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**Datasheet for the decision  
of 3 May 2022**

**Case Number:** T 1406/19 - 3.3.07

**Application Number:** 07804680.2

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A61K31/437, A61K9/28,  
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A61K47/36, A61K47/38

**Language of the proceedings:** EN

**Title of invention:**

USE OF POLYOLS TO OBTAIN STABLE POLYMORPHOUS FORMS OF RIFAXIMIN

**Patent Proprietor:**

Alfasigma S.p.A.

**Opponents:**

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**Headword:**

Use of polyols to stabilise polymorphous forms of rifaximin /  
Alfasigma

**Relevant legal provisions:**

EPC Art. 123(2), 84

RPBA 2020 Art. 11

**Keyword:**

Amendments - added subject-matter (Main request, Auxiliary requests I-III: yes; Auxiliary request IV: no)

Claims - clarity (yes)

**Decisions cited:**

G 0003/14



**Beschwerdekammern**

**Boards of Appeal**

**Chambres de recours**

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Case Number: T 1406/19 - 3.3.07

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.07**  
**of 3 May 2022**

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**Decision under appeal:**      **Decision of the Opposition Division of the  
European Patent Office posted on 4 April 2019  
revoking European patent No. 2059232 pursuant to  
Article 101(3) (b) EPC.**

**Composition of the Board:**

**Chairman**                    D. Boulois  
**Members:**                 E. Duval  
                                  Y. Podbielski

## Summary of Facts and Submissions

- I. European patent 2 059 232 (hereinafter "the patent") was granted on the basis of 14 claims. Claim 1 of the patent related to the use of compounds bearing at least two hydroxy groups (hereinafter "polyols") dissolved in an aqueous solution to stabilize polymorphous forms of rifaximin.
- II. Three oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, it was not sufficiently disclosed and it extended beyond the content of the application as filed.
- III. The appeal was filed by the patent proprietor (appellant) against the decision of the opposition division to revoke the patent.

The decision was based on a main request filed on 1 June 2018, auxiliary requests I to XIII filed on 21 November 2018, and auxiliary request XIV filed during the oral proceedings.

Claim 1 of the main request read as follows:

"Use of one or more compounds bearing at least two hydroxy groups dissolved in an aqueous solution to stabilize polymorphous form  $\beta$  of rifaximin in a solid state independently from the residual water content."

- IV. The opposition division decided the following:
  - (a) Claim 1 of the main request infringed Article 123(2) EPC because the feature "to stabilize polymorphous form  $\beta$  of rifaximin in a solid state

independently from the residual water content" resulted in an undisclosed generalisation.

(b) None of the auxiliary requests I-XIII were admitted into the proceedings, because the amendments in auxiliary requests I-XIII were neither occasioned by a ground for opposition (Rule 80 EPC) nor followed a convergent line of development.

(c) Auxiliary request XIV was not admitted into the proceedings because it was late-filed and *prima facie* raised new issues of dispute very late in the opposition proceedings.

V. With the statement setting out the grounds of appeal, the appellant filed a main request and auxiliary requests I-VIII.

The main request was identical to the main request underlying the appealed decision (see III. above).

Claim 1 of auxiliary request I read as follows:

"Use of one or more compounds bearing at least two hydroxy groups dissolved in an aqueous solution to obtain stabilized polymorphous form  $\beta$  of rifaximin in a solid state having a residual water content lower than 4.5 %."

Claim 1 of auxiliary request II differed from claim 1 of auxiliary request I in that the expression "to obtain stabilized" was replaced with "to stabilize".

Claim 1 of auxiliary request III differed from claim 1 of auxiliary request II in that the polyols were limited to "those having the general formula H-[O-CH<sub>2</sub>-

$\text{CH}_2]_n\text{-OH}$ , wherein n can range between 2 and 14, 1, 2, 3-propanetriol or 1,2-propanediol".

Claim 1 of auxiliary request IV read as follows:

"Use of one or more compounds bearing at least two hydroxy groups selected from those having the general formula  $\text{H-}[\text{O-CH}_2\text{-CH}_2]_n\text{-OH}$ , wherein n can range between 2 and 14, 1, 2, 3-propanetriol or 1,2-propanediol, dissolved in an aqueous solution at a concentration ranging between 5% (w/w) and 50% (w/w) to stabilize polymorphous form  $\beta$  of rifaximin in a solid state having a residual water content lower than 4.5%."

- VI. The Board set out its preliminary opinion in a communication pursuant to Article 15(1) RPBA dated 4 February 2022.
- VII. Oral proceedings were held before the Board on 3 May 2022 in the presence of the appellant and of opponent 2 (respondent 2).
- VIII. The appellant requests that the decision under appeal be set aside and that the patent be maintained on the basis of the main request, or, alternatively, on the basis of one of auxiliary requests I-VIII, all filed with the statement setting out the grounds of appeal.
- IX. Respondent 2 requests that the appeal be dismissed, and that auxiliary requests I-VIII not be admitted into the proceedings. In case the appealed decision should be set aside, respondent 2 requests that the case be remitted to the opposition division.
- X. Respondent 1 (opponent 1) and respondent 3 (opponent 3) did not file any substantive submissions in the appeal proceedings.

XI. The arguments of the appellant may be summarized as follows:

(a) Main request and auxiliary requests I-III, Article 123(2) EPC

The feature "dissolved in an aqueous solution", present in claim 1 of the main request and auxiliary requests I-III, did not amount to an inadmissible intermediate generalization from page 7 of the description as filed, because the application as filed disclosed the dissolution of a polyol in an aqueous solution independently of any specific production process. The disclosure on pages 7 and 8 did not indicate any concentration. The term "suitable" referred to an appropriate dilution for the process considered, or a dilution sufficient to dissolve the polyol in water. Page 5 of the application as filed did not define the concentration of the polyol(s) in water, but its amount relative to rifaximin.

(b) Auxiliary request IV

The filing of auxiliary request IV took into account the objections under Article 123(2) EPC and under Rule 80 EPC as identified by the opposition division, and did not represent a significant deviation from the line of defence followed during the opposition proceedings. Consequently, auxiliary request IV was to be admitted into the proceedings.

In claim 1 of auxiliary request IV, in line with the disclosure of page 5, lines 23-24 of the application as filed, the concentration of polyol(s) had been indicated. This feature was not inextricably linked



with the other features disclosed on that page. Therefore, claim 1 was in line with the provisions of Article 123(2) EPC. This feature was furthermore not unclear, because when reading said passage of the description in the context of the whole application, in particular in relation to the examples, the only technical sensible interpretation was that said concentration referred to rifaximin  $\beta$ . Consequently, the criteria of Article 84 EPC were met.

XII. The arguments of respondent 2 may be summarized as follows:

(a) Main request and auxiliary requests I-III, Article 123(2) EPC

Claim 1 of the main request contravened Article 123(2) EPC among others for the reason that it defines that the polyol(s) were "dissolved in an aqueous solution". In contrast, page 7 of the application as filed required the polyol(s) to be suitably diluted. A general use of polyol(s) in an aqueous solution regardless of the concentration was not disclosed.

(b) Auxiliary request IV

Claims 3-6 of auxiliary request IV contained cosmetic amendments and re-arrangements which contravened the provisions of Rule 80 EPC. Furthermore, auxiliary request IV should have been submitted by the appellant during the first instance proceedings. Hence, auxiliary request IV was not to be admitted into the proceedings.

Auxiliary Request IV contravened Article 123(2) EPC because the concentration of polyols introduced in claim 1 was only disclosed on page 5, lines 23-24 of

the application as filed in combination with the feature "subsequent excess water removal" which was missing in claim 1. Furthermore, the change of dependency in claims 3-8 of Auxiliary Request IV also infringed Article 123(2) EPC.

Auxiliary request IV did not meet the requirements of Article 84 EPC because it was not clear whether the concentration specified in claim 1 referred to the polyols in aqueous solution or to the polyols with respect to rifaximin.

Since the discussion before the opposition division had been limited to Article 123(2) EPC and admissibility, and had not addressed sufficiency, novelty and inventive step, special reasons under Article 11 RPBA existed for remitting the case if the Board decided to set aside the decision.

## **Reasons for the Decision**

1. Main request, Article 123(2) EPC
  - 1.1 Claim 1 of the main request relates to the use of one or more polyols dissolved in an aqueous solution to stabilize polymorphous form  $\beta$  of rifaximin in a solid state independently from the residual water content.

The question is whether the subject-matter of claim 1 of the main request, in particular regarding the feature "dissolved in an aqueous solution", derives directly and unambiguously, using common general knowledge, from the application as filed.

- 1.2 The appellant cites pages 7 and 8 as basis for the feature "dissolved in an aqueous solution".

However, as pointed out by respondent 2, the use of polyols in an aqueous solution is disclosed, in the application as filed, only in combination with a suitable dilution. In contrast, claim 1 of the main request does not limit the polyol dilution, or concentration, in the aqueous solution.

Thus, page 7, lines 1-4, indicates that "one of these polyols, or a mixture of them, can be applied *after a suitable water dilution* with a granulation process in which the solution is opportunely added to the powder containing the active ingredient, or exclusively constituted by it, with suitable mixing" (emphasis added by the Board). The further passages of pages 7-8 (see page 7, lines 8, 22, or page 8, line 17) refer to "the" solution, i.e. the solution resulting from a suitable water dilution.

- 1.3 Contrary to the appellant's opinion, it is not directly and unambiguously derivable from the application as filed that the suitable dilution only refers to a dilution which is merely suitable to solubilize the polyol, or a dilution which is suitable for the process used for contacting the polyol with rifaximin (e.g. the granulation process of page 7, lines 1.4, or any other process according to page 8, lines 16-19). Considering that the purpose of the invention is to stabilise rifaximin, and that the manner in which the polyol is contacted with rifaximin, including the polyol's concentration in water, may play a role in this stabilisation, irrespective of the process used, a reading of "suitable" as a concentration "suitable to achieve stabilisation" cannot be excluded. The fact

that water may be removed after the polyol(s) and rifaximin have been contacted does not mean that the concentration of the polyol in water during the contacting is irrelevant.

Accordingly, page 7 only discloses that the polyol solution may be prepared by a suitable water dilution, but does not disclose that the solution may have any concentration as allowed by claim 1 of the main request.

- 1.4 The remaining parts of the application as filed do not disclose either the use of aqueous solutions of polyols for the stabilisation of rifaximin independently of the concentration of the polyols in the solution.

On the contrary, the examples indicate both the amount of water and the amount of polyol used (see examples 1, 4 and 5, with amounts equivalent to concentrations of 3.3%, 11.1% and 2.9%). Furthermore, the application as filed on page 5 (lines 15-25) states that polyols "can operate as stabilizers for the polymorphous form  $\beta$  [...] by the use of aqueous solutions of polyols at a concentration ranging between 5% (w/w) and 50% (w/w)".

- 1.5 The appellant argued that the passage on page 5 did not relate to the concentration of the polyol(s) in the solution, but to the amount of polyol(s) relative to rifaximin. The Board does not share this view.

The expression "aqueous solutions of polyols at a concentration ranging between 5% (w/w) and 50% (w/w)" does not mention rifaximin. Furthermore, the word "concentration" is consistent with an amount of polyol relative to the solvent with which it is admixed (i.e. water), and not with an amount of polyol relative to

the separate, solid rifaximin. Accordingly, the wording on page 5 normally expresses a concentration relative to the aqueous solution, and not relative to rifaximin.

Taking into account the rest of the disclosure of the application as filed does not lead to a different conclusion. Thus, example 4 discloses a polyol concentration in water (11.1%) within the concentration range of page 5 (5-50% (w/w)), which supports the above interpretation. It is in any case not unusual for an application to contain examples departing from the generally described invention. Here, the fact that the concentration in water in other examples falls outside this water (see examples 1 and 5: 3.3% and 2.9%) does not lead to a reading of page 5 which departs from its wording.

Lastly, the appellant argued that, since rifaximin is to be stabilised by the polyol, it is necessary to define the ratio of polyol relative to rifaximin. However this does not mean that the concentration of polyol in water cannot be relevant (see the reasons in 1.3 above) and is not what is intended on page 5.

Consequently, the passage on page 5 of the application as filed does not disclose either the use of aqueous solutions of polyols for the stabilisation of rifaximin independently of the concentration of the polyols in the solution.

- 1.6 Since the application offers no basis for the generalisation to any concentration as in claim 1 of the main request, this main request does not meet the requirements of Article 123(2) EPC.

2. Auxiliary requests I-III

In each of auxiliary requests I-III, claim 1 defines the use of polyol(s) in an aqueous solution without limit as to its concentration in the aqueous solution. Accordingly, irrespective of their admittance into the proceedings, auxiliary requests I-III infringe Article 123(2) EPC for the same reasons as the main request.

3. Auxiliary request IV

3.1 Admittance into the proceedings

3.1.1 The appellant filed auxiliary request IV with its statement setting out the grounds of appeal on 1 August 2019. This request had not been submitted in the proceedings before the opposition division.

The question as to whether auxiliary request IV should be admitted must be decided on the basis of Article 12(4) RPBA 2007 (see Article 25(2) RPBA 2020). Article 12(4) RPBA 2007 gives the Board discretion to hold inadmissible requests which could have been presented or were not admitted in the first instance proceedings.

3.1.2 For the following reasons, the Board sees auxiliary request IV as an appropriate reaction to the appealed decision.

Auxiliary request IV is analogous to auxiliary request XII underlying the appealed decision. During the oral proceedings before the opposition division, auxiliary request XII (among others) was not admitted into the proceedings in particular because of the rewording of "use [...] to stabilize" (see granted claim 1) into "use [...] to obtain" (see claim 1 of auxiliary request

XII; see the appealed decision, point 6 of the reasons). According to the appealed decision, either this rewording changed the subject of the proceedings, with the consequence that issues under e.g. Article 123(3) EPC arose, or the rewording did not change the subject of the proceedings and thus was not occasioned by any ground for opposition, contrary to Rule 80 EPC.

In present auxiliary request IV, the rewording that led to the non-admittance of auxiliary request XII is cancelled, i.e. claim 1 of auxiliary request IV relates to a "use [...] to stabilise" as in claim 1 as granted. Accordingly, auxiliary request IV is seen as an appropriate reaction to the appealed decision.

- 3.1.3 Furthermore, contrary to the opinion of respondent 2, the Board can identify no cosmetic amendments and re-arrangements in auxiliary request IV.

Whereas claims 9-12 as granted referred to rifaximin "stabilized by one or more compounds according to claims 1 to 5", claims 3-6 of auxiliary request IV relate to rifaximin "according to claim 2". Since claim 2 of auxiliary request IV is limited to rifaximin "stabilized by the use of one or more compounds as claimed in claim 1 and having a residual water content lower than 4.5%", the amendment in claims 3-6 is not a mere rewording but is a limitation of the subject-matter to a residual water content lower than 4.5%.

- 3.1.4 Accordingly, the Board admitted auxiliary request IV.

- 3.2 Article 123(2) EPC

Claim 1 of auxiliary request IV finds basis in claims 1, 4, 5, 6 and 7 as filed, together with the disclosure

on page 5, lines 22-23 of the application as filed. Claim 1 does not recite the step of "subsequent excess water removal", mentioned on page 5, line 24 of the application as filed. However, this step on page 5 does not specify any process or any conditions, such as elevated temperatures. Instead, the mere mention of a water removal on page 5 means nothing more than bringing the water content to 4.5% or below, which is a requirement of claim 1 of auxiliary request IV.

Lastly, irrespective of the change in dependency in claims 3-8, the subject-matter of these claims is directly and unambiguously derivable from the application as filed (namely claims 10-15 together with the same limitations as in claim 1).

Accordingly, auxiliary request IV fulfills the requirements of Article 123(2) EPC.

### 3.3 Clarity, Article 84 EPC

#### 3.3.1 Claim 1 of auxiliary request IV recites the use of one or more defined polyols "dissolved in an aqueous solution at a concentration ranging between 5% (w/w) and 50% (w/w) to stabilize polymorphous form $\beta$ of rifaximin".

The feature "at a concentration ranging between 5% (w/w) and 50% (w/w)" was present in claim 14 as granted, albeit in the context of a differently worded process claim. In the context of claim 1 to the use of polyol(s), the expression "dissolved in an aqueous solution at a concentration ranging between 5% (w/w) and 50% (w/w)" finds no counterpart in the granted claims, and its clarity is open to scrutiny following G 3/14.



- 3.3.2 Respondent 2 considered that the concentration of claim 1 was ambiguous as it could refer to the amount of polyol(s) relative to the aqueous solution, or relative to rifaximin.

The appellant expressed the view that this concentration specified in claim 1 could only refer the amount of polyol(s) relative to rifaximin  $\beta$ .

The Board finds that claim 1 is clear and can only refer to the amount of polyol(s) relative to the aqueous solution. In this respect, the Board is not bound by the interpretations proposed by the parties. Even if both parties consider that a "concentration" relative to rifaximin is a possible interpretation (or even the sole one), the Board is not obliged to accept this interpretation as a possibility.

- 3.3.3 For the reasons already set out above (see 1.5) in relation with the analogous wording of page 5 of the application as filed, the Board considers that claim 1 uses a clear language and refers unambiguously to a concentration of the polyol relative to the aqueous solution.

The expression "dissolved in an aqueous solution at a concentration [...]", with the use of the word "concentration", normally express a concentration in the aqueous solution and are not consistent with a ratio relative to rifaximin. Since the language of claim 1 is clear in itself, it is in no need of interpretation in light of the description. The Board adds nonetheless that, for the reasons given above (see 1.5), neither the examples, nor the alleged necessity to define the ratio of polyols relative to rifaximin,

can lead to the conclusion that a definition of the concentration of polyols relative to the aqueous solution is not technically sensible.

Consequently, auxiliary request IV does not introduce any lack of clarity.

4. Remittal

Since the Board concludes that auxiliary request IV overcomes the issues of added subject-matter noted in the appealed decision, and does not introduce any non-compliance with Article 84 EPC, the question of a remittal to the opposition division arises.

Under Article 11 RPBA 2020, the Board shall not remit a case to the department whose decision was appealed for further prosecution, unless special reasons present themselves for doing so. The Board considers that such special reasons are apparent in the present case because the opposition division has not taken an appealable decision on essential outstanding issues with respect to novelty, inventive step and sufficiency of disclosure.

Accordingly, the Board considers that the case should be remitted to the opposition division for further prosecution.

**Order**

**For these reasons it is decided that:**

1. The decision under appeal is set aside.
2. The case is remitted to the opposition division for further prosecution.

The Registrar:

The Chairman:



B. Atienza Vivancos

D. Boulois

Decision electronically authenticated