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**Datasheet for the decision  
of 23 March 2011**

**Case Number:** T 0778/09 - 3.3.01

**Application Number:** 96905945.0

**Publication Number:** 0813536

**IPC:** C07D 503/18

**Language of the proceedings:** EN

**Title of invention:**

Process for the preparation of pharmaceutically acceptable salts of clavulanic acid

**Patentee:**

LEK Pharmaceuticals d.d.

**Opponent:**

DSM IP Assets B.V.

**Headword:**

Clavulanic acid salts/LEK

**Relevant legal provisions:**

EPC Art. 123(3)(2), 87, 56, 54(2)(3)

**Relevant legal provisions (EPC 1973):**

EPC R. 88, 57a

**Keyword:**

"Novelty (yes)"  
"Inventive step - (yes) - non-obvious solution"  
"Main requests - priority validly claimed"

**Decisions cited:**

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**Catchword:**

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Case Number: T 0778/09 - 3.3.01

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.01  
of 23 March 2011

**Appellant:** DSM IP Assets B.V.  
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**Representative:** Misset, Onno  
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**Respondent:** LEK Pharmaceuticals d.d.  
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**Decision under appeal:** Decision of the Opposition Division of the  
European Patent Office posted 23 January 2009  
rejecting the opposition filed against European  
patent No. 0813536 pursuant to Article 101(2)  
EPC.

**Composition of the Board:**

**Chairman:** C. M. Radke  
**Members:** J.-B. Ousset  
C.-P. Brandt

## Summary of Facts and Submissions

I. The appellant (opponent) lodged an appeal against the decision of the opposition division rejecting the opposition against European patent No. 0 813 536 and maintaining it with two amendments to the description.

II. Relevant prior art is represented by:

- (0) Slovenian priority document (10 March 1995)
- (01) Non-certified English version of the Slovenian priority document
- (02) Certified English version of the Slovenian priority document
- (1) WO-A-97/05142
- (2) WO-A-95/23870
- (5) The 1993 Icheme Research Event, Grant IR, Ison A, Hoare M and Levesley J. pp. 173-175
- (6) WO-A-95/34194
- (10) Handbook of separation techniques for chemical engineers. Second edition, McGraw-Hill Book Company, (1988), 2-4 to 2-15.

III. Claim 1 as granted reads as follows:

"1. A process for preparation of a pharmaceutically acceptable salt of clavulanic acid comprising the steps of:

removing solids from a clavulanic acid containing fermentation broth by microfiltration,  
acidifying the filtrate to a pH between 1 and 3;  
extracting the acidified filtrate with a water immiscible solvent and separating the clavulanic acid containing extract;

mixing the extract with a metal donor and at least one additional dry solvent;  
to obtain metal clavulanate salt by direct reaction of the extract with the metal donor;  
and separating the metal clavulanate salt from the solution."

IV. In the written procedure, the appellant argued as follows:

- The replacement in [0016] of the description of the expression "0.1 mol%" by "0.1 vol%" contravened Article 123(2) EPC.
- Claim 1 as granted contravened Article 123(2) EPC), because the water content below 0.1 mol.% was not mentioned in claim 1.
- The replacement of 0.1 mol.% by 0.1 vol.% (see [0016], line 11 of the patent in suit) as well as the replacement of the word "and" by the word "followed" (see [0017], lines 26-27 of the patent in suit) were not occasioned by a ground of opposition.
- The patent did not sufficiently disclose how to carry out microfiltration.
- The newly filed translation of the priority document should not be admitted. If the board did not agree and considered that the first filed translation had been withdrawn, then no translation would be available and the right to the claimed priority would be lost.

- Claims 1-16 of the patent in suit were not entitled to the priority date.
  - The subject-matter of claim 1 was not novel vis-à-vis document (1) and lacked an inventive step in view of the disclosure of document (6) combined with that of document (2).
- V. In the annex to the summons to oral proceedings, the board gave its provisional opinion as to the validity of the claimed priority, novelty of the claimed subject-matter and on the amendments made by the respondent in its requests.
- VI. With a fax received on 18 March 2011, the appellant declared that it would not be attending the oral proceedings and that it maintained its requests.
- VII. Oral proceedings took place on 23 March 2011 in the absence of the appellant. During these proceedings, the respondent withdrew all previous requests and filed a new and single main request.
- VIII. Claim 1 of the main request reads as follows:
- "1. A process for preparation of an alkali and alkaline earth salt of clavulanic acid wherein an aqueous fermentation broth containing crude clavulanic acid, mycelium, proteins and other suspended solid matter is purified by microfiltration at a pH value between 5.8 and 6.2 and a temperature 20° to 40° C, the purified filtrate is concentrated by reverse osmosis and then directly extracted in a series of countercurrent

centrifugal extractors with a water immiscible solvent at a temperature between 15 to 25°C and a pH between 1 and 3, the extract is then dried to a water content below 0.1%, further concentrated by evaporation and decolorised with active charcoal to obtain a completely dry organic phase, the extract is mixed with a metal donor and at least one additional dry solvent containing between 0% and 4% of water to obtain metal clavulanate salt by direct reaction of the extract with the metal donor;  
and the metal clavulanate salt is separated from the solution."

- IX. The appellant requested the revocation of the patent in suit.
- X. The respondent requested that the patent be maintained in amended form on the basis of the main request (claims 1-10) filed at the oral proceedings on 23 March 2011.
- XI. At the end of the oral proceedings, the decision of the board was announced.

### **Reasons for the Decision**

- 1. The appeal is admissible.
- 2. Amendments
  - 2.1 Claim 1 has now been limited to a process for the preparation of alkali and alkaline earth salts of clavulanic acid (see claim 3 as filed). The making as

well as the treatment of the clavulanic acid until the formation of the salt is based on page 3, lines 17 to 28 of the description as originally filed. The amount of water contained in the dry additional solvent (from 0% to 4%) has a basis on page 4, lines 22 to 23 of the description as originally filed.

The limitation in claim 5 of the word "hexanoates" to the word "2-ethylhexanoates" does not add any new matter, since it is directly and unambiguously derivable from the content of the description as originally filed that "2-ethylhexanoates" are particularly preferred (see page 4, lines 15 to 17 and lines 29 to 30).

2.2 The board therefore concludes that the claims of the main request fulfil the requirements of Article 123(2) EPC.

2.3 Moreover, the scope of claim 1 has been restricted to specific metal salts (alkali and alkaline earth) compared to the granted version of this claim, which encompasses any metal salts. Therefore, Article 123(3) EPC is also fulfilled.

3. Disclosure of the invention

3.1 The handbook (10), published in 1988, relates to microfiltration using a pressure-driven membrane. Therefore, microfiltration formed part of the common general knowledge of the person skilled in the art. Hence, the person skilled in the art using common general knowledge was able to carry out the claimed invention including the step of microfiltration.

3.2 The board concludes that no grounds under Article 100(b) EPC prejudice the maintenance of the patent.

4. Priority document

4.1 Correction of the translation of the priority document

4.1.1 A certified translation of the Slovenian priority (document (02)) claimed by the patent in suit had been filed during opposition proceedings to replace the previous non-certified translation (document (01)). The certified translation (02) differs from the non-certified one (01) in that in the former:

- (1) The third full paragraph on page 5 has been added. This added paragraph is a translation of the first full paragraph on page 7 of document (0).
- (2) A reference to the solvents "methyl ethyl ketone, methyl isobutyl ketone and mixtures thereof" has been added on page 6 in the fourth full paragraph. These solvents are also disclosed in the respective paragraph of the originally Slovenian priority document (0) (see page 8, second full paragraph).
- (3) The expression "...water content below 2 g/l..." has been replaced by the expression "...water content 0.05% w/v..." in example 1 as it is disclosed in the Slovenian priority document (0) (see example 1 on page 10).



4.1.2 Hence, document (02) merely represents a correction according to Rule 88 EPC 1973.

4.2 For these reasons, the board considers document (02) rather than document (01) to be a fair translation of the Slovenian priority document (0) that can be used to assess whether the claimed subject-matter is entitled to the claimed priority.

5. Entitlement of the claimed priority

5.1 The process of claim 1 of the main request is limited to alkaline and alkaline earth metal salts of clavulanic acid. This feature is present in document (02) (see page 6, second full paragraph).

The production and the treatment of the clavulanic until its transformation into a salt also has a real basis in document (02) (see page 5, second full paragraph).

The third full paragraph on the same page of document (02) also mentions that the solvent or mixture of solvents containing the alkaline derivative to be added to the extract of clavulanic acid should have a water content ranging from 0% to 4 % as recited in claim 1 of the main request.

5.2 Thus, claim 1 is entitled to the claimed priority.

5.3 The dependent claims are also entitled to the claimed priority. The corresponding basis for each dependent claim is summarised as follows:

- Claim 2 (see document (02), second full paragraph, two first lines on page 6 and second full paragraph on page 7)
- Claim 3 (see document (02), second full paragraph, last line on page 7)
- Claim 4 (see document (02), second full paragraph, line 3 on page 6)
- Claim 5 (see document (02), second full paragraph, lines 3-4 on page 6)
- Claim 6 (see document (02), second full paragraph, last line on page 6)
- Claim 7 (see document (02), fourth full paragraph, lines 3 and 4 on page 6)
- Claim 8 (see document (02), penultimate paragraph, three last lines on page 6)
- Claim 9 (see document (02), penultimate paragraph, last line on page 6)
- Claim 10 (see document (02), claim 4).

5.4 Therefore, the board takes the view that the claims of the main request are entitled to the claimed priority (Article 87 EPC). This has the effect that document (1) and (6) do not form part of the prior art and that document (2) is prior art under Article 54(3) EPC.

6. Novelty

6.1 Document (2) discloses a process for making a salt of clavulanic acid. However, this process differs from the process of claim 1 of the patent in suit in that the potassium clavulanate obtained requires the intermediate formation of an ammonium salt of the clavulanic acid, whereas in the process of claim 1 of the patent in suit the potassium clavulanate is obtained **directly** (without making an intermediate salt). Furthermore, the amount of water in the solvent containing used to form the final potassium clavulanate is not mentioned in document (2), whereas it is mentioned in the process according to claim 1 of the patent in suit.

Document (5) does not describe the formation of a salt of clavulanic acid but only the formation of the free acid.

Nor does any other cited document disclose the subject-matter of present claim 1.

6.2 Hence, the subject-matter of claim 1 as well as that of the dependent claims 2 to 10 of the main request is novel (Article 54(2)(3) EPC).

7. Inventive step

7.1 Document (2) is prior art according to Article 54(3) EPC. As a consequence, this document is not considered when assessing inventive step.

7.2 Document (5) represents therefore the closest state of the art, since it describes the making of clavulanic acid in a broth of *Streptomyces clavuligerus* by fermentation. The acid formed after the fermentation process is recovered by ultrafiltration. This process differs from the one of the patent in suit in that there is no mention of the further reaction of the said clavulanic acid with an alkaline or an alkaline earth metal salt in different water-immiscible solvents to obtain a metal clavulanate.

7.3 The problem underlying the patent in suit can be considered to be the provision of an alternative process to make available metal clavulanates. In view of the outcome of this decision, it is not relevant whether or not a more ambitious problem is solved.

7.4 The board has no doubt, in particular in view of the example of the patent in suit, that the claimed process leads to the formation of metal clavulanates.

Starting from the disclosure of document (5), the person skilled in the art would not find any hint in this document or in any other prior art document to transform the clavulanic acid contained in the extract to obtain a metal clavulanate in a dry solvent.

Thus, the process of claim 1 cannot be deduced in an obvious manner by the person skilled in the art from the available prior art. It is, therefore, based on an inventive step (Article 56). The same conclusion applies to dependent claims 2 to 10.

8. Amendments to the description

The following should be borne in mind when adapting the description to the amended version of the main request:

- The replacement of 0.1 mol.% by 0.1 vol.% (see [0016], line 11 of the patent in suit) does not seem to be occasioned by a ground of opposition (Rule 57a EPC 1973).
  
- The replacement of the word "and" by the word "followed" (see [0017], lines 26 to 27 of the patent in suit) does not correspond to claim 2 as originally filed ("by successive microfiltration and ultrafiltration") which does not clearly indicate the order of the two filtration steps. This amendment thus contravenes the requirements of Article 123(2) EPC.

**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 with the order to maintain the patent on the basis of the main request (claims 1-10) filed at the oral proceedings on 23 March 2011 and a duly amended description.

The Registrar

The Chairman

M. Schalow

C.M. Radke