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Datasheet for the decision of 8 October 2018

Case Number: T 2343/16 - 3.3.07

Application Number: 05793316.0

Publication Number: 1809307

IPC: A61K33/42, A61P7/08, A61K9/08

Language of the proceedings: EN

Title of invention:
MEDICAL SOLUTION, METHOD FOR PRODUCING AND USE THEREOF

Applicant:
Gambro Lundia AB

Headword:
Medical Solution / GAMBRO

Relevant legal provisions:
EPC Art. 54(2), 56

Keyword:
Novelty - (yes)
Inventive step - (no)

Decisions cited:
G 0002/12, G 0010/93

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Case Number: T 2343/16 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 8 October 2018

Appellant: (Applicant)	Gambro Lundia AB Box 10101 220 10 Lund (SE)
Representative:	Sweden SHS IP Office Gambro Lundia AB P.O. Box 10101 220 10 Lund (SE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 13 May 2016 refusing European patent application No. 05793316.0 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	E. Duval
	L. Bühler

Summary of Facts and Submissions

I. The appeal of the applicant (appellant) lies from the decision of the examining division to refuse European patent application No. 05793316.0.

II. The decision was based on a main request filed on 24 March 2016 and one auxiliary request filed during the oral proceedings held on 28 April 2016.

Claim 1 of the main request read as follows:

"1. A medical solution, obtained by mixing a first single solution comprising at least one buffer chosen from the group comprising acetate, lactate, citrate, pyruvate, carbonate and bicarbonate, with a second single solution comprising an acid, to form a ready-for-use medical solution, wherein said first single solution comprises phosphate ions; said mixing of first and second single solutions is performed after terminal sterilization and up on use; and said ready for-use medical solution comprises phosphate in a concentration of 1.0 - 2.8 mM, is sterile, and has a pH of 6.5~7.6".

In the auxiliary request, the mixing step was further specified to be "performed in its final package by breaking frangible pin or peal seal between first single solution and second single solution".

III. The following documents were among those cited in the decision:

D2: Troyanov S. et al., "Phosphate addition to hemodiafiltration solutions during continuous renal

replacement therapy", Intensive care medicine, vol. 30, no. 8, 2004, pages 1662-1665, XP002677818

D13: Monographs on hemodialysis solutions and hemofiltration/ hemodiafiltration solutions of the European Pharmacopoeia 4.0

IV. The examining division found the subject-matter of the main request to lack novelty over D2, describing a hemodiafiltration solution for continuous renal replacement therapy (CRRT). Though not explicitly mentioned, the solution of D2 would by necessity be sterile because this is mandatory for hemodiafiltration, as shown by D13. The mixing step of claim 1 was held by the examining division to define the solution in terms of the process for its preparation, which process did not result in different properties of the claimed solution.

As to the auxiliary request, the examining division considered that the requirements of Article 123(2) EPC were not met: the addition of the feature regarding the breaking of frangible pins or pealing of a seal was considered as an unallowable intermediate generalisation from the embodiment in which the single solutions were provided in different compartments of a multi-compartment bag. It was added that this additional feature could not overcome the novelty objection, since a particular package was not part of the claimed subject-matter.

V. In its statement setting out the grounds of appeal sent on 23 September 2016, the appellant requested that the decision under appeal be set aside and that examination of the patent application be continued on the basis of a main request or alternatively an auxiliary request

submitted therewith. It furthermore filed *inter alia* the following documents:

D17: Dolan, S. A., et al., APIC, www.apic.org, apicinfo@apic.org, Position paper: sale injection, infusion, and medication vial practices in health care (2016).

D18: United States Pharmacopeia (USP 38), 2015, Chapter <797> Pharmaceutical compounding - Sterile preparations.

The main request was identical to the main request upon which the decision of the examining division was based. The auxiliary request differed from the main request by the following features: the "single solutions are provided in different compartments in a multi-compartment bag" and "said mixing is provided by having the different compartments coupled by frangible pins, which pins could be broken in order to mix the content of the different compartment within the multi-compartment bag, or provided by having a peal seal in-between the different compartments, and peal seals are pealed in order to mix the content in the compartments".

VI. In a communication pursuant to Article 15(1) RPBA issued on 13 September 2018, the Board expressed the opinion that the subject-matter of the main request fulfilled the requirement of novelty over D2, but did not involve an inventive step over the same document. The auxiliary request met the requirements of Article 123(2) EPC, and its subject-matter was likewise novel but not inventive over D2.

VII. Oral proceedings were held on 8 October 2018 in the absence of the appellant who had informed the Board accordingly.

VIII. The appellant's arguments in relation to the main and auxiliary requests, as far as relevant for the present decision, can be summarised as follows:

The subject-matter of the main request fulfills the requirement of novelty: the solution of D2 cannot be considered sterile since it results from a compounding step; D17 and D18 *inter alia* were cited to support this view.

Concerning inventive step, should D2 be taken as the closest prior art, the claimed subject-matter would be distinguished therefrom in that the solution is obtained by mixing a first solution comprising a buffer and the phosphate with a second solution comprising an acid, and the the mixing is performed after the terminal sterilisation and up on use, whereby a sterile medical solution having stability against precipitation of phosphate is provided. In the absence of incentive in D2 to proceed in this was, the subject-matter of the main request fulfilled the requirement of Article 56 EPC.

The auxiliary request addressed the objection of added subject-matter of the decision under appeal. The argumentation presented in connection with novelty and inventive step for the main request was considered applicable to the auxiliary request.

Reasons for the Decision

Main Request

1. Article 123(2) EPC

The main request is identical to the main request upon which the decision of the examining division is based. No objection pursuant to Article 123(2) EPC was raised by the examining division in respect of this request. The Board sees no reason to differ.

2. Novelty

Claim 1 relates to a "medical solution" per se, defined by:
- features pertaining to the process for its preparation, namely it is "obtained by mixing a first single solution comprising at least one buffer chosen from the group comprising acetate, lactate, citrate, pyruvate, carbonate and bicarbonate, with a second single solution comprising an acid, to form a ready-for-use medical solution, wherein said first single solution comprises phosphate ions; said mixing of first and second single solutions is performed after terminal sterilization and up on use", and
- features pertaining to the state and composition of the solution, namely it is a "ready for-use medical solution", it "comprises phosphate in a concentration of 1.0 - 2.8 mM", "is sterile", and "has a pH of 6.5-7.6".

It is uncontested that D2 describes a hemodiafiltration solution for continuous renal replacement therapy (CRRT) containing phosphate in a concentration of

1.24mM and having a pH of 7.06 (cf. page 1663, "Methods"; Table 1, Hemosol B0 with KH_2PO_4/K_2HPO_4). To prepare this solution, "two milliliters of potassium phosphate" were "added to 5-l bags of Hemosol LG2 or B0". The solution was then tested clinically in the CRRT treatment of 20 patients.

D2 does not disclose the process steps defined in claim 1, in particular the mixing of first and second single solutions after terminal sterilization (i.e. after sterilization "in its final package", cf. application page 5 line 31). However claim 1 is not directed at a process but at a solution per se, (*inter alia*) defined in terms of the method used to manufacture that solution. This product-by-process definition cannot in itself give the product novelty, nor can it constitute an inventive step over the prior-art (cf. G2/12, Reasons IV(5) and decisions cited therein). Rather it must be established whether the claimed solution itself meets the patentability requirements of Article 52(1) EPC, i.e. whether the inevitable product of the product-by-process definition can be distinguished from the prior-art.

The Board shares the opinion of the examining division, according to which the product-by-process definition does not impart any additional features to the resulting solution: both the sterilization methods used for said intermediate solutions (i.e. the first and second single solution) and the mixing conditions are left undefined in claim 1. This process will at most contribute to obtaining the final solution as a sterile solution, which is already specified in claim 1 as a "structural" feature of the solution. Additionally the product-by-process feature cannot entail any limitation as to the packaging of the solution: claim 1 being

directed at the solution *per se*, any feature regarding (sterilization together with) the package can hardly characterise the solution contained therein.

However, as noted by the examining division, D2 does not explicitly disclose that the solution is sterile. Nor does D2 give any indication as to how the additions of potassium phosphate to the 5-l bags of Hemosol B0 were carried out.

The examining division nonetheless took the view that D2 implicitly discloses this feature, since sterility is mandatory for hemodiafiltration solution; reference was made to D13 (pages 1283-1284) in this respect. The Board does not share this opinion: for D2 to implicitly anticipate the subject-matter of claim 1, an unambiguous disclosure is necessary, in the sense that, in carrying out the teaching of the prior document, the skilled person would inevitably arrive at a result falling within the terms of the claim. In view of the general requirement of D13, the starting hemodiafiltration solution Hemosol B0 as packaged must be sterile; however the solution of D2 results from the addition of potassium phosphate to Hemosol B0 in undisclosed conditions: the resulting compounded solution, prepared upon use for clinical assessment in D2, does not inevitably comply with the sterility test of D13. The disclosures of e.g. D17 and D18, relating to compounded sterile preparations in general, demonstrate that the preparation may take place in "worse than ISO Class 5 environment", thus leading to non-sterile solutions which, considering the risk of contamination, must be used rapidly. D2 does not exclude such practices during preparation, and therefore does not exclude that the compounded solution be merely prepared in aseptic conditions.

Accordingly, the main request meets the requirements of Article 54 EPC.

3. Inventive step

3.1 Scope of ex parte proceedings

In the first instance decision, lack of novelty over D2 was the sole ground for rejecting the main request. It follows from the above (point 2. supra) that this conclusion of the examining division should be reversed. However, in ex parte proceedings, the Board is not restricted to examination of the grounds for the contested decision, and can include new grounds in the proceedings (cf. G10/93). Considering the circumstances of the case, in particular that the appellant also covered the issue of inventive step over the same document D2 in his statement setting out the grounds of appeal, and in accordance with the appellant's request for continued examination, the Board decides to assess compliance with the requirement of Article 56 EPC, as mentioned in the communication pursuant to Article 15(1) RPBA issued on 13 September 2018.

3.2 D2 represents a suitable starting point for the assessment of inventive step of the claimed invention. D2 relates to hemodiafiltration solutions for CRRT, and addresses the issue of hypophosphatemia as well as the risk for calcium phosphate precipitation (cf. abstract).

As established above for novelty, the claimed solution differs from the solution of D2 merely in that it is sterile. The steps leading to the claimed solution, in particular the mixing, after terminal sterilisation and

up on use, of a first solution comprising a buffer and the phosphate with a second solution comprising an acid, do no characterise *per se* the resulting solution nor do they impart any additional feature to its composition or state.

The effect of this sole differentiating feature is that the risk of infection in a patient is avoided. The objective technical problem to be solved is therefore to provide hemodiafiltration solutions avoiding the risk of infection in a patient.

It is however part of the common general knowledge, as embodied by e.g. D13 (pages 1283-1284) that hemodiafiltration solutions should be sterile.

Thus, the main request does not meet the requirements of Article 56 EPC.

Auxiliary Request

4. The auxiliary request differs from the main request by the addition of the features relating not only to mixing by breaking of frangible pins or pealing of a seal, but also regarding the provision of the single solutions in different compartments of a multi-compartment bag. These features are disclosed, in combination, in the application as filed on page 9, lines 8-14. The requirements of Article 123(2) EPC are therefore met.

These additional features however concern only the process for the preparation of the claimed solution, but do not further limit the claimed solution per se: providing the single solutions in different compartments of a multi-compartment bag and mixing them

by breaking of frangible pins or pealing of a seal does not cause the resulting sterile solution to change. Both the reasoning on novelty and the reasoning on inventive step provided above for the main request thus apply fully to the auxiliary request.

It follows that the auxiliary request does not comply with the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

S. Fabiani A. Usuelli

Decision electronically authenticated