BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

Internal distribution code:
(A) [ ] Publication in OJ
(B) [ ] To Chairmen and Members
(C) [ ] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 16 October 2007

Case Number: T 1772/06 - 3.3.08

Application Number: 97934319.1

Publication Number: 0915899

IPC: C07H 17/08

Language of the proceedings: EN

Title of invention:
Preparation of crystal form II of clarithromycin

Patent Proprietor:
ABBOTT LABORATORIES

Opponents:
Sandoz AG
Ranbaxy(UK) Ltd.
Hexal AG
Stada-Arzneimittel Aktiengesellschaft
Ratiopharm GmbH
NORTON HEALTHCARE LTD
Teva Pharmaceutical Industries Ltd.
Grünenthal GmbH

Headword:
Clarithromycin/ABBOTT

Relevant legal provisions (EPC 1973):
EPC Art. 123(2)

Keyword:
"Added matter (yes)"

Decisions cited:
T 0383/88, T 1046/96, T 1206/01, T 1018/02, T 0731/03

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1772/06 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 16 October 2007

Appellant: (Patent Proprietor)
ABBOTT LABORATORIES
Chad 0377/AP6D-2
100 Abbott Park Road
Abbott Park
Illinois 60064-3500 (US)

Representative:
Wright, Robert Gordon McRae
Elkington and Fife LLP
Prospect House
8 Pembroke Road
Sevenoaks
Kent TN13 1XR (GB)

Respondent I: (Opponent 01)
Sandoz AG
Lichtstrasse 35
CH-4056 Basel (CH)

Representative:
Breuer, Markus
Breuer & Müller Partnerschaft
Patentanwälte
Heimeranstrasse 35
D-80339 München (DE)

Respondent II: (Opponent 02)
Ranbaxy(UK) Ltd.
CP House, 3rd Floor, 97/107 Uxbridge Road
Ealing, London W5 5TL (GB)

Representative:
Cronin, Brian Harold John
CRONIN Intellectual Property
Chemin de Précossy 31
CH-1260 Nyon (CH)

Respondent III: (Opponent 03)
Hexal AG
Industriestrasse 25
D-83607 Holzkirchen (DE)

Representative:
Hamm, Volker
Maiwald Patentanwalts GmbH
Jungfernstieg 38
D-20354 Hamburg (DE)

Respondent IV: (Opponent 04)
Stada-Arzneimittel Aktiengesellschaft
Stadastrasse 2-18
D-61118 Bad Vilbel (DE)

Representative: Hamm, Volker
Maiwald Patentanwalts GmbH
Jungfernstieg 38
D-20354 Hamburg (DE)

Respondent V: Ratiopharm GmbH
(Opponent 05) D-89070 Ulm (DE)

Representative: Best, Michael
Lederer & Keller
Patentanwälte
Prinzregentenstrasse 16
D-80538 München (DE)

Respondent VI: NORTON HEALTHCARE LTD
(Opponent 06) Albert Basin
Royal Docks
London E16 2QJ (GB)

Representative: Cottam, David William
NORTON Healthcare Ltd.
Albert Basin
Royal Docks
London E16 2QJ (GB)

Respondent VII: Teva Pharmaceutical Industries Ltd.
(Opponent 07) 5 Basel Street, P.O. Box 3190
Petah Tiqva 49131 (IL)

Representative: Nachshen, Neil Jacob
D Young & Co
120 Holborn
London EC1N 2DY (GB)

Respondent VIII: Grünenthal GmbH
(Opponent 09) Postfach 500444
D-52088 Aachen (DE)

Representative: Kutzenberger, Helga
Kutzenberger & Wolff
Theodor-Heuss-Ring 23
D-50668 Köln (DE)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 12 September 2006 revoking European patent No. 0915899 pursuant to Article 102(1) EPC 1973.**

Composition of the Board:

Chairman: L. Galligani
Members: M. R. Vega Laso
C. Heath

Summary of Facts and Submissions

I. European patent No. 0 915 899 with the title "Preparation of crystal Form II of clarithromycin" based on European patent application No. 97 934 319.1 (published as WO 98/04574) was granted with 19 claims.

II. The patent was opposed by nine parties on the grounds of Article 100(a) EPC 1973, in particular lack of novelty (Article 54 EPC 1973), lack of inventive step (Article 56 EPC 1973) and non-patentable discovery (Article 52(2)(a) EPC 1973), as well as on the grounds of Article 100(b) and (c) EPC 1973. Opponent 8 withdrew its opposition on 4 April 2006.

III. In a decision announced at the end of the oral proceedings on 29 June 2006 and issued in writing on 12 September 2006, the opposition division found that none of the seven sets of amended claims then on file fulfilled the formal requirements of the EPC 1973. In particular, the sets of claims corresponding to the main request and the second, third and fourth auxiliary requests then on file were found to offend against Article 123(2) EPC 1973, because the feature "solvent free" present in, *inter alia*, claim 1 of each of these requests was not clearly and unambiguously disclosed in the original application. The opposition division held that, by introducing the feature "solvent free" into the claims, the patent had been amended in such a way that it contained subject-matter which extended beyond the content of the application as filed (cf. Article 123(2) EPC 1973). Consequently, the patent was revoked pursuant to Article 102(1) EPC 1973.

IV. The proprietor of the patent (appellant) lodged an appeal against the decision of the opposition division. With its statement setting out the grounds of appeal, the appellant filed five sets of claims, a main request and four auxiliary requests, which replaced the requests considered by the opposition division. New evidence in the form of a declaration and a scientific publication was also filed. In the event that the board was not minded to allow the main request, the appellant requested oral proceedings.

V. The respondents were given the opportunity to comment on the statement setting out the grounds of appeal. The board nevertheless considered it expedient to summon the parties to oral proceedings even prior to expiry of the time limit set for filing comments.

VI. All respondents except for respondent II (opponent 2) submitted observations to the grounds of appeal and/or the amended requests. Respondent V (opponent 5) filed additional documentary evidence. Respondent II announced that it would not attend and would not be represented at the oral proceedings.

VII. In a communication under Article 11(1) of the Rules of Procedure of the Boards of Appeal (RPBA) as it entered into force on 1 May 2003 (OJ EPO 2003, 60), the board provided comments on the amendments introduced into the sets of claims filed with the statement of grounds of appeal, as well as on some of the issues decided upon in the decision under appeal.

VIII. By letter dated 26 September 2007, the appellant withdrew all sets of claims then on file and submitted

six sets of amended claims, a main request and five auxiliary requests, for consideration by the board.

IX. Claims 1 and 17 of the **main request** read as follows:

"1. A method of preparing solvent free 6-O-methylerythromycin A crystal Form II comprising

(a) treating 6-O-methylerythromycin A with a solvent selected from the group consisting of
(i) an alkanol of from 1 to 5 carbon atoms, provided said alkanol is not ethanol or isopropanol
(ii) a hydrocarbon of from 5 to 12 carbon atoms,
(iii) a ketone of from 3 to 12 carbon atoms,
(iv) a carboxylic ester of from 3 to 12 carbon atoms, provided said carboxylic ester is not isopropyl acetate,
(v) an ether of from 4 to 10 carbon atoms of formula ROR', where R and R’ are straight or branched alkyl,
(vi) benzene,
(vii) benzene substituted with one or more substituents selected from the group consisting of
alkyl or from one to four carbon atoms,
alkoxy of from one to four carbon atoms,
nitro, and
halogen,
(viii) a polar aprotic solvent,
(ix) a compound having the formula HNR1R2 wherein R1 and R2 are independently selected from hydrogen and alkyl of one to four carbon atoms, provided that R1 and R2 are not both hydrogen,

(x) water and a water miscible solvent selected from the group consisting of a water miscible organic solvent and a water miscible alkanol,

(xi) methanol and a second solvent selected from the group consisting of
a hydrocarbon of from 5 to 12 carbon atoms,
an alkanol of from 2 to 5 carbon atoms,
a ketone of from 3 to 12 carbon atoms,
a carboxylic ester of from 3 to 12 carbon atoms,
an ether of from 4 to 10 carbon atoms,
benzene, and
benzene substituted with one or more substituents selected from the group consisting of
alkyl of from one to four carbon atoms,
alkoxy of from one to four carbon atoms,
nitro, and
halogen

and

(b) isolating the 6-O-methyl erythromycin A Form II crystals to separate them and remove any remaining solvents.

17. Solvent free 6-O-methylerythromycin A crystal Form II having the following characterizing x-ray 2-theta angle positions: 8.39 ± 0.20, 9.33 ± 0,20, 10.72 ± 0.20, 11.33 ± 0.20, 11.74 ± 0.20,12.24 ± 0.20, 13.62 ± 0.20,13.97 ± 0.20, 15.03 ± 0.20, 16.37 ± 0.20, 16.80 ± 0.20, 17.16 ± 0.20, 17.38 ± 0.20, 17.97 ± 0.20, 18.20 ± 0.20, 18.91 ± 0.20, 19.75 ± 0.20, 20.34 ± 0.20, 22.08 ± 0.20 and 24.79 ± 0.20."

Claims 2 to 16, 18 and 19 were identical to the corresponding claims as granted, and concerned particular embodiments of the method of claim 1 (claims 2 to 16) and specific medical uses of the compound of claim 17 (claims 18 and 19).

X. At the oral proceedings, which took place as scheduled on 16 October 2007, all parties to the appeal except for respondent II were represented.

XI. The parties presented their arguments on issues related to Article 123(2) EPC 1973 with respect to the main request. After the discussion, the appellant submitted an amended set of claims as **auxiliary request 1** which replaced the auxiliary requests previously on file. Claim 1 of this request differed from the corresponding claim of the main request in that the claimed method comprised the additional step of "(a) converting erythromycin A to 6-O-methylerythromycin A;", the previous step (a) becoming step (b), and that step (c) (previous step (b)) read:

"1. ...
(c) isolating the 6-O-methylerythromycin A Form II crystals by filtration and drying in a vacuum oven at a temperature of between ambient temperature (from 20 to 25°C) and 50°C, and a pressure of between 6.8 kPa [2 inches of mercury] and atmospheric pressure to remove any remaining solvent."

Additionally, claim 17 was amended to insert the phrase "... obtainable by the method of any one of claims 1 to 16" at the end of the claim. Dependent claims 2 to 16 and independent claims 18 and 19 remained as granted.

XII. The following documents are referred to in the present decision:

D11: Iwasaki et al., 1993, Acta Cryst. C49, pages 1227 to 1230;

D14: ICH Harmonised Tripartite Guideline "Impurities: Residual Solvents", CPMP/ICH/283/95, published on September 1997, pages 1/18 to 18/18;

D42: WO 98/31699, published on 23 July 1998;

AP2: Witness Statement of Dr Cynthia B. Curty dated 25 September 2007.

XIII. The submissions made by the appellant, as far as they are relevant to this decision, may be summarized as follows:

In coming to the erroneous conclusion that the application did not teach the removal of solvent from a solvate of clarithromycin (6-O-methylerythromycin A) Form II, the opposition division made a distinction between "solvent free" and "solvate free" that was present neither in the application nor in the patent. In the context of the patent, "solvent" referred to the liquid medium used to prepare a supersaturated solution of clarithromycin, from which clarithromycin Form II could be isolated. It was the common practice of the person skilled in the art to dry pharmaceutical active ingredients so that they were essentially free of residual solvents. This was described in various

textbooks of practical organic chemistry cited in opposition proceedings.

However, when concluding that the term "solvent free" could not encompass "solvate free", the opposition division seemed to have assumed that, first, solvates would inevitably be formed by clarithromycin and the solvents mentioned in the process claim, and, second, that under the conditions generally used by the skilled person, this "bound" solvent could not be removed. However, no evidence on the formation of solvates of clarithromycin was filed in opposition proceedings. Although D11 described a methanolate solvate of clarithromycin, this document did not describe how the solvate was produced. Moreover, no evidence was presented showing that "bound" solvent could not easily be removed from a solvate.

The opposition division seemed to have assumed that different conditions were required to remove "bound" solvent from a solvate, relative to the normal conditions for removing "non-bound" solvent from a solid pharmaceutical substance. However, the conditions for removing "unbound" solvent and "bound" solvent could be the same. The ease of removal of solvent depended, amongst other things, on the crystal structure of the pharmaceutical products and on the solvent. The sole document on file describing the preparation of solvates of clarithromycin was D42, and the results therein showed that solvates of clarithromycin could be readily desolvated to give a solvent free form of clarithromycin Form I, under drying conditions which were commonplace for pharmaceutical products and identical to the general

conditions taught in the application as filed, at the top of page 8.

The disclosure of the application, in particular the passage on page 8, lines 1 to 3 left the skilled person in no doubt that clarithromycin Form II was to be dried to remove any remaining solvent. However, the skilled person knew that it was not practicable to remove all remaining traces of solvent. In the context of the patent, the skilled person would construe "dried ... to remove any remaining solvent" to mean remove, as far as practicable, solvent from the clarithromycin. The products obtained in the experiments described in declaration AP2, which corresponded to Examples 8 and 10 of the patent, would be considered by the person skilled in the art to be "solvent free" and to comply with the guidelines for residual solvents set out in D14.

XIV. The submissions by the respondents were as follows:

The term "solvent free" had not been disclosed, let alone defined in the original application. This term was introduced into the claims during the examination proceedings in order to delimit the claimed subject-matter against a prior art document cited by the examining division. During the oral proceedings before the opposition division, the proprietor (appellant) contended that the term "solvent free" was to be construed to indicate that all solvent, ie. not only the free solvent, but also the solvent bound in a solvate had to be eliminated. Thus, independently from the crystal form and the solvent used, the term

"solvent free" had to be understood as "completely free of solvent".

If so construed, the feature "solvent free" could not be clearly and unambiguously derived from the original application. There was neither an explicit nor an implicit disclosure which could serve as a basis for the amended claims 1 and 17. Neither the intended use of 6-O-methylerythromycin A crystal Form II for the manufacture of a medicament nor the drying conditions described in the application implied that the compound must be completely free of solvent. According to D14, crystals of an active substance did not need to be completely free of solvent; rather, residual solvents were often present in medicaments, eg. when the active substance was a hydrate.

XV. The appellant (patentee) requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request filed on 26 September 2007 or auxiliary request 1 filed during the oral proceedings.

XVI. The respondents (opponents) requested that the appeal be dismissed.

Reasons for the Decision

Main and auxiliary request - Article 123(2) EPC 1973

1. Article 123(2) EPC 1973 states that a European patent application or a European patent may not be amended in such a way that it contains subject-matter which

extends beyond the content of the application as filed. According to the established case law of the Boards of Appeal of the European Patent Office (see eg. T 383/88 of 1 December 1992; T 1046/96 of 19 January 1998; T 1206/01 of 23 September 2004 and T 731/03 of 28 July 2005), in order to determine whether or not an amendment offends against Article 123(2) EPC 1973 it is necessary to examine whether the amendment results in the introduction into the specification, and especially into the claims of technical information which a skilled person could not have objectively derived from the application as filed, when account is taken of matter which is implicit to a person skilled in the art in what has been expressly mentioned.

2. At the oral proceedings before the opposition division, the opponents raised a number of objections under Article 123(2) EPC 1973 against the claims then on file, and the opposition division discussed each of the objections in point 6 of the decision under appeal. In particular, the opposition division found that the introduction of the feature "solvent free" in claims 1, 9 and 10 of, *inter alia*, the main request then on file contravened Article 123(2) EPC 1973 because it extended the scope of the request beyond the content of the application as filed (see points 6.2 and 6.6 of the decision).

3. The feature "solvent free", which is present also in claims 1 and 17 of both the main request and the auxiliary request 1 at issue (see sections IX and XI above), has been objected to by the respondents under Article 123(2) EPC 1973 alleging that this feature has no basis in the application as filed.

4. While it was not disputed by the appellant that the original application does not explicitly qualify the 6-O-methylerythromycin A crystal Form II as "solvent free", the appellant contended that the feature "solvent free" was implicit in the passage on page 8, lines 1 to 3 of the application as filed. This passage described the isolation of 6-O-methylerythromycin A crystal Form II by filtration and the particular conditions under which it was dried in a vacuum oven in order "*to remove any remaining solvent*".

5. Thus, the decisive question is whether or not the technical information embodied in the qualifying feature "solvent free" in claims 1 and 17 of both the main request and the auxiliary request 1 at issue is objectively derivable from the cited passage of the application as filed, account being taken of matter which is implicit to a person skilled in the art in what it is expressly mentioned in that passage.

6. In order to answer this question, the board must first examine how the feature "solvent free" is understood by a person skilled in the art when reading claims 1 and 17. The skilled person can be defined here as a pharmaceutical chemist with skills in the preparation of pharmaceutically relevant organic molecules and their subsequent isolation for use as active principle in a medicament. It has not been disputed by the appellant that a pharmaceutical chemist working in the pharmaceutical field must be aware *inter alia* of the content of document D14. In fact, the appellant itself has referred to this document as part of the "mental

furniture" of a skilled person in the pharmaceutical field.

7. In point 4.1 of document D14 (see page 6/18), it is stated that:

"*Solvents in Class I should not be employed in the manufacture of active substances, excipients, and medicinal products because of their unacceptable toxicity or their deleterious environmental effect.*"

In Table I on the same page, several solvents which belong to Class I are listed. In particular, benzene is mentioned as being carcinogenic. Thus, a pharmaceutical chemist is aware of the fact that, at least for some types of solvents, even minute quantities in the final product may render the product unacceptable for medicinal use.

8. With this information as "mental furniture", a person skilled in the art reading the claims, in particular claim 1, which is directed to a method of preparing 6-O-methylerythromycin A crystal Form II using, *inter alia*, benzene as a solvent (cf. item a) vi)), cannot construe the feature "solvent free", which qualifies the product in both claim 1 and 17, to merely mean "possibly having some residual solvent", but rather in absolute terms, as he or she is aware of the consequence of the presence of any residual benzene, namely that 6-O-methylerythromycin A prepared by the method of claim 1 cannot be used for the manufacture of a medicament because of its unacceptable toxicity.

9. The appellant argued that the feature "solvent free" should not be interpreted as "completely free of solvent", but must rather be construed to mean that the solvent is removed, "as far as practicable", from the clarithromycin. In the appellant's view, this interpretation was supported by the passage on page 8, lines 1 to 3 of the application as filed (cf. point 4 above).

10. The board disagrees with this interpretation. In the context of claims 1 and 17, the feature "solvent free" **in itself** imparts a clear, explicit technical indication to the skilled reader, namely that the 6-O-methylerythromycin A crystal Form II prepared by the method of claim 1 must be free of **any** solvent in absolute terms, and not simply as being what results from operating according to the passage on page 8, lines 1 to 3 of the application as filed.

11. In these circumstances, the board follows the rationale of decision T 1018/02 of 9 December 2003, in which it was held that "*[a]lthough a claim must not be interpreted in a way which is illogical or does not make any sense, the description cannot be used to give a different meaning to a claim feature which in itself imparts a clear credible technical teaching to the skilled reader. This also applies if the feature has not been initially disclosed in the form appearing in the claim.*"

12. As stated above, for a person skilled in the field of pharmaceutical chemistry the sole technically sensible interpretation of the feature "solvent free" which qualifies the product in both claim 1 and claim 17 must

be "free from any residual solvents" in absolute terms. Since this interpretation is clear and unambiguous, there is no need to consult the description, which in any case provides no definition whatsoever of the feature in question.

13. The meaning of the feature "solvent free" in claims 1 and 17 for a person skilled in the art having been established, the sole question that remains to be decided is whether this feature has a basis in the application as filed. As stated above (see point 4), the original application does not explicitly disclose the feature in question. As for the passage on page 8, lines 1 to 3 of the application, on which the appellant relied as an implicit basis for the feature "solvent free", it is noted that this passage indicates specific conditions for drying, namely those now recited in step c) of claim 1 in the auxiliary request. However, the product obtained working under these conditions is not necessarily "solvent free" in absolute terms. In fact, the appellant admitted that the phrase "*dried ... to remove any remaining solvent*" in the passage on page 8, lines 1 to 3 is to be understood as "to remove, **as far as practicable**, solvent from the clarithromycin". It follows that, if, even when operating under those conditions, removal of certain solvents is not practicable, the final product would contain residual solvents. This is confirmed by the results of the experiments in the declaration AP2 filed by the appellant (see section XII above), in which residual ethanol (as well as a small amount of methanol) was found in sample B of the product (see point 3 of the declaration). Thus, the passage indicated by the appellant cannot be seen as a basis for the feature

"solvent free" in the sense of "free of any solvent" in absolute terms, as the skilled person would understand it (see point 8 *supra*).

14. It follows from the above that the feature "solvent free", which was added upon grant to further qualify the 6-O-methylerythromycin A crystal Form II, goes beyond what the skilled person would have derived from the passage of the description cited by the appellant, in which he/she is invited to remove "any remaining solvent" with reference to specific conditions (now introduced in step (c) of the auxiliary request 1).

15. Thus, the finding of the opposition division that the introduction of the feature "solvent free" into the claims then on file offended against Article 123(2) EPC 1973 is considered to be justified. Since claims 1 and 17 of both the main request and the auxiliary request 1 include the feature in question, neither request fulfils the requirements of Article 123(2) EPC 1973.

16. At the oral proceedings before the board, the question whether or not the deletion of step (a) ("*converting erythromycin A to 6-O-methylerythromycin A*") from claim 1 as filed offended against Article 123(2) EPC 1973 was discussed in respect of the main request (see section IX above). However, in view of the findings above (see point 15) this issue does not need to be discussed in the present decision.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Wolinski L. Galligani