event we do not have to decide them.

The Legislation: Art. 57 and the Biotech Directive

51. An invention is only patentable if it is "susceptible of industrial application" (EPC Art.52(1). Art 57 of the EPC says:

An invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture.

So if an invention does not comply with that requirement it not a patentable invention and the patent for it may (which in context means "must") be revoked (s.72(1) of the Patents Act 1977).

52. The British Parliamentary draftsman's "translation" of "susceptible of industrial application" is "capable of industrial application" (see s.1 of the Patents Act 1977. Although this is "so framed as to have, as nearly as practicable, the same effect as Art 57 (see s.130(7) of the Act), "capable" does convey a flavour of concrete-

ness about what the invention must be for. Of course the translation cannot be determinative but is it perhaps a straw in the wind as indicating what one of the parties to the EPC had in mind.

53. Neither side took us to the travaux préparatoires of the EPC. This is hardly surprising since the language was carried over, unchanged, from Art. 2 of the Strasbourg Convention of 1993. Whether the travaux to that Convention throw any light on the meaning was also not explored (I am not sure they were ever published, though Dr Justine Pila clearly has had access to them, see Art. 53(b) EPC A Challenge to the Novartis Theory of European Patent History" Oxford University Legal Research Paper Series, Paper 21/200, November 2008). I do not think that matters now, for what matters is the modern interpretation of the phrase, particularly that of the EPO TBAs

54. Whilst no-one suggests that the Biotech Directive (99/44EC) altered the meaning of the EPC (it could hardly do so, given that the EPC is a free-standing international treaty whose signatories do[1] include Member States of the EU), it is common ground that it throws some light on the interpretation of Art 57.

55. Article 5 provides:

"1.The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.

2. An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.

3. The industrial application of a sequence or partial sequence of a gene must be disclosed in the patent application."

56. Art. 5.3 is a key provision. Recitals 22 to 24 put its meaning in context:

22. …. Whereas the industrial application of a sequence or partial sequence [of a gene] must be disclosed in the patent application as filed

23. Whereas a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention;

24. Whereas, in order to comply with the industrial application criterion it is necessary in cases where a sequence or partial sequence of a gene is used to produce a protein or part of a protein, to specify which protein or part of a protein is produced or what function it performs.

57. The upshot, stated broadly, is that you can patent an isolated gene sequence but only if you disclose the industrial application of the protein for which it encodes. 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.

58. Mr Carr suggested the background context of the Directive's provisions about industrial applicability was merely about ESTs. As Professor Joseph Straus describes in his 1995 article Patenting Human Genes – Past Developments and Prospect for the Future, IIC 26, 290 at p.934 at the time of the Directive there was a particular problem about attempts, particularly in the US, to patent ESTs as soon as they were identified and before anyone had any idea what they were for. Professor Straus was not sure that the "susceptible of industrial application" test would not be met by ESTs (because he thought it enough they could be made in industry) but tentatively supported an argument that they were not inventions because they did not solve any technical problem.

59. Mr Carr submitted that this case was quite different from that of an EST. First there was disclosure of the full length gene sequence for the whole protein Neutrokine-α and secondly that this protein was expected to have valuable therapeutic functions.

60. He also submitted that the Art. 57 objection was in effect no different from an objection that the "invention" was a mere "discovery" "as such" (Art.52).

61. Mr Waugh also referred to the background at the time of the Directive. He submitted it was not concerned only with problems about attempts to patent ESTs. The problem was wider with attempts to patent entire genes for proteins with no known function in prospect, for instance by organisations such as that headed by the well-known Dr. Craig Venter. The vice aimed at was not just patents for ESTs but patents for whole genes whose function was unknown.

62. Moreover he submitted the Directive was not a mere manifestation of the rule that a mere "discovery" "as such" cannot be patented (EPC Art. 52). It is about the free-standing objection of lack of susceptibility of industrial application.

63. Further the current EPC implementing Rule 42(1)(f), although pre-dating it (under different numbers) correctly expresses the meaning of the Directive and hence of Art. 57. It says:

(1) The description shall

(f) indicate explicitly, where it is not obvious from the description or nature of the invention, the way in which the invention is industrially applicable.

The Rule itself is of course not the source of the law – that depends and only depends on the true interpretation of Art. 57.

64. The Judge's summary of what emerges from the Directive was as follows:

[185] In a nutshell, the industrial application of a gene must be disclosed in the application. If it encodes a protein then the protein or its function must be specified.

I agree with that, subject to the rider that what matters is a sufficient specification of the function of the protein. Just describing the existence of a protein and its structure is not enough. Nor is it enough to describe the function at a high level of generality – e.g. that the

[1] Editorial comment: the published text reads "do not", but that seems a typorgaphical error

compound must have a significant function biologically and so it (or its antibodies) may be usable to treat some sort of disease. You have to say what it is for with more particularity. What amounts to a sufficient specification of function will depend on the facts of the case and involves a question of degree.

The EPO Case Law on Art. 57

65. This view is consistent with the important case-law of the TBAs. The decision of the TBA concerning the patent in suit does not purport to lay down any new principles. For these it is necessary to go to the main cases involving DNA sequences and proteins discovered by bioinformatics. These are Max-Planck T 0870/04 (May 2005) Johns Hopkins T 1329/04 (June 2005) Genentech T 0604/04 (March 2006), ZymoGenetics T 0898/05 (July 2006), Bayer T 1452/06 (May 2007) and Schering T 1165/06 (July 2007). It is not necessary or useful to refer to any others. Nor to the meagre English case-law on the subject.

66. I take them in turn. Max-Planck was an ex parte appeal from a refusal to grant by the examining division. The applicants had identified what they called a "BDP1 polypeptide". They sought to justify a claim to it on the basis that it could be made and used as a tool for research. That was rejected. It is now settled that the "research tool" justification for a new polypeptide or the nucleotide sequence encoding for it is not enough to satisfy the Art. 57 test. As the Board said:

[*21] In the board's judgment, although 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.*

67. That last sentence is full of importance. If you allow patenting of chemicals whose use you do not really know you will subvert the patent system and be likely to stultify research by others rather than encourage it. A merely "vague and speculative indication of possible objectives" is not enough.

68. The present case indeed provides an example of the danger of what can happen if patenting too far upstream is allowed. Both sides (HGS in collaboration with GlaxoSmithKline) are conducting clinical trials but each is trying a different antibody to Neutrokine-α and for different conditions. As a matter of interest the HGS trials are for the treatment of lupus, one of the few diseases not mentioned in the patent. If the patent were valid, the valuable research and development work done by Lilly into a field apparently not researched (and certainly not taken through to clinical trial) by HGS would potentially be rendered futile. The patent system would not be working as it should. It would be operating to prevent research, not to encourage it.

69. It is also important to note an earlier paragraph of Max Planck, for the Boards still regard it as good law:

[6] In cases where a substance, naturally occurring in the human body, is identified, and possibly also structurally characterised and made available through some method, but either its function is not known or it is complex and incompletely understood, and no disease or condition has yet been identified as being attributable to an excess or deficiency of the substance, and no other practical use is suggested for the substance, then industrial applicability cannot be acknowledged. While the jurisprudence has tended to be generous to applicants, there must be a borderline between what can be accepted, and what can only be categorized as an interesting research result which per se does not yet allow a practical industrial application to be identified. Even though research results may be a scientific achievement of considerable merit, they are not necessarily an invention which can be applied industrially.

70. So the question here is which side of the borderline the case lies – a question of degree turning on the facts and not a pure question of law.

71. Johns Hopkins was another ex parte appeal from the OD. The problem of a speculative claim was considered in the context of obviousness, it being settled law (see AgrEvo T 0939/92) that merely to specify a chemical compound or class without any plausible use for it did not involve an inventive step.

72. The claims were for a defined polynucleotide encoding for a polypeptide which the applicant called GDF-9. It had a degree of homology with a known "superfamily" of polypeptides called "transforming growth factor-ß" ("TGF- ß") and the applicant claimed that a skilled person would recognise that GDF-9 belonged to that "superfamily."

73. I interpolate to say something about the expression "superfamily". It does not appear to have a precise meaning: the general idea is that it includes not only very closely homologous compounds but those with rather less homology – by analogy the contrast is between the "nuclear family" of humans and the wider family including cousins, second cousins, distant uncles and so on. The latter is the "superfamily" thereby indicating that a not particularly high degree of homology may be enough to regard a protein as a member of such a superfamily.

74. Going back to Johns Hopkins, although the members of the TGF-ß superfamily had functional and structural relationships to a known protein called transforming growth factor- ß which was known to have a influence on a wide range of differentiation processes, GDF-9 did not share all those relationships with the class. The Board put it this way at [7] "*it does not exhibit the most striking structural features which serves to establish whether or not a polypeptide belongs to the TGF-ß family*". It was, if you like, at best potentially only a very distant cousin indeed and one could not with any confidence say it had the same use as a member of the family.

75. The Board went on to say this:

[10] Therefore, the issue here is rather how much weight can be given to speculations in the application in the framework of assessing inventive step, which assessment requires that facts be established before starting the relevant reasoning. In the board's judgment, enumerating any and all putative functions of a given compound is not the same as providing technical evidence as regard a specific one.
[11] Accordingly, as 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.
76. The Board went on to hold that one could not supplement the information in the patent by evidence of after-patent work that showed that the compound was indeed a growth differentiation factor. It said:
[12] The appellant filed post-published evidence .... establishing that GDF-9 was indeed a growth differentiation factor. This cannot be regarded as supportive of an (sic) evidence which would have been given in the application as filed since there was not any. The said post-published documents are indeed the first disclosures going beyond speculation. For this reason, the post-published evidence may not be considered at all. Indeed, to do otherwise would imply that the recognition of a claimed subject-matter as a solution to a particular problem could vary as time went by. Here, for example, had the issue been examined before the publication date of the earliest relevant post-published document, GDF-9 would not have been seen as a plausible solution to the problem of finding a new member of the TGF-β superfamily and inventive step would have had to be denied whereas, when examined thereafter, GDF-9 would have to be acknowledged as one such member. This approach would be in contradiction with the principle that inventive step, as all other criteria for patentability, must be ascertained as from the effective date of the patent. The definition of an invention as being a contribution to the art, i.e. as solving a technical problem and not merely putting forward one, requires that it is at least made plausible by the disclosure in the application that its teaching solves indeed the problem it purports to solve. Therefore, even if supplementary post-published 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.
77. The reference to "make at least plausible" should be noted – the Board has carried it over into Art.57 considerations. It should also be noted that in context "at least plausible" means more than a speculation, even if the speculation could be true. The word is not being used in the sense of "not incredible" but in the sense of having significant degree of likelihood to be true.
78. In passing it may also be noted that Lord Hoffmann in the **House of Lords in Conor v Angiotech [2008] UKHL 49** followed this approach: the use of taxol in the coating of a stent as an effective way of preventing restenosis was rendered plausible by the fact that, as disclosed by the patentee, the CAM assay showed that taxol was the best angiogenic (Lord Hoffmann at [39]).
79. The next case is Genentech, an opposition appeal as opposed to one ex parte. I take the facts from the Board's summary:
[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.
80. The Board then referred to Max Planck and specifically quotes [6] cited above. That is why I said earlier that it is still regarded as good law.
81. The Board then held that the Patent alone did not provide enough information to comply with Art 57, though if one added to it the common general knowledge of the skilled man, there was enough. It said:
[15] The board agrees with the criteria defined in T 870/04 and observes that, taken in isolation, the technical data provided in respect of the polypeptides of Figures 4 and 5 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 (see eg. T 338/00 of 6 November 2002) 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.
82. The Board's reference to each case being considered on its own merits is of course not only right but important. It shows that one cannot jog from the facts of one case to the facts of another. What matters is the applicable legal principle, not the detailed facts of a particular case.
83. So what Genentech adds to Max Planck and Johns Hopkins is that one should add, to the disclosure in the patent, the common general knowledge. On the facts of that case, the Board thought the common general knowledge added enough. This was because the claimed polypeptides were related to PF4-related proteins which were:
[17] ... attractive targets for the development of new therapeutic agents. Inhibition of their activity may be an effective anti-inflammatory strategy and promoting that activity might enhance wound healing and tissue repair.
From that the Board reasoned:
[18] It is clear from this statement 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 polypeptides of Figures 4 and 5 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.

84. Mr Carr relied on that. But I cannot accept that the Board is saying that generally it is sufficient for Art 57 that a protein is of interest to the pharmaceutical industry. For any protein of the human body will be of interest to the pharmaceutical industry – it is near certain to have a function and it, or its antibodies, could well have therapeutic potential of some sort or another and so be of interest to the pharmaceutical industry. But that high level of generality is not enough. What mattered in the case itself were the specific facts recited at [17] – the protein was seen as having the specific potential of enhancing wound healing and tissue repair even though how it might achieve this was not well-defined.

85. Mr Carr particularly relied upon the next case, ZymoGenetics. He called it "seminal". So I go to it with some care. It was again an ex parte case. It is worth reminding oneself of the significance of that. It is that there was no one on the other side to present counter-argument or evidence or even to challenge the applicant's assertions. Inherently therefore (just as with decisions in unopposed cases generally) one is disposed to approach the case with caution. Hearing the other side can really make a difference.

86. Before turning to the specific facts of the case, the Board dealt with the law more generally. The following are important passages:

[5] … 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. It would be at odds with the purpose of the patent system to grant exclusive rights to prevent the commercial activities of others on the basis of a purely theoretical or speculative patent application. This would amount to granting a monopoly over an unexplored technical field.

[6] …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. Not only is this the essence of the requirements of Rules 23e(3) and 27(1)(f) EPC, it also corresponds to the requirements of Articles 56 (the need to provide a non-obvious solution to a technical problem), 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.

[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 (made) (cf. [Max Planck], point 10 infra). 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.

87. Mr Carr attaches much importance to the expression "plausibly shown to be usable" - I will return to it later.

88. On the facts of ZymoGenetics, the OD had rejected a claim to a protein called Zcytor1. The Board summarised the OD's reasons thus:

[19] Although recognising that the predicted role of the protein Zcytor1 in proliferation, differentiation and/or activation of immune cells was "reasonably credible", the examining division denied the industrial applicability of the claimed invention on the basis of, essentially, the following two reasons: i) the use of a computer-assisted alignment as disclosed in the application 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; ii) the Zcytor1 receptor was only a research tool whose importance lay in establishing a research programme and whose disclosure was only the first step in the quest for industrially applicable matter.

89. The Board then went on to say:

[20] As seen above with reference to the case law of the boards of appeal, the disclosure of the function of a newly discovered protein is of utmost importance when examining the issue of "industrial applicability" as the function is the gateway to understanding the concrete benefits which may derive from exploiting the invention industrially. As shown by T 870/04 (supra [i.e. Max Planck]), the mere characterisation of the structure of a protein may not be enough to comply with Article 57 EPC if no profitable use of the protein is disclosed. On the other hand, T 338/00 and T 604/04 (supra) show that a positive answer can be given in spite of the ab-

sence of actual experimental data, if a profitable use can readily be identified on the basis of the description taking into account common general knowledge. This demonstrates that this matter can only be decided in each case on its own merits according to the particular technical circumstances (extent of disclosure, background art, post-published evidence etc).

90. This is a re-affirmation of the fact that one cannot go about the problem by working from the facts of one case to another. It is not good enough to say that a "profitable use" was "readily identified" in one or more earlier cases and so should be in the case under review. It all depends on the facts of the case in hand.

91. The reference to a use being "readily identified" is also of importance. It shows that merely providing information from which one can deduce that there might be some sort of use though you have no real idea as to what is not enough.

92. I add, in passing, that I do not understand the reference to "post-published evidence" to include post-published evidence establishing for the first time or adding to what the potential industrial application of the patented subject-matter may be. It is surely axiomatic that whatever the standard for susceptibility to industrial application may be, the information about it must be in the patent (supplemented if necessary by the common general knowledge of the time). Otherwise you could satisfy the Art 57 requirement by just identifying a compound in the patent and finding a use for it later. That would contravene, for example, Art. 5(3) of the Directive. You cannot have a patent for an invention when only years later you or someone else finds out what it is for. The same principle as applied in Johns Hopkins concerning obviousness must apply also to Art. 57.

93. I say that in passing because Mr Carr did not directly invoke the fact that the parties are now in clinical trials for what look like promising medicines as matter he could directly rely on to prove susceptibility of industrial application. The Board decision on this may in part be based on post-patent evidence showing that antibodies to Neutrokine-α have potential as a therapeutic agent. However that does not appear to be crucial to the decision and I do not read the Board as saying that post-patent evidence of utility can itself support a claim to satisfy the Art. 57 requirement.

94. Post-patent evidence may be relevant in other ways, however. For example, if, following the patent, the inventor and others behaved as they had no real idea what the invention was for, that is a powerful indication that the information in the patent (plus common general knowledge) was not in itself enough to tell you that. That would be so if the patentees (or others) conducted research on the basis that they were trying to find out what the substance would do (as opposed to researching and developing what the patent had already sufficiently disclosed the invention could be used for).

95. Turning back to ZymoGenetics, the Board then contrasted Max Planck (where on the facts there was not enough) with Genentech where there was. It then turned to the application in question. It noted that it contained two sorts of information, that derived from computer-assisted sequence homology studies (what the Board called in silico examples) and that based on actual experiments by way of tissue distribution studies which showed expression of Zcytor1 to be at high levels in lymphoid tissues. Based on that information the patent identified the Zcytor1 receptor to be a putative member of the hematopoeitin receptor family and postulated – "reasonably credibly" – that its ligands had "a possible role" in therapeutic conditions. There was evidence about this, the details of which are not recited. This is of some importance – for the words "reasonably credible" are apt to cover anything from "very probably" down to anything which is not impossible. One cannot assess from the report of ZymoGenetics how credible the putative use was on the facts of that case as perceived by the Board.

96. What is clear is that the Board goes out of its way to say that the mere fact that the information is derived by in silico work is not enough in itself to say that the invention is incapable of industrial application. The Board put it this way:

[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. There is no "all-encompassing" approach, and certainly not a "throw-into-the-bin" approach, for these in-silico examples. Their probative value 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.

97. This makes entire sense, provided however one means by "plausible conclusions" more than conclusions which are not impossible. There must be a real likelihood of their being true. For if the suggested use covered anything other than the wholly improbable, patents for research programmes to find a use would be grantable.

98. On the facts of ZymoGenetics the Board concluded that the "educated guess" made in the patent was plausible. It went on to consider whether the role defined (in early thymocyte development and immune response regulation) was too "vaguely defined." In a paragraph relied upon by Mr Carr it said:

[29] Whereas the structural characterization of a protein might be directly derived from the genome, its function cannot normally be derived in a straightforward manner therefrom. 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 (protease, endonuclease, ion channel or pump, etc.), i.e. its molecular function; ii), the function of the protein in cellular processes (apoptosis, secretion pathway, etc.), i.e. its cellular function; and iii) the influence of those cellular processes within a multicel-

lular organism, i.e. in a general and more complex network within a multicellular organism (cancer, inflammation, immune responses, etc.), this being its biological function in a broad sense. Each of these levels, particularly the cellular and biological function, may not be restricted to a very single (objective) function but may encompass multiple functions arising from all the different possible protein complexes (units of macromolecular organization) in which the protein might participate or contribute. In fact the latter is more the rule than the exception.

99. It went on to say:

For the purpose of Article 57 EPC ... none of these levels is more fundamental, i.e. "more specific" or "less vague" in the words of the decision under appeal, than the other ones insofar as at least from one of these levels a practical application (a profitable use in a wider sense, cf. points 5 and 6 supra) is derivable in a straightforward manner.

100. So here the test is expressed as whether "a practical application… is derivable in a straightforward manner". On the facts of ZymoGenetics the Board went on to hold:

[31] In the present case, the suggested role of the Zcytor1 receptor 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 cell-mediated immunity and of lymphocyte proliferation by agonist ligands of Zcytor1 and the suppression of the immune system by antagonists of the Zcytor1 receptor ....

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.

101. Finally I turn to Schering, another ex parte case. The application was to patent a protein called "IL ("interleukin)-17". The Board dealt with Art. 57 briefly, the main question being obviousness. As regards Art 57 it said:

[25] The board is convinced that the requirements of Article 57 EPC are fulfilled. 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 this 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.

102. 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 (i.e. is a member of a family) may satisfy Art.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.

103. Kitchin J reviewed these and other authorities and drew from them a series of propositions which he set out at [226] which I set out here but for readability shortening case names and adding citations where I have not mentioned them before

(i) The notion of industry must be construed broadly. It includes all manufacturing, extracting and processing activities of enterprises that are carried out continuously, independently and for commercial gain (Max-Planck).

(ii) However, it need not necessarily be conducted for profit (Chiron [1996] RPC 535) and a product which is shown to be useful to cure a rare or orphan disease may be considered capable of industrial application even if it is not intended for use in any trade at all (ZymoGenetics).

(iii) The capability of industrial exploitation must be derivable by the skilled person from the description read with the benefit of the common general knowledge (Genentech).

(iv) The description, so read, must disclose a practical way of exploiting the invention in at least one field of industrial activity (/Max-Planck; Salk Institute T 338/00).

(v) More recently, this has been re-formulated as an enquiry as to whether there is a sound and concrete basis for recognising that the contribution could lead to practical application in industry. Nevertheless, there remains a need to disclose in definite technical terms the purpose of the invention and how it can be used to solve a given technical problem. Moreover, there must be a real prospect of exploitation which is derivable directly from the specification, if not already obvious from the nature of the invention or the background art (ZymoGenetics; Bayer T 1452/06).

(vi) Conversely, the requirement will not be satisfied if what is described is merely an interesting research result that might yield a yet to be identified industrial application (Salk Institute). A speculative indication of possible objectives that might or might not be achievable by carrying out research is not sufficient (Max-Planck). Similarly, it should not be left to the skilled reader to find out how to exploit the invention by carrying out a research programme (/ZymoGenetics).

(vii) It follows that the purpose of granting a patent is not to reserve an unexplored field of research for the applicant (Max-Planck) 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 (ZymoGenetics).

(viii) 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 incom-

pletely 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 (Max-Planck).

(xi) Using the claimed invention to find out more about its own activities is not in itself an industrial application (Max-Planck).

(x) Finally, it is no bar to patentability that the invention has been found by homology studies using bioinformatics techniques (ZymoGenetics) although this may have a bearing on how the skilled person would understand the disclosure.

104. We asked Mr Carr whether he challenged these propositions. His answer can be summarised thus: "not exactly". He submitted that phrases like "sound and concrete basis", "immediately suggest a practical application" and "disclose how the invention can be used to solve a given technical problem," and "not be left to the skilled reader to find out how to exploit the invention by carrying out a research programme" were "plastic." One could only see what they meant by seeing how they were applied in other cases.

105. That seems to me to ignore the very thing the Board has emphasised time and time again, that each case must be decided on its own facts. I do not find Mr Carr's criticism of the judge's summary convincing for it invites the court to do the opposite – to decide the case before it by reference to the facts of other cases.

106. Mr Carr's more fundamental attack on the Judge's summary of the law was this: that he had wrongly failed to articulate, in addition to what he did set out in his summary the correct level of the plausibility test. Putting it another way he submitted that the Judge had applied too high a standard of plausibility as compared with the standard applied by the TBA. It was enough if the patentee disclosed (either by the specification or the specification plus common general knowledge) a reasonably credible or educated guess as to a real use for the invention.

107. Mr Carr said this was demonstrated by the fact that Judge had referred to US authority, of course, under the provisions of the US Patents Act, 35 USC s.101. For instance the Judge referred to the USCAFC decision in Fisher v Lalgudi (2005) 04-1465, 09/619,643, where patentability of ESTs encoding proteins and protein fragments of maize plants was denied. The CAFC said this:

It is thus clear that an application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the "substantial" utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public.

And:

Thus, in addition to providing a "substantial" utility, an asserted use must also show that that claimed invention can be used to provide a well-defined and particular benefit to the public.

108. From that the Judge concluded:

[222] So the application must show that the invention is useful to the public as disclosed, not at some future date after further research. The utility must be significant and presently available. It must also disclose a use which is well defined and not so vague as to be meaningless.

109. Mr Carr submitted that showed the Judge thought that in the US more was required than mere plausibility. He did not accept the Judge was right about US law. What mattered here, submitted Mr Carr, is that the Judge was aligning Art.57 with what he thought was a more stringent test.

110. I am by no means convinced of this. "Plausible", as I have observed, is an imprecise word, covering any assertion from that which is not seen as ridiculous or impossible, to that which is well-nigh certain. The Oxford English Dictionary says this by way of definition:

Of an argument, an idea, a statement, etc.: seeming reasonable, probable, or truthful; convincing, believable.

111. Now I am conscious that it is a bit absurd to suppose that Art.57, which does not use the word "plausible" or any other language version of the word, should be interpreted by reference to an English dictionary meaning of the word "plausible". But I think it is legitimate to have regard to the dictionary to see what it is the TBA was intending to convey by its use of the word in the English language cases where it is used. More than "not incredible" is required – there must be some real reason for supposing that the statement is true.

112. Moreover the statement itself must be sufficiently precise. 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.

The Common General Knowledge

113. At [33-99] the Judge set the relevant common general knowledge out largely uncontroversially under four headings: immunology, the TNF superfamily, biological assays and bioinformatics. I do not believe it is necessary to repeat all that here. But it is necessary to set out what the Judge says was known about the "TNF ligand superfamily."

[71] Pulling these various strands together, I derive the following conclusions. I have no doubt that the details of all these publications did not form part of the common general knowledge of the ordinary skilled person in 1996. However, as the experts accepted, they would have been found by any researcher setting out to find or investigate the properties of a new member of the TNF ligand superfamily. Upon reading the publications any such researcher would have appreciated that the activities of the members of the superfamily are extremely complex and had been the subject of extensive research, as reflected in the forest of papers they reference. But some general points about the TNF ligand superfamily members would have emerged:

i) They were all expressed by activated T cells and some by other cells such as activated monocytes and macrophages.
ii) Their activities were mediated by binding to receptors, of which a number had been identified.
iii) They were known to have pleiotropic actions, that is to say a multitude of different effects on different cell types, driving multiple biological processes. 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.
v) Some of the ligands played a role in the regulation of B-cell proliferation and antibody secretion and some took part in T cell dependent 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-β 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 such as septic shock, rheumatoid arthritis, inflammatory bowel disease, tissue rejection, HIV infection, and some adverse drug reactions. 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. It was believed to operate in a particular way, namely by interrupting the cytokine cascade and by controlling the recruitment and trafficking of blood cells to the joint.
[72] Moreover, it 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.

114. I particularly emphasise finding ix). Only one member of the superfamily had been found to have any use at all. And (see later) even that use not proved to be directly linked to a specific role in the regulation of T cell proliferation and T cell mediated immune responses – the common factor of the superfamily which the Board considered was enough to justify its finding of a plausible possible use.

The Patent in suit

115. It is not necessary here to set out much of the lengthy patent itself. The Judge provides some of it at [100-133]. He sums up what the patent says Neutrokine-α might be useful for at [130]:

i) to modulate angiogenesis;
ii) to inhibit immune cell functions and hence have a wide range of anti-inflammatory activities;
iii) to act as an anti-neovascularizing agent to treat solid tumours and other non-cancer indications where blood vessel proliferation is not wanted;
iv) to enhance host defences against resistant chronic and acute infections, for example, myobacterial infections via the attraction and activation of microbiocidal leukocytes;
v) to inhibit T-cell proliferation by the inhibition of IL-2 biosynthesis for the treatment of T-cell mediated auto-immune diseases and lymphocytic leukaemias;
vi) to stimulate wound healing, both via the recruitment of debris clearing and connective tissue promoting inflammatory cells;
vii) to treat other fibrotic disorders, including liver cirrhosis, osteoarthritis and pulmonary fibrosis.
viii) to increase the presence of eosinophils which have the distinctive function of killing the larvae of parasites that invade tissues, as in schistosomiasis, trichinosis and ascariasis;
ix) to regulate hematopoiesis, by regulating the activation and differentiation of various hematopoietic progenitor cells, for example, to release mature leukocytes from the bone marrow following chemotherapy, i.e., in stem cell mobilization; and
x) to treat sepsis.

116. Since the patentees did not actually know whether Neutrokine-α itself would have any therapeutic activity and it was equally in principle possible that its antagonists (such as neutralising antibodies) might have some use, the patentee also provided a list of such uses, summarised by the Judge at [131]:

i) the inhibition of Neutrokine-α;
ii) to inhibit the chemotaxis and activation of macrophages and their precursors, neutrophils, basophils, B lymphocytes and some T-cell subsets, eg activated and CD8 cytotoxic T cells and natural killer cells;
iii) in certain auto-immune and chronic inflammatory and infective diseases: examples of auto-immune diseases including multiple sclerosis and insulin-dependent diabetes; infectious diseases including silicosis, sarcoidosis, idiopathic pulmonary fibrosis;
iv) to treat idiopathic hyper-eosinophilic syndrome by preventing oesinophil production and migration;
v) to treat endotoxic shock by preventing the migration of macrophages;
vi) to treat atherosclerosis by preventing monocyte infiltration in the artery wall;
vii) to treat histamine-mediated allergic reactions and immunological disorders including late phase allergic reactions, chronic urticaria, and atopic dermatitis;
viii) to treat IgE-mediated allergic reactions such as allergic asthma, rhinitis, and eczema;
ix) to treat chronic and acute inflammation chronic and acute inflammatory pulmonary diseases;
x) to treat rheumatoid arthritis by preventing the attraction of monocytes into synovial fluid;
xi) to treat degenerative and inflammatory arthropathies;
xii) to prevent inflammation;
xiii) to inhibit prostaglandin-independent fever induced by chemokines;

xiv) to treat cases of bone marrow failure;
xv) to treat asthma and allergy by preventing oesinophil accumulation in the lung.
117. The key claims of the Patent as now settled by the TBA are in part to nucleic acid sequences encoding for Neutrokine-α or important parts of it and for Neutrokine-α or important parts of it.
118. The Judge drew these important conclusions:
[134] Overall, the Patent contains extravagant and sometimes contradictory claims. By way of illustration, it suggests in paragraph [0123] that Neutrokine-α inhibits immune cell function and in paragraph [0143] that antagonists of Neutrokine-α also inhibit immune cell function. There is nothing by way of experimental evidence to support the claims made and I accept Professor Saklatvala's evidence that the idea that Neutrokine-α and antagonists to Neutrokine–α could be used to treat the extraordinary range of diseases identified was fanciful. He found it hard to believe that anyone could seriously suggest on the basis of no experimental data at all that that Neutrokine-α was the answer to so many conditions, from treating cancer to treating worms. In my judgment 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. It teaches the skilled person nothing useful about its activity other than that Neutrokine-α is another member of the TNF ligand superfamily.
[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. As is apparent from my review in paragraphs [100]-[134] of this judgment, it 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, as I have found, 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 which I have considered in paragraphs [34]-[77] of this judgment. 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, as Professor Saklatvala accepted, 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; and that it would have the same roles, to some degree, as those described in the Gruss paper.
[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, as explained in the Maini publication, 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.
[234] 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.
119. 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 program to see which, if any, of the possible uses of the Neutrokine-α or its antagonists was real.
120. Lilly accepts that the patent does indeed convey enough information to make it plausible that Neutrokine-α is a member of the TNF ligand superfamily. But, it says, that is nonetheless not good enough – for the biological effects and activities of that family were so poorly understood that any actual use should be regard-

ed as purely speculative – as too vague. The very list of possible uses shows that.

121. Mr Carr's response to this was in large part to accept Lilly's case and what the Judge said at [134]. However his submission was to the effect that within the mass of mere speculation, there was a kernel of more substance amounting to a teaching of a practical use which was sufficiently concrete to satisfy an "educated guess" test to the standard applied in the EPO.

122. In this connnection he reminded us of what Lord Walker had said about disentangling extraneous matter in the patent in Conor v Angiotech at [53]. Mr Carr suggested there was a good analogy in this case even though the disregarded matter in Conor, unlike that in this case, was not in part self-contradictory.

123. He then went on to submit that the Judge had made the necessary findings of fact amounting to the kernel he relied on. He therefore submitted that this was not the sort of case where this Court should be slow to reverse a value judgment formed by a first instance judge. Far from it, we should apply the relevant, as he submitted, findings of the Judge.

124. For good measure, he submitted, those findings were the same as those made by the TBA in its decision on this patent. So we should align ourselves with that decision.

125. Mr Carr focussed on just two aspects of potential use, accepting, rightly, that if neither of these got him home, nothing else would. He pointed to the fact that the Patent "incorporated by reference in its entirety" a paper by Gruss and Dower and, of course the patent would be read with the common general knowledge. He summarised his submission thus:

It was plausible, based on the common general knowledge and the disclosure of the patent (including Gruss & Dower) that Neutrokine-□ would, at the cellular level:

1) be expressed on activated T cells and co-stimulate T cell proliferation and hence be involved in regulation of T cell proliferation and T cell mediated immune responses;

2) co-stimulate B cell proliferation and be involved in the regulation of B cell proliferation and humoral B cell activity;

3) be expressed on B cell and T cell lymphomas;

plausibly leading to, at the biological level, application of Neutrokine-□ and/or antagonists (including antibodies):

1) in the regulation of the immune and inflammatory responses and in the treatment and diagnosis of autoimmune diseases (e.g. RA) and inflammatory conditions;

2) in the control of tumours and malignant diseases, including B cell and T cell lymphomas.

126. Gruss and Dower is a general review of the 10 TNF-ligand superfamily members that had been discovered up until its date (1995, just before the priority date of the Patent). Thus it provides a valuable "freeze-frame" picture at just the right time. Table 4 is headed "Role of the TNF Ligand Superfamily Members for T- and B-Cell Activation Involved in the Immune Response". It contains a list of functions of 6 members of the superfamily with a + or – sign indicating whether the function is present for each member. All 6 get a + for T-cell costimulation; for B-cell proliferation one gets a – and one a + with no information given for the other 4 in the table.

127. Gruss and Dower also have this to say about T- and B-cell activity:

Biologic activities related to T-cell-mediated immunity are a unique feature for all members of the TNF ligand superfamily. All ligands and receptors, without exception, are expressed on activated T cells (Table 4). Purified human T cells and T-cell clones show enhanced proliferation when stimulated with any recombinant TNF family ligand or crosslinked with antireceptor antibodies in the presence of anti-CD3 or other mitogens, such as phytohemagglutinin (PHA), phorbol myristate acetate (PMA), or ionomycin. Possible autocrine T-cell activation and growth control might be a common feature of this protein family. The induction of each ligand expression shows unique kinetics consistent with different roles for each of these ligands in the T-cell activation. For example, the induction of CD30L surface expression on activated T cells is slower in comparison to other TNF ligands such as TNF, CD27L, CD40L, and 4-1BBL (maximal expression, 24 hours v 6 hours, respectively). B-cell proliferation and Ig secretion is induced by at least TNF, LT□, and CD40L. Further, several members participate in T-cell-dependent help for B cells, which are known to express TNFR-I, TNFR-II, CD27, CD30, CD40, FAS and 4-1BB (Table 4). TNF, LT□, and CD40L are mitogenic to B cells.

In general, all TNF ligand superfamily members, including FASL and CD40L, are essential for T-cell costimulation and activation. It is of special interest that signals, at least through CD27L, CD40L, and 4-1BBL, can provide costimulation for activated peripheral blood (PB) T cells. Further studies need to be performed to see if other TNF ligand superfamily members are able to transduce a costimulatory signal.

128. In its summary, Gruss and Dower tells the reader that even for T-cell proliferation, the members of the family do not necessarily each act in the same way:

Taken together, TNF superfamily ligands show for the immune response an involvement in the induction of cytokine secretion and the upregulation of adhesion molecules, activation antigens, and costimulatory proteins, all known to amplify stimulatory and regulatory signals. On the other hand, differences in the distribution, kinetics of induction, and requirements for induction support a defined role for each of the ligands for T-cell mediated immune responses. The shedding of members of the TNF receptor superfamily could limit the signals mediated by the corresponding ligands as a functional regulatory mechanism. Induction of cytotoxic cell death, observed for TNF, LT□, CD30L, CD95L, and 4-1BBL, is another common functional feature of this cytokine family. Further studies have to identify unique versus redundant biologic and physiologic functions for each of the TNF superfamily ligands.

129. Of particular importance is Gruss and Dower's assessment of the practical usefulness of the TNF-ligand superfamily as a whole. They only go this far:
Several TNFR superfamily members could be candidates for novel treatment protocols. Recombinant CD30L and CD40L could be by itself antitumorigenic for CD30+ ALCLs and CD40+ B-cell NHLs, respectively. Furthermore, CD30 and CD40 might be used for tumor targeting after conjugation with radioisotypes or cytostatic drugs for CD30+ and/or CD40+ HD and NHLs.
130. That is far from saying that any member of the superfamily (or its agonists) has real or indeed any potential as a therapeutic or diagnostic agent. It is merely saying some identified members may have some use because of their individual known properties. Significantly Gruss and Dower, even though they are putting their minds to potential uses of members of the superfamily do not say that the T-cell proliferation common function or B-cell stimulation is enough to indicate that any member of the family could be "a candidate for a novel treatment protocol" i.e. have a use.
131. The reason this is so important is that it is a statement from the time by real experts with no axe to grind. They are not saying there is a plausible (at least in the sense of reasonably credible) use for any member of the superfamily.
132. Now it is true that it was known that all members of the superfamily were expressed by activated T cells, that they all played a role in the regulation of T cell proliferation and T cell mediated immune responses and that some of the ligands played a role in the regulation of B-cell proliferation and antibody secretion and some took part in T cell dependent regulation of B cells. But it by no means follows that any member of the superfamily has a practical use or that the skilled reader would envisage such a use (other than as a speculation) on being told that a new member of the superfamily had been found. You would have to investigate each of them to find out. It is not impossible they would have such a use of some sort, but no more. It is all too speculative to say, on the basis of the information in the patent and common general knowledge that a newly found member of the superfamily is "capable of industrial application." That view is surely reinforced by the fact that only TNF-α had found any use and that was rather specialised, as I have already noted.
133. The Judge thought his conclusion as to the speculative nature of the claims in the patent was confirmed by the subsequent history of investigations by both HGS and others, particularly into B cells and T cells. He set out the detail (which was not challenged) at [141-175]. His summary is as follows:
[176] The papers and work to which I have referred represent only a very small fraction of the work carried out on Neutrokine-α. Nevertheless, I believe the following general conclusions can be drawn from them and the expert evidence. From 1999 it became increasingly clear that Neutrokine-α is expressed by peripheral blood leukocytes, and in the spleen and lymph nodes. From that time it also became apparent that Neutrokine-α plays a significant and particular role in the proliferation and differentiation of B cells. Subsequently it has also been shown to play a part in the regulation of T cell proliferation and activation. As the activities of Neutrokine-α have gradually been elucidated, and particularly those relating to B cells, it has become increasingly recognised as a potential therapeutic target for diseases that are specifically associated with altered B cell function. Notable amongst these are autoimmune diseases such as rheumatoid arthritis and SLE and B cell malignancies such as lymphoma. 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.
134. It should be noticed that his summary was reached not only by an examination of the papers but also from the expert evidence about them. That evidence included evidence about a paper by Moore et al. in 1999, some years on from the date of the patent. No one from HGS was called as a witness to give evidence about the work done at HGS. Instead HGS's expert, Professor Noelle, gave evidence about the paper, evidence which the Judge rejected at [150] saying "it did him no credit." The significance of the paper is that at that time those at HGS could not find any T-cell effect, thus demonstrating that it was a far from straightforward matter even to establish the first stage of any prediction about usefulness in relation to T-cells.
135. The same paper did report some effect, only in relation to B cells. But of course one could not say that such an effect was a sound prediction at the date of the patent, since at that date only some of the known superfamily had shown an effect in relation to such cells. B-cell activity was not a common factor for all or even a majority of members of the superfamily. The most an educated guesser could say is "it might have a B-cell effect, if so I don't know what that effect might be." It may be noted that the Board did not base its decision to uphold the patent on any potential B-cell effect.
136. Accordingly based on the evidence before him, I conclude that the Judge's decision about Art. 57 cannot be faulted and the appeal falls to be dismissed.
137. Although the Judge and the TBA asked the same key question and identified the same "kernel" the real difference is that the Judge found on the facts before him that the "kernel" did not provide any basis for supposing that the invention was susceptible of industrial application whereas on the facts before it the Board thought there was.
138. Since the Board has come to a different conclusion I should be more specific about this. As I have already

said the Board did not purport to lay down any new principle or even to vary an old one. It is a decision on the facts as the TBA saw them. As I have said those facts include what some would regard as a last minute affidavit by a Dr Kelsoe. I do not know what it said, and of course it was never tested by cross-examination – as was the evidence of HGS's corresponding witness in this case, Prof. Noelle, evidence which in some respects was held to do him no credit.

139. The TBA deals with Art. 57 at [21-34]. It notes that it is common ground that Neutrokine-α is a member of the TNF-ligand superfamily. It then asks the question which I described as "crucial" above, namely "Is that enough?" The Board put it this way, whether this [i.e. being a member of the superfamily] "suffices to suggest a practical way to exploit the claimed invention … thereby providing an immediate concrete benefit [the Board's italics]." So there was no difference at all between the question the Judge and I think are crucial and that which the Board did.

140. The next paragraph makes the by-now-uncontroversial point that cases of this sort are fact-specific and involve questions of degree:

[22] As pointed out in [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.

141. It is clear from this paragraph that the Board rejected the argument that merely allocating Neutrokine-α to the TNF ligand family was enough. A detailed examination of all the facts was required. That is what the Board proceeded to do in the remainder of its decision. So it is clear that the Board's decision depended on their assessment of the facts; and not on any principle of law.

142. In [23] the Board finds that all members of the TNF-ligand superfamily "are known to be … involved in various medical conditions." The evidence in this case was different. Professor Saklatvala said this:

I cannot support Professor Noelle's comment that one would expect Neutrokine-α to be useful in the same way as other members of the TNF ligand superfamily. By 1996 only TNF-α had been shown to be biomedically useful.

Prof Saklatvala was found to be "an outstandingly good witness" and his evidence "of very great assistance.". Prof. Noelle's evidence was less well received.

143. Also in [23] the Board said that although the known members of the TNF ligand superfamily "display a wide range of activities" a "feature common to all members is the expression on activated T-cells and the ability to co-stimulate T-cell proliferation." It refers inter alia to Gruss and Dower as evidence for this. It does not note that the authors themselves do not say that fact is in any way a lead to any practical use for all or even any members of the family – a matter I think of significance as I have said above.

144. In [24] the Board focuses on [63] of the Patent:

(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.

145. It is worth contrasting this statement with what the Patent says at [123]:

Neutrokine-α may also be suitable to inhibit T-cell proliferation by the inhibition of IL-2 biosynthesis for the treatment of T-cell mediated auto-immune diseases and lymphocytic leukemias.

The contrast is remarkable, and surely supports Kitchin J's view that the Patent, even in relation to T-cell activity, is just too speculative to provide anything of practical value other than information upon which a research programme can be based.

146. The Board says about the [63] statement that it is plausible and confirmed by post published evidence. As to being "plausible" it is not impossible, just as all the other things said in the Patent are not impossible as individual items. But that cannot be enough to provide an immediate and concrete benefit.

147. Moreover even Prof. Noelle accepted under cross-examination that the [63] statement was not credible as respects all leukocytes, thus demonstrating its essentially speculative nature.

148. Nor, on the evidence before the Judge do I agree that a skilled reader would read the patent as the Board went on to hold:

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 - in the respondent's view - 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 leukocytes, are the first essential steps at the onset of research work on the newly found TNF ligand superfamily member.

Certainly there was no evidence from either side before Kitchin J that a skilled man would approach the patent with an ability to distinguish the kernel from the rest.

149. I would add, with respect, that "a first step at the onset of research work" is hardly enough to provide "an immediate and concrete benefit".
150. The Board said at [27]:
In the present case, 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.
151. It then rejected two Lilly arguments, first that there were such technical difficulties involved in measuring the co-stimulation of T-cells by Neutrokine-α that they could not be reproduced without undertaking a research programme, and second that you cannot say there will or may be an industrial application from merely knowing about co-stimulation of T-cells.
152. As to the first point, the Board thought that standard assays would do the job. But Kitchin J's finding on the facts was to the opposite effect:
[77] … 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 assess 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.
153. Moreover Kitchin J considered the Moore paper to which I have already referred, showing that in fact HGS could not find T-cell activity by the date of that paper.
154. So the findings of fact before the Board (which include reliance on the late-filed evidence of Dr Kelsoe) and before Kitchin J were different. I have to go by the latter, noting again as I do that his findings were arrived at following an intensive examination of the evidence.
155. As to the second point, I confess I do not really see why the mere fact of the T-cell activity "may represent a valid basis for a possible industrial application" as the Board held. Nor do I consider that such a test is consistent with settled TBA authority, can fairly be said to provide either an "immediate" or "concrete" benefit or, fundamentally, amount to something which is "susceptible of industrial application."
156. In connection with T-cell activity the Board either overlooked (or did not have) the paper by Kalled et al published in 2005. The Judge quotes it at [169-170]. I just pick out a key sentence: "How physiologically relevant this activity is in vivo needs to be further investigated." That seems to me to be a clear statement, nearly 9 years after the date of the patent, that it was not known what significance the T-cell activity had – that seems rather a long way from "an immediate and concrete benefit."
157. There are other differences between the findings of the Judge and the TBA, but what I have said is enough to demonstrate why their results were different. The upshot of all this is that Board, working on different evidence and using a different procedure came to a different conclusion on the facts. We are not bound to follow, or even give deference to, the Board's findings of fact.
158. For the above reasons I have come to the clear conclusion that the Judge was right to hold that the invention failed to comply with Art. 57.
159. It follows that the appeal should be dismissed. It is not necessary to consider the other points argued (insufficiency and AgrEvo type obviousness). I rather suspect they would go hand-in-hand with Art 57, but it is unnecessary to consider whether there are subtle differences given that the invention was not "susceptible of industrial application."
Lady Justice Hallett:
160. I agree.
Mr Justice Lewison:
161. I also agree.