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**Datasheet for the decision  
of 23 July 2012**

**Case Number:** T 2524/10 - 3.3.01  
**Application Number:** 04703805.4  
**Publication Number:** 1602662  
**IPC:** C07J 41/00, C07J 21/00,  
C07J 7/00  
**Language of the proceedings:** EN

**Title of invention:**

Method of obtaining 17alpha-acetoxy-11beta-(4-N,N-dimethylaminophenyl)-19-norpregna-4,9-diene-3,20-dione

**Applicant:**

Crystal Pharma, S.A.

**Opponent:**

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**Headword:**

Purification process/CRYSTAL PHARMA, S.A.

**Relevant legal provisions:**

EPC Art. 56

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

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**Keyword:**

"Inventive step -(yes) - unexpected higher purity grade"

**Decisions cited:**

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**Catchword:**

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Case Number: T 2524/10 - 3.3.01

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.01  
of 23 July 2012

**Appellant:** Crystal Pharma, S.A.  
(Applicant) Parque Tecnológico de Boecillo Parcela 105 A  
Valladolid  
ES-47151 Boecillo (ES)

**Representative:** ABG Patentes, S.L.  
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**Decision under appeal:** Decision of the Examining Division of the  
European Patent Office posted 29 June 2010  
refusing European patent application  
No. 04703805.4 pursuant to Article 97(2) EPC.

**Composition of the Board:**

**Chairman:** P. Ranguis  
**Members:** J.-B. Ousset  
D. S. Rogers

## Summary of Facts and Submissions

- I. An appeal was lodged against the decision of the examining division to refuse the European patent application No. 04 703 805.4.
- II. The examining division found that the subject-matter of the then pending main request as well as auxiliary requests 1 and 2 was lacking an inventive step in view of the disclosure of
- (1) WO-A-96/30390
- And more particularly in view of example 7 of document (1).
- III. In its statement of grounds of appeal, the appellant argued that the claimed process was inventive, since it led to a compound having a better purity than a compound obtained by the process described in document (1).
- IV. In the communication annexed to the summons to oral proceedings, the board was of the preliminary opinion that the claimed matter differed from the one described in the closest prior art document (1) in that VA-2914 isopropanol hemisolvate was not collected by filtration as in step b) of the process of claim 1 of the present application. Since the experimental results provided by the appellant were not considered as relevant to show the presence of an improved effect due to this distinguishing feature, and since filtration was a common physical technique well-known by the person

skilled in the art, the board considered that the claimed matter was lacking an inventive step.

V. In a second letter, the appellant requested that the oral proceedings were cancelled if any of the main and auxiliary requests 1 to 3 were in condition for acceptance and further argued that:

- An inventive step for the claimed process should be acknowledged, because VA-2914 obtained according to the claimed process did not contain p-bromo-dimethylaniline, which was a potentially genotoxic impurity.
- The problem to be solved by the present application is thus the provision of an improved process and not a mere alternative process to make available VA-2914.
- Even if it could be argued that document (1) could be expanded on by the skilled person by the incorporation of well known purification techniques, the person skilled in the art would not have expected this improved purity.
- The experimental data provided supported the improvement of the purity of the obtained VA-2914.

VI. With a fax sent on 20 June 2012, the board notified the appellant that the first auxiliary request filed on 4 June 2012 was regarded as meeting the requirements of the EPC.

VII. With its letter of 21 June 2012, the appellant

- withdrew its request for oral proceedings;
- withdrew its main request and its auxiliary requests 2 and 3 and
- renamed auxiliary request 1 filed with letter of 4 June 2012 as the main request. This request contains six claims. The sole independent claim 1 reads as follows:

"1. A process for purifying  $17\alpha$ -acetoxy- $11\beta$ -(4-N,N-dimethylaminophenyl)-19-norpregna-4,9-diene-3,20-dione (VA-2914) comprising:

- a) forming VA-2914 isopropanol hemisolvate crystals by means of crystallising VA-2914 in isopropanol;
- b) separating the VA-2914 isopropanol hemisolvate crystals by filtration; and
- c) converting VA-2914 isopropanol hemisolvate into VA-2914."

VIII. In view thereof, the board cancelled the oral proceedings scheduled on 3 July 2012.

### **Reasons for the Decision**

1. The appeal is admissible.

The novelty of the claim request before the board is not in dispute, neither is its compliance with the other requirements of the EPC, except Article 56 EPC, which is the sole issue upon which this appeal turns.

*Main and sole request - Inventive step*

2. The board considers that document (1) represents the closest prior art. Example 7 of this document describes that starting from a crude product, a crystalline compound retaining isopropanol is made as in step a) of the process of claim 1 of the main request. Contrary to the appellant's argument, example 7 of document (1) mentions that "...remaining solid, which retained isopropyl alcohol as solvent of **recrystallisation...**" (see page 23, lines 29-30). The board is of the opinion that the word "recrystallisation" implies that the compound obtained is in a crystalline form otherwise, the word "solvation" would have been more appropriate to qualify the retained solvent. Hence, the process described in step a) of claim 1, namely crystallising VA-2914 in isopropanol is identical to the one described in example 7 of document (1) in which a crystalline form of VA-2914 containing isopropanol is also obtained.

The process of recovery of VA-2914 in a non-solvated form is described in example 7 of document (1) (see page 23, lines 30 to 33).

Finally, the process of claim 1 of the main request differs from the process described in example 7 in that the intermediate VA-2914 isopropanol hemisolvate is collected by filtration (see step b) of claim 1 of the main request).

3. The problem underlying the present invention can be seen in the provision of an improved process to obtain VA-2914.

3.1 With its letter of 4 June 2012, the appellant provided experimental data and more particularly purification processes A1 and A3. Purification process A1 was run as follows:

- Syrup containing raw VA-2914 was dissolved in isopropyl alcohol (18ml) at room temperature and evaporated, isopropyl alcohol (18ml) was again added to the resulting residue (which did not dissolve) and the solvent was evaporated, isopropyl alcohol (18ml) was again added to the resulting residue (which did not dissolve) and the solvent was evaporated;
- The resulting residue was dissolved in ethyl acetate (20ml) at room temperature and evaporated to give a residue;
- The resulting residue was dissolved in diethyl ether (200ml) at room temperature and the solution allowed to crystallize at room temperature;
- The solid formed was filtered, washed with diethyl ether (18ml) and dried in an oven at 50°C.

Purification process A3, according to the claimed invention was run as follows:

- Isopropyl alcohol (18ml) was added to the syrup containing raw VA-2914, dissolution was not observed at room temperature, so 18 ml more of isopropyl alcohol were added to dissolve the product. The resulting solution was partially

evaporated at room temperature up to a volume of 18ml, and the solid formed was filtered;

- The resulting residue was dissolved in ethyl acetate (20ml) at room temperature and evaporated to give a residue;
- The resulting residue was dissolved in diethyl ether (200ml) at room temperature and the solution allowed to crystallize at room temperature;
- The solid formed was filtered, washed with diethyl ether (18ml) and dried in an oven at 50°C.

3.2 Purification process A3 differs from process A1 in that the solid obtained in the first step was filtered. This filtration step corresponds to the distinguishing features between the prior art and the claimed matter.

Moreover, another difference appears from the respective first steps of processes A1 and A3, which could invalidate the relevance of the comparison. However, the board contends that this is not the case here for the following reasons.

In process A1 and according to example 7 of document (1), the syrup was dissolved in isopropyl alcohol and this alcohol was evaporated to yield a solid retaining the said alcohol as solvent of crystallisation. This dissolution and evaporation were repeated three times. The dissolution/evaporation process was carried out only once in process A3. If the dissolution/evaporation would have affected the grade of purity of the crystalline hemisolvate of VA-2914, then the compound



obtained after removal of the alcohol present in the solvate should be purier in the case of process A1 than in the case of process A3. In view of the results submitted by the appellant, it is the compound obtained according to process A3, which does not contain any p-bromo-dimethylaniline.

- 3.3 It can be concluded therefrom, that the distinguishing feature between the process described in example 7 of document (1) and the process claimed in the current application is responsible for the improved grade of purity of VA-2914.
- 3.4 The question is therefore whether such an improvement could be deduced or not in an obvious manner from the available state of the art.
- 3.5 A filtration of the crystalline hemisolvate is not mentioned and cannot be inferred from the disclosure of document (1), since a filtration step occurs only to recover the final compound, namely the non-solvated crystalline form of VA-2914. As a consequence, an improvement in the grade of purity, due to this filtration, is even less deducible from the content of the prior art than the repeating of the dissolution and evaporation step.
- 3.6 The board concludes that claim 1 of the main request fulfils the requirements of Article 56 EPC. Since claims 2 to 6 all depend on claim 1, their subject-matter is also considered to be inventive.

**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 grant a patent with the present main request and a description to be adapted.

The Registrar

The Chairman

M. Schalow

P. Ranguis