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D E C I S I O N
of 20 April 1994

Case Number: T 0212/92 - 3.4.2

Application Number: 86903560.0

Publication Number: 0224590

IPC: G01N 33/577, G01N 33/68, G01N 33/53, C05K 15/04, C12P 21/00, C12N 15/00, A61K 39/395

Language of the proceedings: EN

Title of invention:
Method for assaying human pulmonary surface active substance and reagent kit therefor

Applicant:
Teijin Limited

Opponent:
-

Headword:
-

Relevant legal norms:
EPC Art. 83

Keyword:
"Disclosure sufficiently clear and complete - yes"

Decisions cited:
-

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0212/92 - 3.4.2

D E C I S I O N
of the Technical Board of Appeal 3.4.2
of 20 April 1994

Appellant: Teijin Limited
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Decision under appeal: **Decision of the Examining Division of the European Patent Office dated 27 September 1991 refusing European patent application No. 86 903 560.0 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: C. Black
Members: R. Zottmann
M. Lewenton

Summary of Facts and Submissions

I. European patent application No. 86 903 560.0 (publication No. EP-A-0 224 590) was refused by decision of the Examining Division on the ground that it did not meet the requirement of Article 83 EPC.

II. The present appeal against the said decision is based on the following documents, which are unamended as compared with those under consideration in the decision:

Description pages 1, 20 and 25 as originally filed,
Description pages 2, 3, 5-7, 9, 10, 12-19, 21-24 as filed with the letter dated 19 December 1989,
Description page 8 filed with the letter dated 9 January 1991,
Description pages 4 and 11 filed with the letter dated 1 May 1991,
with amendments to pages 3, 5, 19 and 20 requested on page 2 of the letter dated 9 January 1991,
Claims 1 to 7 received with the letter dated 3 May 1991,
Claims 8 to 10 received with the letter dated 11 July 1990,
Drawing sheets 1/4 to 4/4 as originally filed.

III. Independent Claims 1 and 7 read as follows:

"1. A method of quantisation of human pulmonary surfactant characterized by determining the quantity of human pulmonary surfactant in the test substance in an immunoreaction system that comprises primary and secondary monoclonal antibodies both of which recognize as an antigen a human pulmonary surfactant apoprotein with a molecular weight of about 62,000 and/or about 34,000 to 37,000, but each of which binds to a different

epitope of said apoprotein, wherein said primary and secondary monoclonal antibodies are either PC6 and PE10, respectively, or PE10 and PC6, respectively.

7. A reagent kit for the immunological determination of human pulmonary surfactant in a test substance, comprising (1) a primary monoclonal antibody which is fixed to a carrier and recognizes a human pulmonary surfactant apoprotein with a molecular weight of about 62,000 and/or about 34,000 to 37,000, (2) a labelled secondary monoclonal antibody which, though it recognizes said apoprotein, binds to a different epitope from the one to which the primary monoclonal antibody binds, wherein said primary and secondary monoclonal antibodies are either PC6 and PE10, respectively, or PE10 and PC6, respectively, and (3) reagents to be used for detecting said labelled antibodies, if necessary.

IV. The Examining Division argued that inventive step of the claimed subject-matter could be seen as residing in the particular properties of the two monoclonal antibodies PC6 and PE10 only. However the only disclosure in the description as originally filed, which relates to the production of the said monoclonal antibodies is that of Example 1 on pages 12 to 16. If the skilled person were to follow this protocol he would certainly produce a large number of monoclonal antibodies with specificities for different epitopes on the human pulmonary surfactant molecule(s). He would not, however, be able to select which of these had identical epitopic specificities to the PC6 and PE10 antibodies, as their specificities are not sufficiently disclosed in the application as originally filed. The information furnished by the unsubstantiated statement on page 16, lines 20 to 24 is, of itself, inadequate to allow the unequivocal production of said antibodies. The technical information provided with the letter of reply dated 9 January 1991

gives sufficient detail to allow the skilled person to establish the epitopic specificity of PC6 and PE10. This information cannot, however, be included in the application (Article 123(2) EPC). Hybridomas which produce the said monoclonal antibodies, and which also could have been deposited within the meaning of Rule 28 EPC, would also provide sufficient information to enable the said epitopic specificity to be established (cf. Official Communication dated 4 March 1991, paragraph 3). There has been no deposition, however, and even if there had it would no longer be possible to include such information in the application as originally filed without contravening Article 123(2) EPC.

The skilled person is thus unable to reproduce the claimed invention.

V. The gist of the argumentation of the Appellant (Applicant) is that the skilled person can obtain the monoclonal antibodies PC6 and PE10 by following the procedure as described on pages 12 to 16 of the description. In particular, contrary to the view of the Examining Division that the skilled person would produce a large number of antibodies but be unable to select those with identical epitopic specificities, only a few monoclonal antibodies will be produced, as is evidenced by the Journal of Japanese Medical Society for Biological Interface, Vol. 16, No. 2, pages 19 to 33, two of the authors being inventors of the present application. This document indicates that only three antibodies are produced from which PC6 and PE10 have to be selected.

VI. The Appellant requests in effect that the decision under appeal be set aside and a patent granted on the basis of the documents set out in paragraph II above. Oral proceedings are requested as an auxiliary measure.

Reasons for the Decision

1. The appeal is admissible.

2. In paragraph 1 of the reasons for the decision, the Examining Division found that the amended claims under consideration met the requirements of Article 123(2) EPC. The Board sees no reason to dispute this. The amendments to the description bring it into conformity with the amended claims or are cosmetic in nature and here too the requirements of Article 123(2) EPC are complied with.

3. Since the sole ground for refusal of the application was non-conformity with Article 83 EPC, the only issue with which the Board has to concern itself is whether the appealed decision is correct or not in this respect.

4. This requires investigating whether the description is sufficiently clear and complete to enable the skilled person to obtain the antibodies PC6 and PE10 required by Claims 1 and 7.

5. On page 3, line 25 of the specification as originally filed there begins the disclosure of the invention and page 4, line 33 to page 12, line 2 discloses in some detail what is stated to be the best mode of carrying out the invention, which is then more particularly described in the Examples.

Example 1, page 12, line 8 to page 14, line 11 contains detailed instructions as to how the human pulmonary surfactant apoproteins having molecular weights of about 62,000 and about 36,000 are extracted from lungs and bronchi of patients with alveolar proteinosis. These

apoproteins are then used to produce hybridomas by the standard Köhler and Milstein technique, those hybridomas producing antibodies recognising the said apoproteins being selected by ELISA and cloned in limiting dilution to monoclonality (page 14, line 16 to page 15, line 26).

6. The Examining Division argues that the skilled person, having followed the protocol thus far, would certainly produce a large number of antibodies with specificities for different epitopes on the human pulmonary surfactant molecules, but would be unable to select which of these had identical epitopic specificities to the PC6 and PE10 antibodies, as their specificities were not sufficiently disclosed in the application as originally filed (point 4 of the Reasons for the Decision). The Appellant argued that the assertion that a large number of antibodies with different specificities would be produced is entirely unsubstantiated, and in support of the contention that only a few were produced, cited the Journal of Japanese Medical Society article referred to in paragraph V above. This indicates that three antibodies were produced, including PC6 and PE10 and the Board can accept that, in the absence of evidence to the contrary, "three" means "three and only three". The Board also accepts that, again in the absence of evidence to the contrary, only a few antibodies are produced when following the protocol according to Example 1 of the application in suit, because the said article is in substance disclosing the subject-matter of the application.

7. As to the specificity of the antibodies PC6 and PE10, Section (4) of Example 1 (on pages 16 and 17) indicates that these recognise, using the Western blotting technique, the same apoproteins 36K and 62K obtained from the IB fraction of bronchoalveolar lavage fluid of patients with alveolar proteinosis. They also recognised

the apoproteins 37K, 34K and 62K in human amniotic fluid and normal human bronchoalveolar lavage fluids. (K means kilo Daltons). The antibodies were specific to human pulmonary surfactant apoproteins, not reacting with apoproteins of other mammals or human serum proteins.

Moreover by the dot-immunobinding method it is shown that PC6 and PE10 recognise different epitopes on the antigen apoproteins. This is not described in detail, but was a technique known at the priority date of the application in suit for investigating the cross-reactivity (or cross-inhibition) of different antibodies with antigenic determinants. It is considered that this would not be disputed and does not require documentary substantiation. A further characterising feature of the antibodies PC6 and PE10 is that the different epitopes on the antigens which they recognise are neighbouring (page 16, line 22). This is not a feature of Claim 1 but played a role in assessing inventive step. It is a property of the antibodies PC6 and PE10 in just the same way as melting point is a property of a chemical compound and its correctness is confirmed by the experiments described in the annex to the Applicant's letter dated 9 January 1991 in the examination proceedings. Moreover if one sees the average skilled person in this art as being a team including or having access to a protein chemist, then this property of the antibodies would have been verifiable at the priority date of the application by just such experiments as are described in the said annex.

8. In view of the foregoing the Board does not agree that the passage on page 16, lines 20 to 24 is an unsubstantiated statement which is inadequate to allow the unequivocal production of antibodies PC6 and PE10. This, in combination with the finding (paragraph 6 above) that only a few antibodies are produced from

which PC6 and PE10 have to be selected, leads the Board to the conclusion that the requirement of Article 83 EPC is met.

9. Since the Board has found in favour of the Appellant, the auxiliary request for oral proceedings does not require to be considered.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to grant a patent on the basis of the documents set out in paragraph II above.

The Registrar: The Chairman:

P. Martorana C. Black