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**Datasheet for the decision  
of 30 November 2012**

**Case Number:** T 0977/09 - 3.3.02

**Application Number:** 01994654.0

**Publication Number:** 1335706

**IPC:** A61K 9/16, A61K 38/46

**Language of the proceedings:** EN

**Title of invention:**

Microspheres of pancreatic enzymes with high stability

**Patentee:**

Aptalis Pharma S.r.l.

**Opponent:**

Abbott Products GmbH

**Headword:**

Microspheres of pancreatic enzymes/APTALIS PHARMA S.R.L.

**Relevant legal provisions:**

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

-

**Keyword:**

"Sufficiency of disclosure - (no): examples not enabling"

**Decisions cited:**

-

**Catchword:**

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Case Number: T 0977/09 - 3.3.02

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.02  
of 30 November 2012

**Appellant:**  
(Opponent)

Abbott Products GmbH  
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**Representative:**

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**Respondent:**  
(Patent Proprietor)

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**Representative:**

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**Decision under appeal:**

Interlocutory decision of the Opposition  
Division of the European Patent Office posted  
23 February 2009 concerning maintenance of  
European patent No. 1335706 in amended form.

**Composition of the Board:**

**Chairman:** U. Oswald  
**Members:** A. Lindner  
R. Cramer

## Summary of Facts and Submissions

- I. European patent No. 1 335 706, based on application No. 01 994 654.0, was granted on the basis of 8 claims.
- II. Notice of opposition was filed against the patent. The patent was opposed under Article 100(a) EPC for lack of novelty and inventive step and Article 100(b) EPC for insufficient disclosure.
- III. The documents cited during the opposition and appeal proceedings included the following:
- (1) EP-A-0 256 127
  - (2) WO 01/25412
  - (3) US-A-4 280 971
  - (12) Science Lab.com, "Material Safety Data Sheet Polyethylene glycol 400 MSDS"
  - (23) K.-J. Steffens, "Ergänzendes Gutachten zur Vorlage beim Europäischen Patentamt", dated 20 September 2011
  - (24) Zanchetta Rotolab, "One step ahead".
- IV. The appeal lies from an interlocutory decision of the opposition division pronounced on 16 December 2008 and posted on 23 February 2009, maintaining the European patent on the basis of auxiliary request I.
- V. In said decision, the opposition division decided that the main request did not meet the requirements of Article 84 EPC, as it was not clear whether the lipase according to claim 1 was pancreatic. Regarding auxiliary request I, the opposition division concluded that the requirements of Articles 123(2), 83 and 84 EPC

were met. Moreover, the subject-matter claimed was novel, as neither of documents (1) and (2) related to pancreatic lipase. As regards inventive step, the provision of an alternative process for the production of a highly active pancreatic lipase was defined as the problem to be solved over document (3), which was considered to constitute the closest prior art. The combination of document (3) with document (1) would not render the claimed subject-matter obvious, as there was no reasonable expectation for the skilled person to obtain a lipase activity of >90%.

VI. The appellant (opponent) lodged an appeal against that decision.

VII. With a letter dated 27 June 2012, the respondent (patentee) filed a main request and an auxiliary request. Their sole independent claims read as follows:

*(i) Main request*

"1. A process for the production of microspheres containing pancreatic lipase or mixtures thereof with other pancreatic enzymes, one or more hydrophilic low melting polymers, and optionally excipients for pharmaceutical use, said microspheres having diameter comprised between 10  $\mu\text{m}$  and 1500  $\mu\text{m}$  and enzymatic title equal to or higher than 90% of the title of the solid mixture of their components, characterised in that a solid mixture formed by said lipase or mixtures thereof with other pancreatic enzymes, one or more hydrophilic low melting polymers, and optional excipients, is heated to a temperature equal to or higher than the melting temperature of said hydrophilic low melting

polymer, in stirring condition, where said hydrophilic low melting polymer has a melting point between 20°C and 90°C."

*(ii) Auxiliary request*

"1. A process for the production of microspheres containing pancreatic lipase or mixtures thereof with other pancreatic enzymes, one or more hydrophilic low melting polymers, and optionally excipients for pharmaceutical use, said microspheres having diameter comprised between 10 µm and 1500 µm and enzymatic titer equal to or higher than 90% of the titer of the solid mixture of their components, characterised in that a solid mixture formed by said lipase or mixtures thereof with other pancreatic enzymes, a hydrophilic low melting polyethylene glycol, and optional excipients, is heated to a temperature equal to or higher than the melting temperature of said hydrophilic low melting polyethylene glycol, in stirring condition, where said hydrophilic low melting polyethylene glycol has a melting point between 20°C and 90°C."

VIII. Oral proceedings took place on 30 November 2012.

IX. Regarding sufficiency of disclosure, the appellant's arguments can be summarised as follows:

In order to meet the requirements of sufficiency, it had to be possible to carry out the invention essentially over the whole area claimed. This could not be done, however, as the claimed invention encompassed quantities of hydrophilic low melting polymer which, according to paragraph [0019] of the contested patent,

were as low as one percent. Moreover, the skilled person was not in a position to determine the enzymatic title. Finally, none of the examples related to subject-matter encompassed by the claims.

- X. Regarding sufficiency of disclosure, the respondent's arguments can be summarised as follows:

The skilled person would be able to reproduce the claimed invention in the light of examples 3 and 4. The hydrophilic polymer defined in claim 1 of the main request was characterised by a melting point in the range of 20 to 90°C, so that the skilled person immediately recognised that PEG 400, having a melting point of 4 to 6°C, was erroneously used in example 3. He also knew that it had been intended to take PEG 4000 instead, which was the hydrophilic polymer used in subsequent example 4. As a consequence, taking PEG 4000 instead of PEG 400, the skilled person would follow the instructions given in example 3 and arrive at a product as claimed.

Regarding example 4, it was important to note that paragraphs [0044] and [0045] of the patent in suit related to two different procedures involving two different mixers. As a consequence, document (23) was irrelevant.

- XI. The appellant requested that the decision under appeal be set aside and that the European patent No. 1 335 706 be revoked.

The respondent requested that the decision under appeal be set aside and that a patent be granted on the basis

of the main request or alternatively on the basis of the auxiliary request, both filed with the letter of 27 June 2012.

### **Reasons for the Decision**

1. The appeal is admissible.
2. Admission of auxiliary requests I and II submitted at the oral proceedings before the board

These requests were submitted at a late stage of the oral proceedings of 30 November 2012. Their admission is therefore at the board's discretion and depends upon the overall circumstances of the case under consideration, including the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy (see Article 13(1) of the Rules of Procedure of the Boards of Appeal (RPBA)). The respondent did not give any reason for their late submission except that the amendments made were straightforward and simple and would not take the appellant by surprise. The board notes that the amendments were not based on any new facts or arguments put forward for the first time at the oral proceedings. All the objections raised by the appellant at the oral proceedings had already been submitted in writing, so that the respondent could have filed these requests much earlier. As a consequence, the board decided not to admit them into the proceedings.

3. Admission of documents (23) and (24)
  - 3.1 Document (23) was submitted with the letter dated 30 September 2011, i.e. after the statement of the grounds of appeal. The intention to submit document (23) had already been announced in the letter dated 23 May 2011. In both letters, the appellant explained that its late submission was caused by the non-availability of a Zanchetta Rotolab P-50, which was necessary for reworking example 4 of the contested patent. Despite this difficulty, the appellant managed to submit document (23) more than one year before the oral proceedings, so that the respondent was not taken by surprise. As a consequence, the board decided to admit document (23) into the proceedings.
  - 3.2 Document (24), which was submitted with a letter dated 28 June 2012, concerns copies of a catalogue relating to various types of Zanchetti Rotolab machines. However, it is not clear whether the submitted copies were all taken from the same document. In particular, it is not clear whether the last four pages (pagina 1 to pagina 4) belong to the same original document as the first four pages. Moreover, it is not clear that document (24) was published before the effective filing date of the contested patent. The first four pages do not appear to contain any publication date, whereas the last four pages comprise two dates: each table carries the header "Roto P year2000" and the footer "15/02/2009". As it is not possible to determine with certainty whether either of these dates constitutes a publication date, and if so, which one, the board decided not to admit document (24) into the proceedings.



4. Sufficiency of disclosure

4.1 Main request

An invention is in principle sufficiently disclosed if at least one way is clearly indicated enabling the skilled person to carry out the invention over essentially the whole claimed range. The skilled person, trying to rework the invention defined in the main request, would first direct his attention to the examples, in which the invention is described in its most concrete form. The patent in suit contains four examples, of which examples 1 and 2 are reference examples and therefore irrelevant for the present invention.

Example 3 describes the preparation of pancreatin pellets using PEG 400 (polyethylene glycol) as hydrophilic low melting polymer. In view of the fact that according to document (12) PEG 400 has a melting point of 4 to 6°C, which was not contested by the respondent, example 3 is also not encompassed by the invention defined by the main request, which requires a hydrophilic low melting polymer having a melting point between 20°C and 90°C. Regarding the respondent's argument that the reference to PEG 400 was an obvious error which the skilled person, knowing the melting point of PEG 400, would have immediately recognised as such and, as a consequence, would have understood PEG 4000 instead, the board notes that claim 1 as granted does not contain any lower limit regarding the melting point of the low melting hydrophilic polymer. The skilled person did therefore not have any reason to assume that example 3 was defective. He would rather

have concluded that it was representative of the invention according to claim 1 as granted, but no longer relevant for the invention now defined in the main request. Therefore, he would have dismissed example 3 and turned his attention to example 4 in which PEG 4000 is used as low melting hydrophilic polymer.

The appellant argued that it was not possible to prepare pancreatin pellets by following the instructions given in example 4. The fact that the maximum rotation speed of the mixer-granulator Zanchetta Rotolab P-50 (see page 6, line 31 of the patent) was limited to 315 rpm, so that the required 900 rpm (see page 6, line 26 of the patent) was not obtainable, was offered as the principal reason for this failure. Reference was made to document (23).

The respondent counter-argued that example 4 involved two different mixers, namely a high-energy mixer-granulator Zanchetta Rotolab with a maximum rotation speed of 1150 rpm, mentioned in paragraph [0044] of the contested patent, and a mixer-granulator Zanchetta Rotolab P-50 depicted in paragraph [0045] of the contested patent. Paragraphs [0044] and [0045] related to two separate procedures involving two different mixers. As a consequence, the appellant, having erroneously used the mixer-granulator Zanchetta Rotolab P-50 for both procedures, had not correctly reworked example 4, so that document (23) was completely irrelevant.

However, the fact that paragraphs [0044] and [0045] relate to two separate procedures involving two

different mixer-granulators is a piece of information which the skilled person is not able to extract from the wording of example 4. Paragraph [0044] describes the preparation of pancreatin pellets involving the steps of placing pancreatin and PEG 4000 in the tank of a high-energy mixer-granulator Zanchetta Rotolab, processing the mixture under the specific conditions described therein and finally unloading the pellets thus obtained. Then, at the beginning of paragraph [0045], example 4 continues with the wording "Using the described process, with a mixer-granulator Zanchetta Rotolab P-50 spherical pellets are obtained which are afterwards coated with a gastroresistant membrane formed by HP-55, triethylcitrate and talc...." The skilled person, reading example 4 as a whole, would necessarily assume that the same mixer-granulator is used, in the sense that the high-energy mixer-granulator Zanchetta Rotolab according paragraph [0044] is a generic denomination of the apparatus which is then specifically defined as mixer-granulator Zanchetta Rotolab P-50 in paragraph [0045]. Confronted with the problem that the mixer-granulator Zanchetta Rotolab P-50 does not allow a rotation speed of 900 rpm, he would conclude that example 4 was not enabling, as either said rotation speed of 900 rpm or the designation of the mixer-granulator Zanchetta Rotolab P-50 was incorrect.

Sufficiency of disclosure must be assessed on the basis of the patent as a whole. As a consequence, the absence of enabling examples does not necessarily mean that the claimed invention is not sufficiently disclosed. If, however, as in the present case, where the process in question involves the processing of an instable enzyme

under relatively harsh conditions (high rotational speed, elevated temperatures) without any significant loss of its activity, the claimed invention is of a complex nature, then the skilled person is in need of clear and precise instructions. These are lacking, on account of the deficiencies in examples 3 and 4 mentioned above. Trying to carry out the invention only on the basis of the general teaching of the description would, taking into account the technical complexity of the present case, amount to an undue burden. As a consequence, the requirements of Article 83 EPC are not met.

#### 4.2 Auxiliary request

The reasoning of point 3.1 applies *mutatis mutandis* to the invention defined in the auxiliary request. Limiting the hydrophilic low melting polymer to polyethylene glycol does not change the fact that an unreasonable amount of experimentation would be necessary for carrying out the invention in the absence of specific examples. The requirements of Article 83 EPC are therefore not met.

**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:

N. Maslin

U. Oswald