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D E C I S I O N
of 11 June 1999

Case Number: T 0936/96 - 3.3.5

Application Number: 87100215.0

Publication Number: 0225867

IPC: B01J 20/32

Language of the proceedings: EN

Title of invention:
Adsorbent and process for preparing the same

Patentee:
Kanegafuchi Kagaku Kogyo Kabushiki Kaisha

Opponent:
Asahi Medical Co Ltd

Headword:
Adsorbent for LDL/KANEGAFUCHI

Relevant legal provisions:
EPC Art. 56

Keyword:
"Inventive step - no"
"Obvious improvements"
"Problem - solution approach"

Decisions cited:
T 0021/81, T 0766/92, T 0192/82

Catchword:

Once a realistic technical problem is defined and once it is established that a particular solution to such a problem would have been envisaged by a person skilled in the art in the light of the relevant state of the art, then this solution lacks an inventive step, and this assessment cannot be altered by the fact that the claimed invention inherently also solves further technical problems.

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0936/96 - 3.3.5

D E C I S I O N
of the Technical Board of Appeal 3.3.5
of 11 June 1999

Appellant: (Opponent)
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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 16 August 1996 rejecting the opposition filed against European patent No. 0 225 867 pursuant to Article 102(2) EPC.**

Composition of the Board:

Chairman: R. K. Spangenberg
Members: G. J. Wassenaar
M. B. Günzel

Summary of Facts and Submissions

I. The appeal is from the decision of the Opposition Division to reject the opposition and maintain European patent No. 0 225 876 with claims 1 to 9 as granted. Claim 1 of the patent in suit reads as follows:

"An adsorbent for removing low and/or very low density lipoprotein from body fluid in extracorporeal circulation treatment, which comprises a water-insoluble porous hard gel except with a porous cellulose gel with exclusion limit of 10^6 to 10^9 daltons on which a dextran sulfate, a salt thereof or a mixture of the dextran sulfate and the salt thereof having a sulfur content of not less than 15% by weight is immobilized by a covalent linkage."

II. In the decision, inter alia, the following prior art documents were considered:

D1: US-A-4 103 685

D2: JP-A-57-190003 (In this decision reference is made to the English translation filed with the notice of opposition)

D4: Kosoku Ekitai Kuromatogurafi(1978), pages 212-217

D10: J. clin. Path. Vol. 17(1964), pages 627-643

D13: Journal of Lipid Research, Vol. 11(1970), pages 583-595

III. In the statement of the grounds of the appeal, the appellant maintained that the product according to granted claim 1 lacked an inventive step over D1 in combination with D2. Inter alia, the following document was submitted to show that the dextran sulphate used in D1 fulfilled the requirements of claim 1.

D21: Product brochure of Pharmacia Fine Chemicals titled "Dextran Fractions, Dextran Sulphate, DEAE-Dextran, defined polymers for biological research" printed Dec. 1974.

IV. The respondent refuted the appellant's arguments and maintained that there was no proof that the dextran sulphate used in D1 fulfilled the requirements of the claims as granted. To show that different dextran sulphates having different molecular weights and different sulphur contents were usual products at the priority date of D1, reference was made to the following document:

D19 Römpps Chemie-Lexikon 7th ed. (1973), pages 807-808.

V. Oral proceedings took place on 11 June 1999. The respondent's arguments with respect to inventive step of the adsorbent according to claim 1, put forward during the written and oral proceedings, can be summarised as follows:

D1 related to the batch-wise treatment of human blood for removing lipoproteins therefrom by contacting the blood with an adsorbent comprising a calcium complex of a sulphated polysaccharide coupled to a soft gel. Such

an adsorbent was not suitable for removing low density lipoproteins (LDL) from body fluid in a continuous extracorporeal circulation treatment. The technical problem which the invention tried to solve was to provide an adsorbent, suitable for such a continuous treatment, which could be used without the formation of a calcium ion complex. This problem was solved by the adsorbent according to claim 1. Essential for solving the problem was the use of a porous hard gel with an exclusion limit between 10^6 to 10^9 daltons and a dextran sulphate with a sulphur content of at least 15% by weight. Porous hard gels as carrier for an adsorbent were known from D2, but it was not obvious to combine this teaching with the teaching of D1, since D2 did not relate to the removal of lipoprotein. There was no evidence that the dextran sulphate used in D1 had a sulphur content of at least 15% and it could not be foreseen that by using such a high sulphur content the adsorption of the low-density lipoproteins could be improved to such an extent that it could be used without the need to add calcium ions to form the calcium dextran sulphate complex, as taught in D1 and other relevant literature such as D10 and D13. The addition of calcium ions in the extracorporeal circulation treatment could be dangerous for the patient and should be avoided. It was, therefore, not obvious that the above-mentioned problem could be solved by an adsorbent according to granted claim 1.

VI. The appellant requested that the decision under appeal be set aside and European patent No. 0 225 867 be revoked.

The respondent requested that the appeal be dismissed

and the patent be maintained.

At the end of the oral proceedings the decision to revoke the patent was announced.

Reasons for the Decision

1. The appeal is admissible.

2. *Inventive step*

2.1 The only ground of opposition in dispute in these appeal proceedings was lack of inventive step. The Board agrees with the parties that D1 represents the closest prior art. This document relates to a method for the extracorporeal treatment of blood with an adsorbent in order to remove lipoproteins therefrom. In particular it discloses an adsorbent comprising sodium dextran sulphate, covalently bound to activated agarose beads. Specifically disclosed is a dextran sulphate having a molecular weight of 500,000 purchased from Pharmacia Fine Chemicals on beads of hydrated "BIOGEL® A-5m" (Example 1, column 6, line 56 to column 7, line 36). This hydrated gel, normally used for high performance liquid chromatography, has a molecular weight exclusion limit of 5,000,000, which is equivalent to 5.10^6 dalton (D4, page 215).

2.2 According to the patent in suit it is difficult to obtain a sufficient flow rate for an extracorporeal treatment if the adsorbent carrier is a soft gel such as agarose. Accordingly, a particular modification in column shape is required in order to obtain a large

flow rate and the risk of an occasional clogging still remains. Therefore, a stable extracorporeal circulation cannot be achieved with agarose beads (column 1, line 58 to column 2, line 14). Soft carriers such as agarose beads have the further disadvantage that they cannot be sterilised by autoclaving without destroying the pore structure (column 2, lines 55 to 56). Thus on the basis of the information given in the patent in suit, the problem underlying the invention can be seen in providing an adsorbent for removing LDL from body fluid in extracorporeal circulation treatment, allowing improved flow rate without clogging in a packed column and sterilisation by steam autoclaving. In the patent in suit it has been demonstrated that flow rate and stability against sterilisation by steam autoclaving are satisfactory (test Example 1 and Example 4). The Board is therefore satisfied that the product of claim 1 actually solves the above-mentioned problem.

2.3 It remains to be decided whether the claimed solution was obvious to a person skilled in the art. The problems of agarose gels as carrier in adsorbents for extracorporeal circulation treatment of body fluids such as blood has been discussed in detail in D2. It discloses that agarose gels (for example, Sepharose, trade name of Pharmacia Co., Sweden) activated with bromcyan which have been used in the past for this purpose are not suited for thermal sterilisation and do not allow a high rate of flow of body fluids. It proposes to solve this problem by replacing the agarose beads with beads of an activated porous hard gel of a cross-linked copolymer whose main structural component is a vinyl alcohol unit (pages 2 to 5 and 17 to 19). The hard gels of D2 have a molecular weight exclusion

limit of 10^3 to 10^8 (daltons); see page 12. Specifically disclosed is a hard gel with an exclusion limit of 30.10^5 (Example 7, page 24). Although D2 does not mention the removal of lipoproteins but relates to the removal of proteins in general from body fluids, the skilled person trying to solve the above-mentioned problem will certainly take D2 into account. The problem relates to the carrier beads and is not specific for the removal of lipoproteins, but concerns all adsorbents used in extracorporeal circulation treatment of body fluids. The Board holds therefore that, in order to solve the problem underlying the invention, it was obvious to the skilled person to replace the bromocyan activated agarose beads used in Example 1 of D1, amongst which Sepharose® is mentioned, with beads of the porous hard gels according to D2 having an exclusion limit of at least 10^6 daltons.

2.4 Present claim 1 further requires that the dextran sulphate has a sulphur content of not less than 15 % by weight. The sulphur content of the sodium dextran sulphate used in Example 1 of D1 is not revealed. What is disclosed however, is that it has a molecular weight of 500,000 and was purchased from Pharmacia Fine Chemicals. In D21, a sales brochure of Pharmacia Fine Chemicals from December 1974, relating to Dextran and Dextran derivatives, only dextran sulphate having an average molecular weight of 500,000 and a sulphur content of approximately 17% is offered (pages 10 and 32). D21 further discloses that the dextran sulphate is suitable for the removal of LDL (â-lipoprotein); see page 12. There is no evidence that before the filing date of D1 (5 January 1976) Pharmacia Fine Chemicals ever sold dextran sulphate with another sulphur

content. References D10(page 630), D13(page 584) and D19, cited by the respondent do not teach otherwise.
D10 discloses that one of the three laboratory scale preparations of dextran sulphate has a sulphur content lower than 15% (12.2%) but confirms that the two commercial preparations, having molecular weights of 500,000 and 2.10^6 (obtained from Pharmacia Ltd, see page 643 left column), contained 17±0.5%.
D13 discloses "sodium dextransulfate 2000 (mol wt 2 x 10^6; Pharmacia, Uppsala, Sweden)" without revealing its sulphur content.

D19 discloses that the commercial dextran sulphate products are sodium salts thereof having a molecular weight of 500,000 to 2,000,000 but does not reveal their sulphur content either.

From the evidence on file, the Board concludes that the use of dextran sulphate with a sulphur content of about 17% for an adsorbent for the removal of LDL from body fluids is, if not the only choice, certainly the first choice. Thus the skilled person, trying to solve the above-mentioned problem, not only **could** use dextran sulphate with a sulphur content of about 17%, but **would** use it.

2.5 On the basis of the experimental report dated 22 June 1995, the respondent argued that the claimed products solved not only the technical problems set out in the patent in suit, but, in addition, the further problem of providing a possibility to remove LDL from body fluid without the need to add further calcium ions, since, as was surprisingly found, at a sulphur level above 15% by weight the complex between dextran

sulphate and LDL was stable enough to allow the use of the adsorbent without the addition of calcium ions. Test Example 1 shows that the adsorbent does remove LDL from human plasma without added calcium ions. However it also shows that the removal efficiency is rather low (Table 1). On that basis, the additional problem solved cannot be considered to be an **efficient** removal of LDL without adding calcium ions, but only that of providing a product which can be used without additional calcium ions, but at the cost of efficiency. Since it was known in the art that dextran sulphate would form a complex with LDL and that this complex tended to re-dissolve on standing in the absence of added calcium ions (D10, page 629, left column), it is doubtful whether the claimed product, proposed as a solution to the problem of providing a product which can be used without additional calcium ions, but at the cost of efficiency, was not obvious.

2.6 However, even if the Board would have accepted, in the respondent's favour, that an additional problem had been effectively solved in a manner not suggested by the state of the art relevant in respect of the solution to this problem, the claimed product would not thereby become inventive. In the Board's judgment, the proper question to be asked in respect of the assessment of the presence of an inventive step within the meaning of Article 56 EPC is what a skilled person **would** have done in a particular situation. The problem-solution approach established by the Boards of Appeal provides an objective basis for answering this question (see T 24/81, OJ EPO 1983, 133, reasons point 4). Bearing this in mind, the Board holds that, once a realistic technical problem is defined and once it is

established that a **particular** solution to such a problem **would** have been envisaged by a person skilled in the art in the light of the relevant state of the art, then this solution lacks an inventive step, and this assessment cannot be altered by the fact that the claimed invention inherently also solves further technical problems (see also T 21/81, OJ EPO, 1983, 15, point 6; T 192/82, OJ EPO 1984, 415, point 16, and T 766/92 of 14 May 1996, point 2.3(ii)).

2.7 In the present case, as explained in paragraphs 2.3 and 2.4 above, the skilled person would have combined the disclosures of D1 and D2 and thereby have arrived at a product as claimed in claim 1 that had the properties of enabling increased flow rate and steam sterilisation, which are highly desirable in the relevant technical field, as acknowledged in the patent in suit (see paragraph 2.2 above). In that situation the claimed unexpected effect put forward by the respondent, allegedly providing a solution to an additional technical problem, cannot be regarded as an indication of the presence of an inventive step because the skilled person not only could, but would, have made a product comprising a dextran sulphate having a sulphur content of about 17% on a porous hard gel, without knowing about an additional advantage provided by the said sulphur content.

2.8 The Board agrees with the respondent that in view of D1 and D10 the skilled person would probably have added calcium ions to the adsorbent to form the calcium complex before using it for the precipitation and filtration of lipoproteins, whereas the patent in suit does not require the addition of calcium ions. However,

having regard to the fact that claim 1 is directed to a product as such and is not limited to the use of that product, the possibility of using the claimed product without the addition of calcium ions has no impact on the question of the obviousness of the subject-matter of that claim.

2.9 For these reasons the Board holds that the subject-matter of claim 1 does not involve an inventive step within the meaning of Article 56 EPC so that the patent cannot be maintained with the claims as granted.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

S. Hue R. Spangenberg