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Bezeichnung der Erfindung: Method for assaying antigen-antibody reactions and reagent therefor.
Title of invention:
Titre de l'invention :

Klassifikation / Classification / Classement : G01N 33/53, G01N 33/68

ENTSCHEIDUNG / DECISION

vom / of / du 19 September 1989

Anmelder / Applicant / Demandeur :

Patentinhaber / Proprietor of the patent / Titulaire du brevet : Mitsubishi Chemical Industries Limited

Einsprechender / Opponent / Opposant : Boehringer Mannheim GmbH

Stichwort / Headword / Référence :

EPÜ / EPC / CBE Article 54 EPC

Schlagwort / Keyword / Mot clé : "Novelty (denied) - Consideration of prior art document as a whole"

Leitsatz / Headnote / Sommaire

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Case Number : T 12/88 - 3.4.1

D E C I S I O N
of the Technical Board of Appeal 3.4.1
of 19 September 1989

Appellant : (Proprietor of the patent)
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Respondent : (Opponent)
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Representative :

Decision under appeal : Decision of Opposition Division of the European Patent Office dated 16 September 1987 revoking European patent No. 0 064 274 pursuant to Article 102(1) EPC.

Composition of the Board :

Chairman : K. Lederer
Members : H. Reich
L. Mancini

Summary of Facts and Submissions

I. European patent No. 0 064 274 was granted on the basis of European patent application No. 82 103 639.9.

II. The patent was revoked by a decision of the Opposition Division on opposition by the Respondent, on the grounds that the subject-matter of independent Claim 1 of both the main and the subsidiary requests filed on 16 September 1987 was lacking an inventive step having regard to document DE-A-3 022 681, hereafter D1, and that furthermore the subject-matter of independent Claim 4 of the main request was not novel in view of the same document.

III. The Appellant (Patentee) lodged an appeal against this decision.

IV. Oral proceedings were held on 19 September 1989, at the end of which the Appellant requested that the decision under appeal be set aside, and the patent be maintained on the basis of a first set of claims numbered 1 to 3 handed over at the oral proceedings (main request) or alternatively on the basis of a second set of claims numbered 1 to 3 also handed over at the oral proceedings (auxiliary request).

The Respondent requested that the appeal be dismissed.

V. Claim 1, the only independent claim of the main request, reads as follows:

"1. A method for assaying an antigen-antibody agglutination reaction wherein an antigen to be assayed is reacted with the corresponding antibody in a reaction mixture, characterized in that a sample containing the antigen to

be assayed is treated with natural or synthetic polymers having therein plural sulfonyl or carboxyl anions and which are soluble in the reaction medium and the treated sample is used to conduct the reaction of a reverse passive agglutination, with the proviso of excluding the methods wherein a reducing agent is used."

The sole independent claim, Claim 1, of the auxiliary request reads:

"1. A method for assaying an antigen-antibody agglutination reaction wherein an antigen to be assayed is treated with a polyanion and reacted with the corresponding antibody in a reaction mixture, characterized in that the polyanion is a natural or synthetic polymer having therein plural sulfonyl or carboxyl anions and which is soluble in the reaction medium and the treated sample is used to conduct the reaction of a reverse passive agglutination."

VI. At the beginning of the oral proceedings and in response to a question from the Board as to the precise meaning of the expression "reverse passive agglutination" used in the independent Claims 1 of both his main and auxiliary requests, the Appellant stated that a reverse passive agglutination in the light of the present patent has to be interpreted as an antigen-antibody agglutination reaction in which carrier particles supporting antibody molecules were caused to agglutinate when contacted with antigen molecules contained in the reaction mixture.

His arguments in support of novelty of the claimed subject-matter can be summarised as follows:

(a) in the method set out in Claim 1 of the main request, no reducing agent is used in addition to the polymers containing the sulfonyl or carboxyl anions, whereas

document D1 discloses the use of such polymers only in combination with a reducing agent, as set out in particular in independent Claim 13, and in the specific examples on description pages 21 and 25, first paragraph.

The description of document D1 only on page 17, paragraph 3, refers to the use of a serum buffer which contains a polyanion and/or a reducing agent. However, in view of the specific examples disclosed in the description of document D1 which examples consistently use both additives simultaneously, the skilled person would not see in said wording a realistic hint to an alternative use of either a polyanion or a reducing agent but a precautionary measure of the patent drafter, being without technical significance.

Moreover, according to the common practice of the EPO in the field of chemistry, a generic definition in a prior art document is not regarded as disclosing specific embodiments which fall under this generic definition, so that selection inventions may be patented. Accordingly, document D1 should be considered to disclose not more than what has been explicitly described in view of the specific examples, i.e. the simultaneous use of a polyanion and a reducing agent.

(b) Furthermore, the claimed subject-matter differs from the method disclosed in document D1 in that it does not necessarily require a non-immune serum to be present in the reaction mixture, which presence is an essential feature of the known method, as can be seen from document D1, Claim 1.

(c) It cannot be excluded that the non-immune serum used in accordance with the known method may have an effect upon the antigen-antibody agglutination reaction. Therefore, the latter might well not be of the reverse passive type as in the present invention.

VII. (a) The Respondent contested that the reference to a "reverse passive" agglutination reaction in the claims actually leads to a clear definition of the claimed subject-matter.

(b) However, if the Appellant's interpretation of the contested term is accepted, the claimed subject-matter would lack novelty. For, on the one hand, document D1 clearly teaches on page 21, paragraph 2, that an addition of polymers comprising sulfonyl polyanions - such as dextran sulphate - produces similar results as heat treatment in suppressing a non-specific agglutination caused by heat sensitive serum factors. The heat treatment is said to be a time-consuming procedure. On the other hand, the same document (on page 21, lines 9 to 11) explicitly states that heat treatment also produces an inactivation of the non-specific agglutination when used alone. Accordingly, a disclosure of the use of polyanions without a reducing agent unambiguously follows from a mere combination of these two separate teachings.

Reasons for the Decision

1. The appeal is admissible.

A. Main request

1. Interpretation of Claim 1

The expression "reverse passive agglutination" used in Claim 1 was not shown to have a definite meaning which is generally recognised in the art. Neither is this term explicitly defined in the patent specification itself.

But, all specific examples described in the description are consistently directed to agglutination reactions wherein antibody molecules are supported on carrier particles which are caused to agglutinate in the presence of an antigen to be assayed. Thus, the Appellant's submission that the disputed expression is meant to designate the only disclosed specific type of agglutination reaction can reasonably be accepted. The Respondent did not adduce any different interpretation.

2 Novelty

2.1 Document D1 discloses in the wording of Claim 1 of the main request "a method for assaying an antigen-antibody agglutination reaction" wherein an antigen (a microbian antigen; page 8, third paragraph) to be assayed is reacted with the corresponding antibody in a reaction mixture, characterised in that a sample containing the antigen to be assayed (together with a liquid reagent which comprises antibody carrying particles, a physiologically compatible buffer system and non-immune serum) is treated with (for example, dextran sulphate or heparin, which in the specification of the patent in suit, column 2, lines 34 to 37, are specified to constitute examples of) natural or synthetic polymers having therein plural sulfonyl or carboxyl anions and being soluble in the reaction medium".

2.2 Though being referred to in the description of document D1 as a "direct particle agglutination" (page 6, first paragraph), the known reaction clearly involves the use of carrier particles on which antibody molecules are adsorbed (page 10, third paragraph) and which agglutinate in the presence of antigen (page 11, lines 6 to 9). This reaction therefore also constitutes a "reverse passive agglutination" in the sense of Claim 1, as defined in paragraph 1 above. In this respect, the Appellant's unsupported argument that the presence of non-immune serum in the reaction mixture might result in a different agglutination reaction (point VI (c)) could not convince the Board, because document D1 also encompasses methods in which antibody-sensitised carrier particles are caused to agglutinate when contacted with antigen, even in the presence of non-immune serum (Claim 13 in connection with Claim 9).

Hence, the feature according to the further wording to Claim 1: "and the treated sample is used to conduct the reaction of a reverse passive agglutination" is considered to be known from document D1 as well.

2.3 It remains to be examined whether the last feature of Claim 1: "with the proviso of excluding the methods wherein a reducing agent is used" is also known from document D1.

In this respect, the Board indeed accepts the Appellant's submission that the use of the alternative preposition "und/oder" at a single location of the description cannot by itself be considered to unambiguously disclose the use of polyanions in the absence of a reducing agent (point VI (a)), because in order to correctly assess its technical teaching, a document should always be considered as a whole, in which way it would also be interpreted by a

skilled person. In view of this very principle, however, the Board cannot follow the Appellant's opinion (see point VI (a) above) that the disclosure of document D1 is limited to the described specific examples for the reasons indicated below:

An integral assessment of document D1 shows that, for generally proposing a method which exhibits improved sensitivity for assaying antigen molecules in a body liquid (page 8, third paragraph), the document in particular addresses the problem of avoiding the occurrence of a non-specific agglutination during the actual antigen-antibody reaction. For alleviating this problem document D1 discloses a number of separate measures: (I) the addition of a non-immune serum to the sensitised carrier particles, (II) the addition of serum buffer comprising a polyanion and/or a reducing agent directly to the reaction mixture, and/or (III) heat treatment of the serum (page 17, third paragraph). More specifically, document D1 teaches on page 21, lines 8 and 9, that the use of a reducing agent alone reduces the occurrence of non-specific agglutination to 38%, and on page 21, lines 9 to 11 that a similar reduction is obtained by heat treatment alone. Thus, a skilled person clearly derives from document D1 that a heat treatment of the reaction mixture and an addition of reducing agent to the reaction mixture are two measures, which have been separately realised with similar success. Furthermore, document D1 explicitly states on page 21, paragraph 2, that because of the time-consuming character of heat treatment an alternative measure for replacing it was developed in the form of an addition of polyanions. In the Board's view, a skilled person is able to logically assemble the two separate statements in document D1 - i.e. that on the one hand heat treatment can be performed alone, and that on the other hand polyanion addition is an

alternative to heat treatment - and to integrate them into the technical fact that polyanions have really been added alone to the reaction mixture with reasonable success.

For the above reasons, the Board is convinced that also said last feature of Claim 1 is known from document D1.

2.4 The fact that all the specific examples of the description in which a polyanion is used also involve an addition of a reducing agent (page 22, second paragraph; page 25, first paragraph), cannot be construed as necessarily implying that both additives must always be used simultaneously, but only that their combined use is a preferred embodiment of the described method, as derivable from the term "zweckmäßig" in the description page 21, last paragraph.

When referring (see point VI (a) above) to a practice of the EPO of considering generic disclosures in a prior art document which are not supported by specific examples as not novelty destroying, the Appellant obviously addresses a different situation, namely the case in which the mere disclosure in a prior art document of a whole class of chemical compounds, defined only by a generic formula, is not considered to destroy the novelty of specific compounds falling under the generic formula and not specifically exemplified in the document, whereby selection inventions are rendered possible.

Finally, the Appellant's submission (see point VI (b) above) that the method of Claim 1 is further distinguished from the state of the art according to document D1 in that no non-immune serum is used, cannot be accepted either, because a skilled person derives from document D1, (cf. page 19, lines 9 to 22 where a variety of measures to reduce non-specific agglutination and the results obtained with each of these measures are discussed separately) that

the addition of a non-immune serum represents only a preferred measure which in principle can be omitted. Moreover, Claim 1 of the patent in suit does not state that also non-immune serum addition shall be excluded.

2.5 For the reasons set out in points 2.1 to 2.4 above, the subject-matter of Claim 1 is considered to lack novelty in the sense of Article 54 EPC.

2.6 The subject-matter of dependent Claims 2 and 3 considered in connection with Claim 1 lacks novelty as well. In the method of document D1, the agglutination reaction is conducted in the presence of natural or synthetic polymers as claimed in Claim 2 (see document D1, Claim 13), and dextran sulphate is exemplified as a suitable polymer as claimed in Claim 3 (see document D1, Claim 15).

3. Thus, Claims 1 to 3 of the Appellant's main request do not meet the requirements of Article 52(1) EPC and for this reason cannot form the basis of a patent maintained in amended form according to Article 102(3) EPC.

B. Auxiliary request

Claim 1 according to the Appellant's auxiliary request corresponds in substance to Claim 1 of the main request, except for the fact that it lacks the last feature: "with the proviso of excluding the methods wherein a reducing agent is used". Accordingly, its subject-matter is not novel either, for the reasons indicated in connection with Claim 1 of the main request in points A-2.1 and 2.2 above. Claims 2 and 3 of the auxiliary request having the identical wording as in the main request, are shown to be known from document D1 in point A-2.6.

For these reasons, the patent also can not be maintained as amended in accordance with Appellant's auxiliary request.

Order

For these reasons, it is decided that:

The appeal is dismissed.

The Registrar: **The Chairman:**

M. Beer **K. Lederer**