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**Datasheet for the decision
of 11 January 2007**

Case Number: T 0993/03 - 3.3.02

Application Number: 94112519.7

Publication Number: 0642792

IPC: A61K 31/28

Language of the proceedings: EN

Title of invention:

Stabilized solutions of platinum(II) antitumor agents

Patentee:

Bristol-Myers Squibb Company

Opponent:

PLIVA - Lachema, a.s.

Headword:

Stabilized solutions of platinum(II) antitumor agents/BRISTOL-
MYERS SQUIBB

Relevant legal provisions:

EPC Art. 99, 114(1)

EPC R. 68(2), 55(c)

Keyword:

"Substantial procedural violation (yes)"

"Reimbursement of both appeal fees (yes)"

Decisions cited:

G 0009/91

Catchword:

-



Case Number: T 0993/03 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 11 January 2007

Appellant:
(Opponent)

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Decision under appeal:

Interlocutory decision of the Opposition
Division of the European Patent Office posted
14 August 2003 concerning maintenance of
European patent No. 0642792 in amended form.

Composition of the Board:

Chairman: U. Oswald
Members: M. C. Ortega Plaza
P. Mühlens
J. Willems
J. Riolo

Summary of Facts and Submissions

- I. European patent EP-0 642 792, based on European application No. 94 112 519.7, was granted on the basis of 16 claims.

Claim 1 as granted reads as follows:

"1. A stable injectable composition of a malonato platinum(II) compound comprising:

- (a) an antitumor effective amount of the platinum(II) compound,
- (b) a stabilizing amount of 1,1-cyclobutanedicarboxylic acid of an alkali metal salt thereof,
- (c) sufficient pH modifier to maintain a pH of 4 to 7, and
- (d) a pharmaceutically acceptable carrier."

Claim 9 as granted reads as follows:

"9. A method of stabilizing a solution of a malonato platinum(II) compound comprising:

- (1) adding a stabilizing amount of 1,1-cyclobutanedicarboxylic acid or an alkali metal salt thereof to the solution, and
- (2) adjusting the pH and maintaining it at 4 to 7."

Claim 16 as granted reads as follows:

"16. A process for stabilizing a malonato platinum(II) compound of a solution comprising the steps of:

- (1) dissolving the platinum compound in a carrier and adjusting the pH to 4 to 7,
 - (2) purging the product of step (1) with at least one of air or oxygen gas, and
 - (3) placing the purged solution into a container so that at least 50 volume % is unfilled with liquid, but saturated with air or oxygen."
- II. Opposition was filed and revocation of the patent in its entirety was requested pursuant to Article 100(a) EPC. In the "Anlage VII" to the form filed on 30 January 1998, the opponent filed its grounds of opposition, where it opposed the patent in suit for lack of novelty and lack of inventive step ("Erfindungshöhe") (Articles 52, 54 and 56 EPC).
- III. The appeals lie from the interlocutory decision of the opposition division maintaining the patent in amended form (Articles 102(3) and 106(3) EPC) on the basis of the sets of claims of the second auxiliary request filed during the oral proceedings before the opposition division.
- IV. The opposition division considered that the subject-matter of claim 1 of the main request (set of claims as granted) did not meet the requirements of novelty (Article 54 EPC). Basically, the opposition division considered the prior use claim put forward by the opponent to be proven and that the Batch No 321191 fulfilled the criteria set out by claim 1 of the main request, in particular in respect of carboplatin and 1,1-cyclobutanedicarboxylic acid (CBDCA).

The opposition division considered that the batch No 321191 did not anticipate the subject-matter of claim 1 of the first auxiliary request, which was filed as "auxiliary request" with the letter of 3 August 1999, in view of its lower content of CBDCA. As regards inventive step, the opposition division did not explicitly define the closest prior art. However, it would appear that it considered the previously mentioned production batch as appropriate starting point. The opposition division defined the problem underlying the opposed patent as "the provision of stabilized solutions of platinum **of structure II** antitumor agents" (emphasis added by the board). The opposition division considered that the solution claimed in the set of claims of the first auxiliary request (claim 1) was obvious in the light of document B20.

Although document B20 was not identified in the opposition division's decision, it appears to correspond to the Review article: "Stability of solutions of antineoplastic agents during preparation and storage for in vitro assays", by A. G. Bosanquet, published in Cancer Chemother. Pharmacol. (1989), 23, pages 197-207, which was filed by the opponent as annex to its letter of 29 September 2000.

The only text in the opposition division's decision concerning the second auxiliary request (filed during the oral proceedings before the opposition division) is the following ("Reasons for the decision", points 3.6 to 4):

"3.6 The Opponent did not comment on novelty (already acknowledged by the opposition division for auxiliary request I), but considered auxiliary request II obvious at least in so far as the claimed air saturation was concerned and in view of B22 according to which N₂ is used. Moreover no surprising effect has been shown in the patent.

3.7 To demonstrate an inventive step of new claim 1, the Patentee referred to data present in the patent indeed showing a surprising, unpredictable effect related to the feature d) [*sic*] of new claim 1. According to Group II of Table 1A on page 6, the result when filling the headspace in the container with Air or oxygen is a colorless [*sic*] solution compared to nitrogen which did not show the same beneficial effect on the physical stability of the aqueous solutions tested.

4. The Opposition Division decided to maintain the patent in amended form on the basis of the second auxiliary request whose claims meet the requirements of the EPC, Article 100a) namely Articles 54 as well as 56 EPC."

V. Claim 1 of the (first) auxiliary request (filed with the letter of 3 August 1999 reads as follows:

"1. A stable injectable composition of a malonato platinum(II) compound comprising:

- (a) 1 to 20 mg/ml of the platinum(II) compound,
- (b) 0.25 to 4 mg/ml of 1,1-cyclobutanedicarboxylic acid or an alkali metal salt thereof,

- (c) sufficient pH modifier to maintain a pH of 4 to 7, and
- (d) a pharmaceutically acceptable carrier."

Claim 1 of auxiliary request II (filed during the oral proceedings before the opposition division) reads as follows:

"1. A stable injectable composition of a malonato platinum(II) compound comprising:

- (a) 1 to 20 mg/ml of the platinum(II) compound,
 - (b) 0.25 to 4 mg/ml of 1,1-cyclobutanedicarboxylic acid or an alkali metal salt thereof,
 - (c) sufficient pH modifier to maintain a pH of 4 to 7, and
 - (d) a pharmaceutically acceptable carrier,
- in which the solution and the headspace of the container in which the solution is contained is saturated with air or oxygen."

Independent claim 6 of the auxiliary request II (filed during the oral proceedings before the opposition division) reads as follows:

"6. A method of stabilizing a solution of a malonato platinum(II) compound comprising:

- (1) adding 0.25 to 20 mg/ml of 1,1-cyclobutanedicarboxylic acid or an alkali metal salt thereof to the solution, and
- (2) adjusting the pH and maintaining it at 4 to 7, and
- (3) purging the solution with air or oxygen."

Independent claim 11 of the auxiliary request II (filed during the oral proceedings before the opposition division) reads as follows:

"11. A process for stabilizing a malonato platinum(II) compound of a solution comprising the steps of:
(1) dissolving the platinum compound in a carrier and adjusting the pH to 4 to 7,
(2) purging the product of step (1) with at least one od [sic] air or oxygen gas, and
(3) placing the purged solution into a container so that at least 50 volume % is unfilled with liquid, but saturated with air or oxygen."

- VI. The patent proprietor (appellant patentee) and the opponent (appellant opponent) lodged an appeal against said decision and filed grounds of appeal.

- VII. The appellant opponent and the appellant patentee filed counterarguments to the other party's appeal.

- VIII. A board's communication dated 15 May 2006, which conveyed the board's preliminary opinion, was sent to the parties. In this communication the board expressed its intention to remit the case to the department of first-instance due to a substantive procedural violation.

In the said communication both appellants were requested to inform the board as to whether under the circumstances previously depicted they maintained their requests for oral proceedings.

IX. Both appellants filed responses to the board's communication.

The appellant opponent's letter of 11 July 2006 reads as follows:

"I further inform the Board that OP 01 does not maintain his request for oral hearings if the opposed patent is revoked in its entirety **or if the case is remitted back to the first instance.**" (*emphasis added*)

The appellant patentee's letter of 19 July 2006 reads as follows:

"We herewith inform the Board that the proprietor does not maintain his request for oral proceedings if the case is remitted back to the first instance."

X. The appellant patentee requested that the decision under appeal be set aside and the patent be maintained as granted, or, alternatively, on the basis of the first or second auxiliary requests filed during the opposition proceedings before the opposition division.

The appellant opponent requested that the decision under appeal be set aside and the patent be revoked in its entirety.

Reasons for the decision

1. The appeals are admissible.
2. It appertains to the board's main duties to determine which is the legal and factual framework of the appeal procedure.

The present appeal lies from an interlocutory decision of an opposition division maintaining the patent in an amended form (on the basis of the second auxiliary request) and concerns two appellants: patent proprietor and opponent.

Therefore, when determining which is the legal and factual framework of the appeal in the present *inter partes* case it should be investigated whether the requirements of Rule 68(2) EPC are met by the first instance decision, and whether the opposition division duly exercised its discretionary power within the meaning of Article 114(1) EPC. The latter concerning *inter alia* the admission and examination of grounds of opposition, and the determination of the extent of the opposition.

- 2.1 The board agrees with the opposition division in that the opposition is admissible since it meets the requirements of Article 99(1) and Rule 55 EPC. This has not been disputed by the appellant patentee.
- 2.2 As regards the content of the notice of opposition in the present case, EPA form 2300 was filed in German language ("Einspruch gegen ein europäisches Patent"),

together with an annex ("Anlage VII") and an additional sheet ("Zusatzblatt zu IX B"), attached thereto.

It becomes evident from the reading of form 2300 (point V in 2300.2) that the patent was **opposed in its entirety** (this concerns the statement of the extent to which the patent is opposed within the meaning of Rule 55(c) EPC) pursuant to the grounds under Article 100(a) EPC (point VI in 2300.2).

However, although only lack of novelty (Articles 52(1); 54 EPC) was crossed in the form 2300.2, it becomes immediately evident from the reading of the annex "Anlage VII" that lack of inventive step ("Mangelnde Erfindungshöhe", see *inter alia* point 7 of the said annex) was also filed and reasoned as a ground of opposition within the due opposition period (Article 99(1) and Rule 55(c) EPC).

- 2.3 The opposition division's opinion that it had to be assessed whether the opposition ground concerning inventive step was admissible in view of the fact that "the inventive step analysis was not substantially drawn into question" in the notice of opposition (see paragraph under the heading "Article 100(a) EPC(inventive step)", point 3 of the "Reasons for the decision"), is not correct.

Whether the reasons given in the notice of opposition were likely to lead to a revocation of the contested patent on the grounds of lack of inventive step is not a prerequisite when examining the admissibility of this opposition ground in relation to the requirements of Article 99 and Rule 55(c) EPC.

2.4 The set of claims as granted contains three independent claims (claims 1, 9 and 16). The set of claims of the (first auxiliary request contains three independent claims (claims 1, 7 and 13) and the set of claims of the second auxiliary request contains three independent claims (1, 6, 11).

As regards the set of claims as granted, claim 1 concerns a "stable injectable **composition** of a malonato platinum(II) compound". Claim 9 relates to a "**method of stabilizing** a solution of a malonato platinum(II) compound" and claim 16 relates to a "**process for stabilizing** a malonato platinum(II) compound of a solution".

It may be open for discussion whether or not the composition obtained when stabilizing the solution of a malonato platinum(II) compound by the method steps indicated in claim 9 turns to be the "injectable composition of claim 1", since claim 9 does not require a functionally defined minimum amount of malonato platinum(II) ("antitumor effective amount"), but it is beyond doubt that the "process for stabilizing a malonato platinum(II) compound of a solution" according to claim 16 does not lead to the "stable injectable composition" of claim 1. The very simple reason is that the 1,1-cyclobutanedicarboxylic acid (or its alkali metal salt; see component (b) in claim 1) is never added.

In case of a negative result in the assessment of patentability for independent claim 1, the set of

claims may be rejected without further investigation of the other independent claims.

- 2.5 Hence, assuming a lack of novelty for claim 1 as granted (or lack of inventive step for amended claim 1 of the first auxiliary request) it would not be necessary for the opposition division to decide on the other independent claims, but the appealed decision is a maintenance of the patent based on the second auxiliary request.

Claim 11 of the second auxiliary request corresponds identically to claim 16 as granted, i.e. the process for stabilizing a malonato platinum(II) compound of a solution does not make use of 1,1-cyclobutane-dicarboxylic acid (or its alkali metal salt), nor is this ingredient necessarily present in the solution.

Claims 1 and 6, although different in scope owing *inter alia* to different amounts of the platinum(II) compound, or to the fact that a purging step (claim 6, step (3)) does not necessarily end up in a headspace of the container saturated with air or oxygen as required by amended claim 1, share the presence of 1,1-cyclobutanedicarboxylic acid in the solution.

Therefore, even if reading the only passages dedicated in the opposition division's decision to the second auxiliary request (points 3.6 to 3.7 and conclusion paragraph in point 4, all quoted *verbatim* in the present decision under "Facts and submissions") within the context of the whole reasons given in the first instance's decision, there is **no reasoning at all in the whole decision** in respect of the assessment of

novelty and inventive step **for the subject-matter of independent claim 11** (claim 16 as granted).

- 2.6 The extent of opposition as laid down in the notice of opposition concerned the patent in its entirety (see point 2.1 above). This is confirmed by the reasoning in point 7 of the annex "Anlage VII" of the notice of opposition, where the second type of stabilization claimed (reflected by claim 16 as granted) is opposed for lacking inventive step.
- 2.7 Therefore, the opposition division's decision does not meet the requirements of Rule 68(2) EPC, since it is not reasoned for the second auxiliary request, in particular in respect of the subject-matter of independent claim 11.
- 2.8 Moreover, this failure amounts to a major procedural violation requiring the decision to be set aside and the case to be remitted to the department of the first instance.
3. Additionally, the board wishes to express that it has serious doubts about the validity of the technical reasoning provided by the opposition division in its decision since it has obviously mistaken the number (II) appearing together (without a space) with the metal platinum in the expression a "malonato **platinum(II)** compound" as a reference to "formula (II)" of the description. However, the only chemical meaningful sense for the number (II) in the expression "malonato platinum(II) compound" is the valency number of the metal ("platinum(II)") constituting the compound.

- 3.1 It has also to be considered that the primary purpose of the appeal procedure in *inter partes* is to give the losing party the possibility of challenging the decision of the opposition division on its merits (G 9/91, OJ EPO, 1993, 408, point 18).
- 3.2 Therefore, the board considers that the lack of reasoning in respect of the decision of maintenance based on the second auxiliary request does not allow the losing party appellant opponent the possibility of properly challenging the decision of the opposition division on its merits.
- 3.3 Moreover, the board considers it to be equitable under the circumstances of the present case and by reason of the major procedural violation, as well as in view of the factual deficiencies detected by the board in the opposition division's decision (see *inter alia* points 3 and 3.1 above), to reimburse both appeal fees.

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 for further prosecution
3. Both appeal fees are to be reimbursed.

The Registrar:

The Chairman:

A. Townend

U. Oswald