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Datasheet for the decision of 17 December 2007

Case Number: T 1344/05 - 3.3.02

Application Number: 97600009.1

Publication Number: 0916347

IPC: A61K 47/10

Language of the proceedings: EN

Title of invention:
Pharmaceutical injectable solutions containing paracetamol and combinations of paracetamol with other active substances

Patentee:
Uni-Pharma Kleon Tsetis A.B.E.E.,

Opponents:
BIOSPRAY SA
HELP S.A.

Headword:
-

Relevant legal provisions:
EPC Art. 56

Relevant legal provisions (EPC 1973):
-

Keyword:
"Main and auxiliary request - inventive step - no: obvious to try"

Decisions cited:
-

Catchword:
-

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Case Number: T 1344/05 **-** 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 17 December 2007

Appellant: (Opponent 01)
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Representative:
-

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Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 17 August 2005 rejecting the opposition filed against European patent No. 0916347 pursuant to Article 102(2) EPC.

Composition of the Board:

Chairman: U. Oswald
Members: J. Riolo
P. Mühlens

Summary of Facts and Submissions

I. European patent No. 0 916 347 based on application No. 97 600 009.1 was granted on the basis of six claims.

Independent claim 1 as granted read as follows:

"1. Solution suitable for parenteral administration, comprising paracetamol and benzyl alcohol, glycerol formal and water."

II. Notices of opposition were filed against the granted patent by the appellant (opponent 1) and opponent 2, which is party as of right to the appeal proceedings.

The patent was opposed under Article 100(a) EPC for lack of novelty and inventive step and under Article 100(c) EPC on the grounds that the patent extends beyond the content of the application as originally filed.

The following documents *inter alia* were cited during the proceedings:

(1) GR-B-1 001 523
(2) GR-B-1 002 731
(3) WO 95/05812
(24A) Lambiotte & Cie, supplier of Glycerol Formal, Technical Bulletin, August 1996.
(30) Amer. Jour. Pharm., December 1952, p. 399-403

III. The Opposition Division's decision posted at the EPO postal service on 11 August 2005 rejected the oppositions under Article 102(2) EPC.

Concerning the objection under Article 100(c) EPC, the Opposition Division observed that the notice of opposition contained no argumentation to substantiate this objection, which thus had to be disregarded. It added that the subject-matter of the patent as filed did not *prima facie* extend beyond the content of the application as filed.

The Opposition Division took the view that the subject-matter of the patent in suit met the requirements of Articles 52(1), 54 and 56 EPC having regard to the available prior art cited by the opponent.

As to novelty, it considered that none of the cited prior art disclosed a solution comprising paracetamol and benzyl alcohol, glycerol and water, so that the claimed subject-matter was novel.

It regarded documents (1) or (2), which differed from the subject-matter of claim 1 solely in the use of ethanol instead of benzyl alcohol in combination with glycerol formal and water, as the closest state of the art.

The problem to be solved vis-à-vis said document was seen in the provision of a further solution containing paracetamol and suitable for parenteral administration.

This problem was solved by the combination of paracetamol with benzyl alcohol together with glycerol formal and water.

As document (3), which disclosed the use of benzyl alcohol as a solvent, related to a totally different use, namely the injection of abamectin in sheep and cattle, the Opposition Division concluded that the skilled person would not combine document (3) with documents (1) or (2), so that the claimed subject-matter was inventive.

IV. The appellant lodged an appeal against the said decision.

V. The respondent (patentee) submitted two sets of claims as main and auxiliary request with its letter dated 16 November 2007.

The set of claims in the main request is identical to the set of claims as filed and as granted, with the correction of a clerical error in claim 5.

Claim 1 in the auxiliary request reads:

"1. Solution suitable for parenteral administration, comprising paracetamol and benzyl alcohol, glycerol formal and water, wherein the ratio of benzyl alcohol: glycerol formal: water is 10:50:40 by volume."

VI. In a fax dated 12 November 2007, the appellant informed the Board that it would not attend, and would not be represented at, the oral proceedings.

VII. Oral proceedings were held before the Board on 17 December 2007.

VIII. In summary, the appellant submitted in the written procedure that nothing inventive could be seen in the replacement of a solvent with another known one.

Opponent 2 did not submit arguments during the appeal proceedings.

IX. The respondent mainly shared the Opposition Division's conclusions and arguments.

In addition, it held that the good properties of the paracetamol solution with benzyl alcohol had not been foreseeable since the parenteral solution was a complex mixture of various chemical compounds.

It further sought to argue that the replacement of ethanol with benzyl alcohol represented an improvement vis-à-vis the prior art in the process for manufacturing the parenteral paracetamol formulation.

X. The appellant requested that the decision under appeal be set aside and the patent revoked.

The respondent requested that the patent be maintained in amended form on the basis of the main or auxiliary request filed with letter dated 16 November 2007.

Reasons for the Decision

1. The appeal is admissible.

2. Main request

2.1 Article 123(2) and (3) EPC

No new arguments under Article 123(2) and (3) EPC were provided by the appellant against the set of claims in the main request, which correspond to the set of claims as filed and granted. The Board sees no reason to disagree with the Opposition Division's conclusions.

2.2 Novelty

No new arguments under Article 54 were provided against this set of claims during the appeal proceedings and the Board sees no reason to disagree with the Opposition Division's conclusions.

2.3 Inventive step

2.3.1 The patent provides for a paracetamol formulation suitable for parenteral administration. Claim 1 of the contested patent claims a solvent mixture comprising benzyl alcohol, glycerol formal and water. The solvent mixture used in the examples in the patent in suit for the preparation of a 4 ml solution of 600 mg paracetamol consists of a mixture of benzyl alcohol (0,4 ml in 4 ml), glycerol formal (1,5 ml in 4 ml) and water (q.s. ad. 4 ml)

Document (1) also relates to a paracetamol formulation for parenteral administration. The solvent mixture used in document (1) for the preparation of a 4 ml solution of 600 mg paracetamol consists of a mixture of ethanol(0,4 ml in 4 ml), glycerol formal (1,5 ml in 4 ml) and water (q.s. ad 4 ml)(see examples 1 and 2).

The Board therefore considers that document (1) represents the closest prior art.

2.3.2 Thus, the only difference in the claimed formulation according to the contested patent and those of prior art document (1) lies in the presence of benzyl alcohol as a solvent instead of ethanol.

The patent in suit and the respondent's written submissions are silent about any further or equivalent effect achieved by the presence of benzyl alcohol in the formulation instead of ethanol.

It follows that the problem to be solved as against document (1) can only be seen as the provision of a further solution suitable for parenteral administration of paracetamol.

2.3.3 This problem is solved by the subject-matter of claim 1 and, in the light of the working examples in the patent in suit, the Board is satisfied that the problem has been solved.

2.3.4 Thus, the question to be answered is whether the proposed solution, i.e. the replacement of the solvent ethanol by benzyl alcohol, was obvious to the skilled person in the light of the prior art.

In that respect, the Board observes that document (3) discloses formulations containing benzyl alcohol, glycerol formal and the drug abamectin (examples 3 to 7).

Moreover, the patent in suit itself indicates that "among the tested solvents proved suitable Ethanol, Benzyl Alcohol and GLYCEROL FORMAL Ethanol and Benzylic Alchohol are already used as solvents for parenteral administration of drugs…" (page 3, lines 7 and 8).

Accordingly, as the skilled person is free, for the purpose of preparing of a further formulation, to choose any solvent which is *prima facie* suitable for the intended use, the Board is satisfied that the skilled person would replace the solvent ethanol disclosed in document (1) by another alcohol, namely benzyl alcohol, without an inventive step being involved, since both document (1) and the patent itself make it clear that benzyl alcohol is a solvent suitable for use in the parenteral administration of drugs.

2.3.5 The main arguments raised by the respondent were that the skilled person would not consider benzyl alcohol as a suitable solvent for two reasons: because it was pharmaceutically more risky than ethanol and because it had not been mentioned in the same context as paracetamol, so that its compatibility with paracetamol and the other ingredients of the preparation could not be foreseen.

During the oral proceedings, it also maintained that benzyl alcohol was in any case better than ethanol as a

solvent because it was less volatile, which was an advantage in the preparation of the paracetamol solution.

2.3.6 The Board cannot share the respondent's opinion.

In fact, document (3) and the reference to the use of benzyl alcohol as a solvent for parenteral administration of drug in the patent itself show that, even if benzyl alcohol might be more risky than ethanol, there was no technical prejudice against its use in parenteral solutions.

Nor does the Board accept the argument that the skilled person would not consider benzyl alcohol merely because it had not been mentioned in the same context as paracetamol in the prior art. Indeed, as shown by the working examples, the main solvent is glycerol formal (50% by volume), in which alcohols are described as being fully soluble (see document (24) under miscibility). Since paracetamol and benzyl alcohol both have an alcohol group, the skilled person would not *prima facie* disregard benzyl alcohol as an additional solvent in a solvent system comprising mainly Glycerol Formal, particularily because testing such a preparation by mixing the ingredients together is a routine experiment.

As regards the last point, the Board notes that the alleged effect has not been substantiated, that it would concern advantages during the process of preparation and not in the product *per se*, which is the subject-matter claimed, and that the said advantages were raised for the first time during the oral

proceeding in the absence of the appellant, with the result that the alleged effect cannot be taken into account for the assessment of inventive step.

In view of the foregoing, the Board concludes that the subject-matter of claim 1 of the main request does not involve an inventive step as required by Article 56 EPC.

3. Auxiliary request

3.1 Article 123(2) and (3) EPC

No objection under Article 123(2) and (3) EPC was raised by the appellant against the set of claims in the auxiliary request and the Board sees no reason to object.

3.2 Novelty

No objection under Article 54 was raised against this set of claims and the Board sees no reason to disagree.

3.3 Inventive step

The findings under 2.3.4 also hold good for the auxiliary request. Indeed, the mere indication in claim 1 of a ratio in which benzyl alcohol represents 10% in volume does not render obvious subject-matter inventive in the absence of any effect linked to this particular amount.

In that respect, the Board does not share the respondent's view that the skilled person would not envisage an amount greater than 5% of benzyl alcohol in the light of document (30).

It is indeed correct that document (30) mentions that benzyl alcohol has been used in concentrations up to 5% in parenteral solutions.

In this document, however, this value is disclosed in connection with the use of benzyl alcohol as an anaesthetic and as bacteriostatic, and not as a solvent (page 399, lines 2 to 5). Moreover, document (30) never refers to this amount as a limit which cannot be exceeded.

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

A. Townend | U. Oswald