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**Datasheet for the decision  
of 7 December 2010**

**Case Number:** T 1744/08 - 3.3.02

**Application Number:** 02773579.4

**Publication Number:** 1429749

**IPC:** A61K 9/51

**Language of the proceedings:** EN

**Title of invention:**

Preparation of submicron sized nanoparticles via dispersion  
and solvent or liquid phase removal

**Applicant:**

Baxter International Inc.

**Opponent:**

-

**Headword:**

Preparation of submicron sized nanoparticles/BAXTER  
INTERNATIONAL INC.

**Relevant legal provisions:**

EPC Art. 83, 54, 56, 111(1)

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

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**Keyword:**

"Main request - Novelty, inventive step, sufficiency of  
disclosure - (yes)"  
"Remittal - (yes): undecided issues"

**Decisions cited:**

-

**Catchword:**

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Case Number: T 1744/08 - 3.3.02

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.02  
of 7 December 2010

**Appellant:** Baxter International Inc.  
One Baxter Parkway  
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Illinois 60015 (US)

**Representative:** Dee, Ian Mark  
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**Decision under appeal:** Decision of the Examining Division of the  
European Patent Office posted 10 April 2008  
refusing European patent application  
No. 02773579.4 pursuant to Article 97(2) EPC.

**Composition of the Board:**

**Chairman:** U. Oswald  
**Members:** A. Lindner  
J. Van Moer

## Summary of Facts and Submissions

I. European patent application No. 02 773 579.4 was refused by a decision of the examining division pronounced on 22 February 2008 on the basis of Article 97(2) EPC on the grounds that the subject-matter of the main request and of auxiliary requests 1 to 3, all filed with letter of 22 January 2008 lacked inventive step.

II. Claim 1 of the main request reads as follows:

"1. A process for preparing submicron sized particles of a pharmaceutically active compound comprising the steps of:  
providing a multiphase system having an organic phase and an aqueous phase, the organic phase containing a pharmaceutically active compound dissolved in a water immiscible solvent; and  
sonicating the multiphase system to evaporate a portion of the water immiscible solvent of the organic phase to cause precipitation of particles of the pharmaceutically active compound having an average effective particle size of less than 2  $\mu\text{m}$  in the aqueous phase and wherein the sonicating step is effective to remove nearly all the water immiscible solvent in the system."

III. The documents cited during the examination and appeal proceedings included the following:

- (1) WO 98/14174
- (2) US-A-6 139 870
- (3) WO 96/20698

- (4) WO 99/00113
- (5) WO 94/20072
- (6) J. Dispersion Science and Technology, 15(1), 89-117 (1994)
- (7) Journal of Pharmaceutical Sciences, 82(6), 584-589 (1993)

IV. The arguments in the first-instance decision may be summarised as follows:

Document (1), which constituted the closest prior art, described a process for preparing nanoparticles of a pharmaceutical agent, comprising the steps of dissolving an active agent in a water immiscible solvent, adding an aqueous phase comprising a stabilising agent and forming a crude oil-in-water emulsion by sonication. Subsequently, the solvent was evaporated. The problem to be solved by the present invention consisted in the provision of a simplified process for preparing submicron sized particles. The problem was solved by a process, wherein the sonication process was performed such that precipitation of the particles occurred in the aqueous phase due to evaporation of the water immiscible solvent. None of documents (1) to (7) gave any hint to modify the sonication process according to document (1) such that the water immiscible solvent was almost entirely evaporated. In these documents, emulsification and solvent removal were carried out in two separate process steps.

However, the application under appeal did not contain any evidence that the above problem was indeed solved. In the examples, the residual organic phase was either

removed by evaporation or was not removed at all. Hence, the technical effect on which the applicant based an inventive step had not been proven. As a consequence, the requirements of Article 56 EPC were not met.

- V. The appellant (applicant) lodged an appeal against this decision. He essentially argued as follows:

The examining division, although acknowledging that the prior art did not give any hint to modify the sonication process in such a way that it caused the water immiscible solvent to be evaporated almost in its entirety, nevertheless refused the application on the grounds of inventive step by reasoning that the technical effect on which the acknowledgement of an inventive step was based had not been established. As a consequence, the refusal was based on an objection of insufficiency rather than lack of inventive step. An invention was sufficiently disclosed if at least one way was clearly indicated enabling the skilled person to carry out the invention. In the present case, the description of the application under appeal clearly and unambiguously disclosed the sonication step in a manner that would enable the skilled person to reproduce it. Moreover, the application under appeal contained further information regarding suitable sonication devices and how to operate them.

- VI. The appellant requested in writing that the decision under appeal be set aside and that the case be remitted to the examining division for further prosecution of the main request filed with letter of 22 January 2008.

## Reasons for the decision

1. The appeal is admissible.
2. Main request:

The refusal of the main request and of all auxiliary requests was based on the conclusion that there was no evidence in the original application that the sonicating step was able to remove nearly all the water immiscible solvent in the system. The examining division concluded therefrom that there was lack of inventive step (see point IV above). If, however, the sonicating step is not able to remove nearly all the water immiscible solvent in the system, then the process as a whole cannot be carried out, as the said solvent removal step is an essential part of the process as claimed. As a consequence, the refusal is factually based on insufficiency of disclosure (Article 83 EPC) rather than lack of inventive step (Article 56 EPC).

- 2.1 Sufficiency of disclosure:

The examining division correctly pointed out that none of the specific examples of the application under appeal referred to a process in which nearly all the water immiscible solvent is removed by sonication. However, the description as a whole provides sufficient information for the skilled person to carry out the process of present claim 1. Thus, the passage on page 11, line 21 to page 12, line 17 gives detailed instructions concerning specific sonication devices, the frequency range to be used and the probe size.

Moreover, the description (see paragraph bridging pages 9-10) gives further guidance, as far as the choice of the water immiscible solvent is concerned. In view of this teaching, the skilled person should be able to reproduce the process as claimed in claim 1 of the main request without undue burden. As a consequence, the requirements of Article 83 EPC are met.

## 2.2 Novelty:

As was correctly pointed out in the decision under appeal (see point 2(e) of the Reasons for the decision), documents (1) to (7) relate to a process for preparing submicron sized particles, in which emulsification and solvent removal are carried out in two separate steps. As a consequence, the subject-matter of claim 1 of the main request is novel (Article 54 EPC).

## 2.3 Inventive step:

2.3.1 The present invention relates to a method for preparing submicron sized particles by providing a multiphase system having a liquid phase comprising an organic phase and an aqueous phase, the organic phase having a pharmaceutically active compound therein and removing nearly all the organic phase by sonication to obtain submicron sized particles (see page 5, lines 18-22 and page 12, lines 16-17 of the original application).

2.3.2 Document (1), which constitutes the closest prior art, discloses a method for preparing nanoparticles of a pharmaceutical agent, comprising the steps of dissolving an active agent in a water immiscible solvent, adding an aqueous phase comprising a



stabilising agent and forming a crude oil-in-water emulsion by sonication. Subsequently, the solvent is evaporated, e.g. by means of rotary evaporators, falling film evaporators, spray driers or freeze driers (see claims 1-3, page 18, lines 20-25 and example 2).

2.3.3 As was correctly pointed out in the decision under appeal, the problem to be solved by the present invention as claimed in the main request can be defined as the provision of a simplified process for preparing submicron sized particles comprising a pharmaceutically active agent. The solution to this problem proposed by the subject-matter of claim 1 concerns combining particle formation and solvent removal, which in document (1) comprise two separate steps involving sonication and a further step of solvent removal (see example 2) to a single step, in which the multiphase system is sonicated such that particle formation occurs and additionally nearly all the water immiscible solvent is removed. In view of the disclosure on page 11, line 21 to page 12, line 17 and the paragraph bridging pages 9 and 10, the board is convinced that the above problem was plausibly solved (see point 2.1 above).

2.3.4 It was correctly pointed out in the decision under appeal that none of documents (1) to (7) gave any hint to modify the sonication process according to document (1) such that particle formation and solvent removal in almost in its entirety could be carried out in a single step. As a consequence, the subject-matter of claim 1 of the main request meets the requirements of Article 56 EPC.

3. Since the main request as a whole, including all the claims has to fulfil the requirements of the EPC, the board, exercising its discretionary power according to Article 111(1) EPC, remits the case to the first instance for further prosecution as requested by the appellant.

## **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.

The Registrar:

The Chairman

N. Maslin

U. Oswald