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**Datasheet for the decision
of 7 December 2005**

Case Number: T 1111/02 - 3.3.04

Application Number: 91908963.1

Publication Number: 0527839

IPC: C12Q 1/70

Language of the proceedings: EN

Title of invention:

Recombinant library screening methods

Patentee:

Biosite Incorporated

Opponent:

Cambridge Antibody Technology Limited

Headword:

Library Screening Methods/BIOSITE

Relevant legal provisions:

EPC Art. 83, 100(b), 112

EPC R. 88

Keyword:

"Correction under Rule 88 EPC - (no)"

"Sufficiency of disclosure - (no)"

"Referral to Enlarged Board of Appeal - (no)"

Decisions cited:

-

Catchword:

-



Case Number: T 1111/02 - 3.3.04

DECISION
of the Technical Board of Appeal 3.3.04
of 7 December 2005

Appellant: Cambridge Antibody Technology Limited
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 23 September 2002
rejecting the opposition filed against European
patent No. 0527839 pursuant to Article 102(2)
EPC.

Composition of the Board:

Chairman: S. Perryman
Members: G. Alt
B. Claes

Summary of Facts and Submissions

I. The appeal was lodged by the opponent against the decision of the opposition division of 23 September 2002 to reject the opposition against European patent No. 0 527 839 under Article 102(2) EPC. The patent had been granted on the basis of claims 1 to 12. It had been opposed under Article 100(a) EPC on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC), Article 100(b) EPC and Article 100(c) EPC.

II. Independent claims 1 and 2 as granted read:

"1. The use of a bacteriophage to display a multichain protein, wherein a first chain of the multichain protein is fused to a coat peptide on the outer surface of the bacteriophage, and a second chain of the multichain protein is complexed with the first chain."

"2. A method for screening a DNA library for nucleotide sequences which encode a multichain protein comprising first and second polypeptide chains, which multichain protein binds specifically to a ligand, comprising:

effecting bacteriophage expression vector transformation of a host cell with:

(i) a first nucleotide sequence member of the library that encodes the first chain fused to a sequence encoding a coat peptide of the bacteriophage; and

(ii) a second nucleotide sequence member of the library that encodes the second chain fused to a sequence

encoding a signal peptide that directs periplasmic secretion of said second chain;

cultivating the transformed cell under conditions suitable for expression and assembly of bacteriophage particles and the multichain protein, wherein the multichain protein is displayed on the outer surface of the bacteriophage particles, optionally wherein expression of DNA library sequence members is inducible, induction of expression of the DNA library sequences preferably being delayed until assembly of at least one complete bacteriophage particle has occurred;

selecting bacteriophage particles encoding the multichain protein by means of the ligand and, if desired, further comprising the step of isolating the nucleotide sequences which encode the first and second chains of the multichain protein from the selected bacteriophage particles; optionally wherein the bacteriophage are harvested from the host cell culture before the selecting step."

- III. In its decision rejecting the opposition, the reasoning of the opposition division relating to reproducibility in its section 3 extends over seven and a half pages, and can be briefly summarized as being that though it was undisputed that the only example in the patent was flawed and that the exact repetition of its protocol would not lead the skilled person to the subject-matter of claim 1, declarations such as D26, D27, D28, D30, D31 and D32 by experts on behalf of the patentee, persuaded the opposition division that, given that the skilled person would as a matter of routine perform very precise checks on the protocol to be performed,

the information in the patent and the general knowledge would have been enough for the skilled person without undue burden to successfully correct the errors in the example, and, even with the flawed example, to reliably reproduce the claimed invention. The opposition division also considered and took into account that it had never been disputed that the general strategy disclosed in the patent worked.

- IV. On 25 October 2002 a notice of appeal was filed by the appellant (opponent) and the appeal fee was paid. Grounds of appeal were filed on 3 February 2003. Subsequently further submissions and evidence were filed by the parties.
- V. With the submission dated 4 November 2005 the respondent (patent proprietor) requested correction of the patent under Rule 88 EPC by introduction of the following statement after the description of the oligonucleotide at page 7, lines 55 to 56: "The sequence of the oligonucleotide shown above contains an error and should be corrected to ensure a functional junction between the signal sequence and the heavy chain."
- VI. In the course of the oral proceedings which were held on 6 and 7 December 2005 the respondent submitted the following two sets of questions for referral to the Enlarged Board of Appeal:
- Set A:
- "1. In a prophetic case with only a single but defective specific example can sufficiency of description in accordance with Article 83 [sic] ever be

acknowledged if there is a prevailing technical opinion against?

2. If the answer to question (1) is "yes", under what circumstances; for example, is the answer "yes" if the body of the specification contains a general description which, in practice, would be enough for the skilled person to perform the invention using his common general knowledge?"

Set B:

"1. For the purposes of Article 83 EPC when the single Example in a patent specification is defective and there is a prevailing technical opinion against the invention working, can the skilled person be expected, nevertheless, to attempt to carry out the teaching in the rest of the specification using his common general knowledge?"

2. If the answer to question (1) is "yes", are the requirements of Article 83 EPC satisfied if:
(a) evidence shows he can succeed; and
(b) there are no serious doubts substantiated by verifiable facts."

VII. The following documents are relevant for this decision:

D5: Parmley, S.F. and Smith, G.P., Gene, vol. 73,
1988, pages 305 to 318

D22: Declaration of Prof. Sir Aaron Klug dated
25 August 1999

D26: Declaration of Dr Glaser (I) dated 13 November
2000

D27: Declaration of Dr Gray (I) dated 13 November 2000

D28: Declaration of Dr Donoghue dated 9 November 2000

D30: Declaration of Dr Kang dated 10 April 2002

D31: Declaration of Prof. Stirling dated 12 April 2002

D32: Declaration of Dr Glaser (II) dated 11 April 2002

D34: Declaration of Dr Stinchcombe dated 16 January
2004

D35: Declaration of Dr Mudgett dated 15 January 2004

D36: Declaration of Dr Wendland dated 15 January 2004

D37: Declaration of Dr Darsow dated 27 January 2004

D38: Declaration of Dr Glaser (III) dated 12 January
2004

D40: Declaration of Dr Gray (II) dated 6 April 2004

VIII. The appellant's arguments, as far as they are relevant
for the present decision, may be summarized as follows:

Main request

Correction under Rule 88 EPC

- The error in the sequence of the oligonucleotide on page 7, lines 55 and 56 was not immediately evident. Neither could it be recognized upon simply reading the patent nor was it sure, whether, had the irregularity indeed been detected, it was an error or not. The change could have been introduced deliberately in order to overcome the reported problems of display of large fragments on the phage surface.

- Even if the error was detected and attempts are made to rectify it, it could be corrected in several ways. For example, instead of completing the missing residues of the signal sequence, one could have replaced it completely with a signal sequence of a different protein as taught on page 3, line 15 of the patent in suit. Consequently, the intended correction was not obvious.

Sufficiency of disclosure

- If the procedure in the example was taken step by step none of the claimed subject-matter would be achieved.

- The state of the art, especially document D5, indicated that inserts over 100 amino acids could not be displayed. Given the prevailing opinion that taught the skilled person to expect failure in the first place and given that the specification lacked any step of verification of the presence and function of something displayed, the skilled person had no motivation to seek out errors in the protocol and to correct them.

- Evidence from molecular biologists putting forward that they would usually perform checks of a protocol before starting a cloning experiment, and that they therefore would have detected the errors and would have easily corrected them, did not represent a realistic approach because in contrast to the situation at the priority date of the patent in suit the declarants were aware of later work demonstrating successful phage display of large multichain protein fragments.

Auxiliary Request

Questions for referral to the Enlarged Board of Appeal

- The answer to each of the questions was dependent on the circumstances of a case, for example, on the detailedness of the general disclosure. Thus, since there was no generally valid answer to the questions, they were questions of fact and not of law.

IX. The respondent's arguments, as far as they are relevant for the present decision, may be summarized as follows:

Main Request

Correction under Rule 88 EPC

- The skilled person was a cautious and conservative molecular biologist and would therefore always check new protocols. Real life support for this behaviour came from declarations D26, D27 and D34 to D40. Given that the skilled person would also keep in

view what he was trying to achieve, he would have immediately recognized the errors and would have realized their obvious correction, namely, on the one hand the modification of the oligonucleotide sequence of page 7, lines 55 to 56 in order to allow for complete expression of the signal sequence and on the other hand additional expression of the missing antibody residues. Thus, the error and its correction were immediately evident.

Sufficiency of disclosure

- The protocol given in the example contained errors with the effect that if the skilled person had followed it literally a functional F_{ab} antibody fragment would not have been displayed on the phage surface.

- Nevertheless, there would be no failure when carrying out the example because the skilled person had checked the protocol before starting, had detected the errors and simply corrected them. Since this way of proceeding is a routine course of action, the skilled person would not have been influenced in his behaviour by the technical opinion of the prior art.

- Moreover, the general disclosure of the patent in suit was detailed enough so that the skilled person could have designed its own protocol. Evidence for this view came from declarations D30 and D31.

Auxiliary Request

Questions for referral to the Enlarged Board of Appeal

- The questions addressed an important question of law, namely whether or not the attitude and behaviour of the skilled person, when he is faced with a deficient example, is dependent upon the surrounding circumstances.
 - The EPC had no requirement equivalent to that under US law that an invention had to be reduced to practice. Requiring a workable example would be to introduce such a requirement. Thus prophetic examples such as the example in the patent were allowable.
- X. Oral proceedings took place on 6th and 7th December 2005. First, the parties were heard on the respondent's request for correction under Rule 88 EPC, and after deliberation by the board it was indicated that this request for correction was not allowable.

- XI. At the end of the oral proceedings the following requests were maintained:

The appellant (opponent) requested that the decision under appeal be set aside and that the European patent No. 0 527 839 be revoked

The respondent (proprietor) requested as main request that the appeal be dismissed and as auxiliary request that the questions submitted at the oral proceedings on

6th and 7th December 2005 be referred to the Enlarged Board of Appeal.

Reasons for the Decision

1. The appeal is admissible

Correction under Rule 88 EPC

2. Rule 88 EPC reads "Linguistic errors, errors of transcription and mistakes in any document filed with the European Patent Office may be corrected on request. However, if the request for such correction concerns a description, claims or drawings the correction must be obvious in the sense that it is immediately evident that nothing else would have been intended than what is offered as the correction".
3. This means that it must both be obvious that there is an error, and it must be immediately and unambiguously clear what the correct version should be, if the European Patent Office is to exercise its discretion under Rule 88 EPC to allow the requested correction.
4. As agreed by the parties the erroneous sequence of the oligonucleotide and further errors, be they all related to the first one or not, would have only been brought to light after checking of the protocol. This is at odds with the notion that the mistake must be "immediately evident". Thus, the first of the two requirements for allowance of a correction under Rule 88 EPC is not fulfilled. Therefore, further

considerations whether or not the intended correction is immediately clear are not necessary.

5. The request for an amendment by correction is refused.

Sufficiency of disclosure

6. The two independent claims of the patent in suit are directed to the use of a bacteriophage to display a multichain protein and to a method for screening a DNA library for nucleotide sequences which encodes a multichain protein, respectively.
7. Compared to the invention that the patent is directed to as set out in paragraph 6 above, the state of the art as represented by document D5 discloses the expression of peptides coded for by DNA fragments as fusion proteins with coat protein III of phage fd. The authors saw breakdown products when a protein of 111 amino acids was expressed, and stated in the discussion bridging pages 314 and 315 (Remark by the board: The abbreviation "aa" means "amino acid".):

"The new fusion phage vectors, fUSE1 and fUSE2, accept inserts in gene III with little or no loss of phage function; inserts are stable. The foreign aa encoded in the inserts are expressed on the surface of the phage; two clones carrying fragments of a target gene were shown to express determinants recognized by antibody to the gene product. These results demonstrate the ability of fUSE vectors to accept inserts up to 335 bp (perhaps more) and express the foreign aa encoded in the inserts on the surface of the virion.

Some inserts by their very nature will affect pIII function. Inserts that contain anchor domains or other hydrophobic segments may stop transfer of pIII into the host membrane (Davis and Model, 1985) and presumably would not be tolerated. Inserts that exceed 335 bp may lead to excessive breakdown of the fusion protein or otherwise impair pIII function, so for the time being we recommended using fragments of 100-300 bp."

8. It is not disputed that the patent's contemplated and claimed display of multichain proteins is something more difficult and complex than anything suggested in the prior art including document D5. What the patent requires to be done for the first polypeptide chain corresponds to what is suggested in document D5, but without regard to observing the recommended range of 100-300bp for the fragment. In addition, the proposal of the patent requires effecting bacteriophage expression of the same host cell with a second nucleotide sequence that encodes the second chain of the multichain protein, fused to a sequence encoding a signal peptide that directs periplasmic secretion of said second chain, and cultivating the transformed cell under conditions suitable for expression and assembly of bacteriophage particles and the multichain protein so that this is displayed on the outer surface of the bacteriophage particles.

9. The claimed subject-matter is disclosed in the patent specification by a generic description, including references to other publications, and a single example with a detailed protocol indicating the choices to be made in the cloning strategy, including choice of phage, of vector, and of splicing sites to display a

particular multi-chain protein. The question is whether these instructions are sufficient to enable the skilled person to carry out the invention, i.e. to achieve the display of functional, conformationally correct, large multichain proteins on a phage surface.

10. The generic description refers very generally to methods and elements used in the prior art in the framework of cloning and expression of proteins without giving any specific hint however as to how these should be applied and combined in order to achieve successful expression in the present case.

11. As regards the single example, document D22, a declaration by Professor Sir Klug, reports several errors in this protocol which existence is not contested by the respondent. The main errors and their consequences are:
 - The introduction of a BstX1 site by site-directed mutagenesis with the oligonucleotide given on page 7, lines 33 to 34 of the patent specification changes the three amino acids prior to the signal cleavage from "Ser-His-Ser" to "Trp-His-Ser" and introduces a wrong gene III sequence after the first four amino acids downstream of the signal cleavage.

 - The ligation into the BstX1 site of the oligonucleotide given on page 7, lines 55 to 56 of the patent specification providing XhoI and SpeI sites for insertion of the antibody heavy chains results in the introduction of an amber stop codon in the signal peptide of gene III. Moreover, the six

first amino acids of gene III are changed from "Ala-Glu-Thr-Val-Pro-Val" to "His-Asp-Val-Leu-Val-Leu".

- It is disclosed on page 8, lines 16 to 17 that the cDNA sequences representing the antigen binding domains of the heavy and light antibody chains are synthesized from the RNA of antibody-producing cells in the manner described in a paper authored by Huse and others. This paper sets out a number of primers for amplification of the immunoglobulin domains. The primers described by Huse for annealing to the 5' end of the antibody gene all use the same reading frame. The use of these primers for amplification and finally, the subsequent cloning of the obtained antibody encoding cDNA into the XhoI site of the defective vector described above create the following problems: (i) The amber codon in the gene III leader sequence prevents expression of gene III protein so that no antibody-gene III protein fusion is generated; and (ii) When the sequence fragments obtained with the primers disclosed in the paper by Huse mentioned above are inserted into the XhoI-SpeI-digested vector of the patent in suit, the heavy chain antibody sequences go out of frame so that no functional heavy chain is produced.
12. As already noted above in paragraph 8, the invention set out in the disputed patent requires the adaptation of the method disclosed in document D5 for the expression of **longer** proteins and the generation of biologically active **multichain** proteins on the phage surface. There is no description in the prior art that any of these two goals has ever been achieved. The generic description of the patent in suit recites

standard methods and elements which, without any indication as to how they are to be applied and combined in the present case, do not give a basis for assuming that they are suited to assist the skilled person to successfully achieve the required complex cloning and expression procedure. Finally, the errors in the single example as outlined above in paragraph 11 are such as to hit the core of the present invention because they concern the correct putting together of all cloning elements, a prerequisite for obtaining correct protein expression. Therefore, there is no guidance from this example, either. The board judges that in the absence of a workable example and adequate knowledge from the prior art or the generic description of the patent, it puts an undue burden on the skilled person to carry out the claimed invention.

13. The respondent has sought to avoid the conclusion that therefore the patent must fail for insufficiency, by arguing that a skilled reader, firstly, would have noticed the errors in the example and have had the knowledge to correct them easily, so that he would in fact have had a working example, and secondly, would in any case have had enough knowledge from the generic description in the patent and his own general knowledge to be able to carry out the invention.

14. The respondent relies on various declarations to support sufficiency, i.e. on documents D26, D27, D28, D30, D31, D32, D34, D35, D36, D37, D38 and D40, given by scientists after the priority date of the patent in suit. The general tenor of these can be seen from the following extracts of the declaration of Dr Scott Glaser of 3 November 2000 (document D26):

- "7. I now describe how I analyzed the Example 1 of the Dower patent [patent in suit], identified certain errors in it, and how these errors can be corrected. My general experience of performing procedures from journals or given to by others is that the procedures often contain minor errors. In my experience, if such errors are spotted before performing a procedure or early on in the procedure, they are usually easy to correct, but that if left undetected until later in the procedure (e.g., when attempting to express a sequence) can cause significant wasted time. Accordingly, it is my routine practice (and was in May of 1990) to perform certain checks before and during the early stages of a cloning procedure. Specifically, before performing a cloning procedure, my routine practice was to write down the sequence (or sometimes the restriction map if this was all that was available) of all initial DNA components to be joined, and the resulting sequences of all hybrid molecules following manipulations, such as cleavage and ligation. I would then check the hybrid sequences against the initial sequences to ensure an appropriate joining between the two free ends to avoid inadvertently introducing unwanted amino acid residues, stop codons, or frameshift mutations. I would perform these checks either with pen and paper or using commercial software. If I discovered errors, my practice was to correct them conceptually, and go through the same checking process for the corrected sequences to identify any further errors introduced by the corrections. Eventually, after satisfying myself that my conceptual construct would have the

sequence I intended, I would proceed to synthesize the construct. Thereafter, I would sequence the construct, or at least key components of it, and compare the actual sequence with what I had intended. Only if the two matched would I then proceed with subsequent steps, such as producing a cell line expressing the construct." and

- "17. I disagree with Dr Klug's conclusion that considerable intellectual effort and considerable experimentation would be required to overcome errors in the disclosure of the patent. As I have indicated above, I recognized the errors in the patent simply by performing my usual checks before a cloning experiment of this type. Further, to me, correction of the errors was a simple matter that would not require any experimentation. As previously discussed, the heavy chain errors can be corrected by changing a segment of an oligonucleotide, and the light chain error by deleting a pair of extraneous restriction sites before performing other steps. Thus, to my mind, the procedure described in the Dower patent is workable. I would expect that I or a colleague prepared to exercise standard precautions to detect errors and common sense to correct them would have succeeded. Moreover, if I had not succeeded at the first attempt, I would not have concluded that the procedure described in the patent was fatally flawed, but would rather have re-examined the constructs employed to check for additional errors of the type described above."

15. The only contemporary evidence that is before the board relating to what type of experimental protocol a skilled person would come up with at the priority date of the patent in suit on the basis of the generic description in the patent and his own general knowledge is the single example that is actually in the patent in suit. The only certain fact in this case is that the single example of the patent does not work. As it must be assumed that the skill of the inventors is representative of at least average skill, the presence of this unworkable example is inconsistent with the argument advanced by the respondent that the average skilled person would have noticed the errors in the example and have had the knowledge to correct them easily, or that the average skilled person would in any case have had enough knowledge from the generic description in the patent and his own general knowledge to carry out the invention. For the board the evidentiary value of this one certain fact outweighs all the declarations relied on by the respondent, as these are little more than speculation many years later as to what a skilled person might have done or succeeded in, and leads the board to the conclusion that the patent describes the invention insufficiently for the skilled person to carry it out.

16. It appears to the board that the respondent is seeking to set too high a standard for the abilities of the skilled person in getting a patented invention to work and the efforts that can be expected from him to achieve success. Even if the board had been persuaded, which it has not been, on the evidence that the skilled person would have checked the protocol and recognized unambiguously the errors in the example, this would

have made the skilled person realize that the patent contains nothing to show that success is possible. On the facts of this case, where the invention involves achieving something more complex than the state of the art considered possible, the skilled person would be left in doubt whether any reasonable efforts would bring success or whether he would be embarking on research with quite uncertain outcome. This would also lead the board to the conclusion that the patent describes the invention insufficiently for the skilled person to carry it out without undue burden.

17. The board is aware that there have been cases where, on the facts, sufficiency has been acknowledged despite the description containing no example or only a defective example. But sufficiency in each case depends on the particular facts. That an example may be important has been recognized by the legislator, as the requirements for the content of the description of a patent as stated in Rule 27 EPC include "(f) describe in detail at least one way of carrying out the invention claimed using examples where appropriate...". In this case, the board considers that a workable example would have been both appropriate and necessary.

18. Further the respondent has submitted that the EPC had no requirement equivalent to that under US law that an invention had to be reduced to practice, and that requiring a workable example would be to introduce such a requirement. Thus, prophetic cases such as the patent in suit and its example were allowable. Taking "example in a prophetic case" and "prophetic example" as euphemisms for an example in a patent specification in the form of a protocol which has not been

experimentally verified as workable, the board would agree that a prophetic example can be taken into account for the purposes of considering whether the description is sufficient to meet the requirements of Articles 83/100(b) EPC. The negative conclusion of the board in this case is not due to the example being "prophetic" (that is unverified experimentally), but due to the fact that it is unworkable. Obviously, someone who provides only a prophetic example is at greater risk of not being found to have met the requirements of Articles 83 EPC because it turns out to be unworkable, than someone who has provided only experimentally verified examples of proven workability. This is a question of the value of the information content of the patent and not of introducing a requirement that the invention had to have been reduced to practice.

19. The Opposition Division in its decision stated that it considered and took into account that it had never been disputed that the general strategy disclosed in the patent worked. It is not clear to the board what the opposition division meant by "general strategy", what time they were referring to or what evidence they were relying on. However, since the appellant had disputed the sufficiency of the description of the patent in suit, this is the relevant question and not, whether or not the general strategy worked. Moreover, that the general strategy could be got to work at a later time when the art was more advanced does not mean that the description of the patent was sufficient.

20. The board thus concludes that the invention is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

Auxiliary Request

Questions for referral to the Enlarged Board of Appeal

21. Article 112(1) EPC stipulates that the Board of Appeal shall, during the proceedings on a case following a request from a party to the appeal, refer any question to the Enlarged Board of Appeal if it considers that a decision is required in order to ensure uniform application of the law, or if an important point of law arises.
22. Whether for the purposes of Article 83 EPC the invention is disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art is a question which, for the board in this case, turns essentially on the view taken of the facts of this particular case, and not on any point of law, and is thus a question which is to be answered by this board. The board sees no question of law that needs to be referred to the Enlarged Board of Appeal in order for this board to come to decide on sufficiency.
23. The questions proposed by the respondent do not relate to any uniform application of the law, as this board does not take any view of the law different to earlier cases. It is doubtful whether they are questions of law at all, and they are certainly not questions whose answers would assist this board.

24. Specifically, Set A, question 1 "In a prophetic case with only a single but defective specific example can sufficiency of description in accordance with Article 83 [sic] ever be acknowledged if there is a prevailing technical opinion against?", if not rejected as inadmissible by the Enlarged Board of Appeal as being too hypothetical, would in the opinion of this board invite the answer that it depends on the facts of the case, which would leave this board no wiser. The less likely answer "no, never" would not change the outcome of this appeal.
25. Set A, question 2 "If the answer to question (1) is "yes", under what circumstances; for example, is the answer "yes" if the body of the specification contains a general description which, in practice, would be enough for the skilled person to perform the invention using his common general knowledge?" is unsuitable as it would require the Enlarged Board of Appeal to speculate as to hypothetical facts not relevant to this case. On the facts of this case as found by this board, the skilled person cannot perform the invention using his common general knowledge.
26. The questions of Set B: "1. For the purposes of Article 83 EPC when the single Example in a patent specification is defective and there is a prevailing technical opinion against the invention working, can the skilled person be expected, nevertheless, to attempt to carry out the teaching in the rest of the specification using his common general knowledge?" and "2. If the answer to question (1) is "yes", are the requirements of Article 83 EPC satisfied if: (a) evidence shows he can succeed; and (b) there are no

serious doubts substantiated by verifiable facts?"
again amount to an attempt to get the Enlarged Board of
Appeal to answer questions on the basis of hypothetical
facts, and so are not suitable for a referral.

27. Consequently, the request for referral of questions to
the Enlarged Board of Appeal is refused.

Order

For these reasons it is decided that:

1. The request for referral of questions to the Enlarged
Board of Appeal is refused.
2. The decision under appeal is set aside
3. The patent is revoked.

Registrar:

Chair:

P. Cremona

S. Perryman