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**Datasheet for the decision  
of 5 November 2019**

**Case Number:** T 0998/16 - 3.3.07  
**Application Number:** 05009311.1  
**Publication Number:** 1582204  
**IPC:** A61K9/107, A61K9/19, A61P31/10  
**Language of the proceedings:** EN

**Title of invention:**

Echinocandin pharmaceutical formulations containing micelle-forming surfactants

**Patent Proprietor:**

Eli Lilly & Company

**Opponents:**

Actavis Group PTC ehf  
Grund, Dr., Martin  
Galenicum Health S.L.

**Headword:**

Echinocandin formulations/ LILLY

**Relevant legal provisions:**

EPC Art. 100(c), 76(1), 123(2), 100(b), 111(1)

**Keyword:**

Grounds for opposition - extension of subject-matter (no) -  
insufficiency of disclosure (no)

Appeal decision - remittal to the department of first instance  
(yes)



**Beschwerdekammern**

**Boards of Appeal**

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Case Number: T 0998/16 - 3.3.07

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.07**  
**of 5 November 2019**

**Appellant:** Eli Lilly & Company  
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**Decision under appeal:**      **Decision of the Opposition Division of the  
European Patent Office posted on 24 February  
2016 revoking European patent No. 1582204  
pursuant to Article 101(3) (b) EPC.**

**Composition of the Board:**

**Chairman**                    E. Duval  
**Members:**                 A. Uselli  
                                  P. Schmitz

## Summary of Facts and Submissions

I. European patent No. 1 582 204 was granted on the basis of 11 claims. Independent claim 1 read as follows:

"1. A freeze-dried formulation comprising:

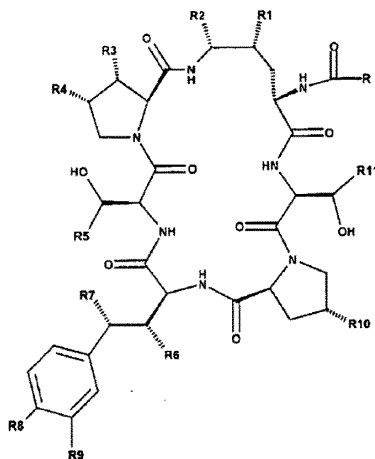
(i) an echinocandin compound, or a pharmaceutically acceptable salt thereof;

(ii) a pharmaceutically acceptable micelle-forming surfactant which is polysorbate 80, polysorbate 40 or polysorbate 20 in an amount greater than 5% by weight of the formulation; wherein the weight ratio of (i) to (ii) is from 1:1.75 to 1:25; and

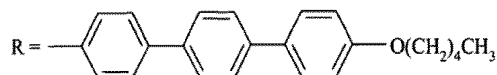
(iii) a bulking agent which is mannitol;

(iv) a buffer which is tartaric acid;

wherein said echinocandin compound is represented by the following structure:



wherein:



R1, R2, R3, R6, R7, and R10 are hydroxy;  
R4 is methyl;

R5 and R11 are methyl;  
R8 is -OH;  
R9, is -H; and  
pharmaceutically acceptable salts thereof."

II. Three oppositions were filed against the patent on the grounds that its subject-matter was not sufficiently disclosed, lacked inventive step, and extended beyond the content of the application as filed and of the earlier application. The following documents were among those cited during the first-instance proceedings:

D22: Experimental report of 24 June 2014

D24: Declaration of Dr Nathaniel Milton

D28: Experimental report of 1 April 2015

D31: Affidavit of Dr Nathaniel Milton

III. The appeal of the patent proprietor (appellant) lies against the decision of the opposition division to revoke the patent. The decision was based on the patent as granted as main request, on auxiliary requests 1 to 5, filed on 16 February 2015, and on auxiliary requests 6 and 7, filed during the oral proceedings held on 18 January 2016.

The opposition division came to, *inter alia*, the following conclusions.

- (a) The claims of the main request complied with the requirements of Articles 123(2) and 76(1) EPC. However, the description contained subject-matter extending beyond the content of the application as filed.
- (b) The process disclosed in the patent could not be successfully used to solubilise free anidulafungin.

It was therefore not possible to prepare the freeze-dried composition according to claim 1 on the basis of the information disclosed in the patent. Hence, the requirement of sufficiency of disclosure was not met. This conclusion applied to the patent as granted and to auxiliary requests 1 to 5.

(c) The claims of auxiliary requests 1 to 7 did not comply with Article 123(2) EPC.

IV. In the statement setting out the grounds of appeal submitted on 29 June 2016, the appellant maintained the patent as granted as the main request and filed 28 auxiliary requests. On the same date, it submitted the following documents:

D52: Second declaration of Dr Nathaniel Milton

D53: WO 2016/079749

D54: Declaration of Dr Carl Deering

V. In their replies to the appeal of the patent proprietor, the opponents (respondents) requested, *inter alia*, that the appeal be dismissed and that documents D52 to D54 not be admitted into the appeal proceedings.

VI. In its communication pursuant to Article 15(1) RPBA issued on 6 September 2019 the Board observed that the opposition division's conclusion that the requirement of sufficiency of disclosure was not met, was essentially based on the fact that the procedure disclosed in Method C did not enable the skilled person to prepare the composition of example 13. The Board further observed that in its opinion the skilled person seeking to produce the formulation of claim 1 would

have considered not only the teaching of Method C but also the teaching provided in other parts of the description.

VII. Oral proceedings were held on 5 November 2019. They were not attended by respondents 2 and 3, which had informed the Board to this effect.

VIII. The appellant's arguments, as far as relevant to the present decision, can be summarised as follows:

(a) Admittance of documents D52 to D54

In the experimental reports filed by respondent 3 (documents D22 and D28), it was not stated whether anidulafungin was used in free form or as a complex. This issue was clarified only during the oral proceedings before the opposition division. Therefore, the patent proprietor, could not properly address the allegations of respondent 3 during the first instance proceedings. Documents D52 to D54 were in direct response to the experiments of respondent 3. For the reasons explained above, these documents could not have been submitted earlier.

(b) Article 100(c) EPC

The subject-matter of claim 1 was based on the core disclosure on page 3 (lines 6 to 15) of the original application. The precise definition of components (i) to (iv) of the composition was based on the preferred embodiments disclosed in the original description. The combination of these preferred embodiments did not add any new information and was in conformity with the requirements of Articles 76(1) and 123(2) EPC.



(c) Sufficiency of disclosure

The decision of the opposition division was based on the results of the experiments of respondent 3 which were focused on the repetition of Method C of the patent. This approach was wrong in that it disregarded important information disclosed in other parts of the patent, in particular in the "Solubility studies". Furthermore, the attitude of a skilled person facing some problems in dissolving anidulafungin by following the procedure of Method C, would have been to modify some parameters of this method, such as temperature and pH. The appellant's experiments showed that it was possible to solubilise anidulafungin both as a complex and in free form. It was not clear why respondent 3 did not succeed in its experiments to solubilise the free form. The appellant could not accept the respondents' conclusions based on the experiments disclosed in D22 and D28.

IX. The respondents' arguments, as far as relevant to the present decision, can be summarised as follows:

(a) Admittance of documents D52 to D54

The appellant had plenty of time during the first instance proceedings to file a response to the experiments of respondent 3. Contrary to what the appellant affirmed, it had always been clear that the product used in the experiments was the free-anidulafungin because this was the product used in Method C of the patent. Hence, documents D52 to D54 should not be admitted into the appeal proceedings, since they should have been filed earlier.

(b) Article 100(c) EPC

The original application did not provide a direct and unambiguous disclosure of the combination of ingredients recited in claim 1 of the patent. The original application disclosed several options with regard to the surfactant, the bulking agent and the buffer. Thus, several selections were necessary within the original disclosure in order to arrive at the subject-matter of claim 1. Moreover, the examples did not provide a pointer towards the claimed combination of features and the vast majority of them fell outside the scope of the claims. Accordingly, claim 1 of the patent did not meet Articles 76(1) and 123(2) EPC.

(c) Sufficiency of disclosure

The experiments submitted by respondent 3 showed that Method C of the patent did not work because it was not possible to dissolve the active ingredient. The patent did not provide any instruction on how to solve this problem. Methods A and B were of no relevance because a different buffer was used, and paragraphs [0055] to [0057] did not add any relevant information on the dissolution of the active ingredients. The "Solubility studies" disclosed in the patent did not contain any detailed information, and in any case they did not relate to the preparation of the freeze-dried compositions of claim 1. Thus, in order to prepare the formulation of claim 1 the skilled person would have been obliged to modify the parameters disclosed in Method C without any clear guidance from the other parts of the description.

- X. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the

basis of the patent as granted, or on the basis of one of auxiliary requests 1 to 28, filed on 29 June 2016 with the statement setting out the grounds of appeal. The appellant further requested remittal to the opposition division in relation to the compliance of any claim request with Article 56 EPC.

- XI. The respondents requested that the appeal be dismissed. They further requested that documents D52 to D54 not be admitted into the appeal proceedings.

### **Reasons for the Decision**

1. Admittance of documents D52 to D54

- 1.1 The appellant filed documents D52 to D54 on 29 June 2016, together with its statement setting out the grounds of appeal. D52 and D54 are expert declarations containing experimental data. D53 is a patent application published after the filing date of the patent in suit disclosing, *inter alia*, a process involving the dissolution of anidulafungin.

These documents have been filed by the appellant in an attempt to demonstrate that it is possible to solubilise free anidulafungin according to the procedure disclosed in Method C of the patent, contrary to the conclusion drawn by the opposition division in point 7.9 of its decision on the basis of the experiments submitted by respondent 3 (documents D22 and D28).

- 1.2 It follows from Article 12(4) RPBA that everything presented for the first time by a party with the statement setting out the grounds of appeal is to be

taken into account by the Board unless it is concluded that it should have been submitted in the first instance proceedings.

The respondents observe that experimental reports D22 and D28 were submitted by respondent 3 at an early stage of the opposition proceedings. Thus, in their view, the appellant should have already filed its response to these experiments during the first instance proceedings.

In this regard the Board notes that the appellant did respond to the experiments of respondent 3 during the first instance proceedings. In particular, in the declaration and in the affidavit of Dr Nathaniel Milton (D24 and D31), the appellant confirmed that it was possible to prepare a freeze-dried product according to claim 1 by following the procedure described in Method C of the patent (point 4 of D31). It further observed that very little information was provided in the experimental reports of respondent 3 regarding, for instance, the nature of the materials used, their quantities and purity (points 24 of D24 and D31). This was a legitimate response from the side of the appellant. The Board sees no reasons to consider that the appellant was under an obligation to respond to experimental reports D22 and D28 by filing its own experiments.

- 1.3 At the end of the oral proceedings, the opposition division concluded that the requirement of sufficiency of disclosure was not met. It is apparent from point 7.9 of the decision that an important aspect of the discussion held during the oral proceedings concerned the question of whether, in Method C of the patent, anidulafungin was used in free form or as a complex.

This issue was not addressed before the oral proceedings.

The experiments described in D52 and D54 concern procedures for the solubilisation of anidulafungin in free form or as a complex with fructose. They basically show that free anidulafungin can be solubilised in an aqueous solution containing polysorbate 80 (D52) and that Method C can also be used when starting from free anidulafungin (D54). These results confirm the position held by the appellant during the first instance proceedings. Hence, the respondents are not faced with a fresh case.

- 1.4 In view of the above, the Board decides to admit documents D52 to D54 into the appeal proceedings.

#### MAIN REQUEST - PATENT AS GRANTED

2. Article 100(c) EPC in combination with Articles 123(2) and 76(1) EPC

- 2.1 In paragraph 5.4 of its decision, the opposition division identifies, in the embodiment disclosed on page 3, lines 6 to 14 of the description of the parent application (identical to the description of the application as filed), the starting "core" for the definition of the formulation of claim 1 of the patent.

This embodiment relates to a freeze dried composition comprising: (i) an echinocandin compound, (ii) a micelle forming surfactant, and (iii) a bulking agent. This passage further indicates that the amount of the surfactant is greater than 5% by weight and that the ratio of echinocandin to surfactant is from 1:1.75 to 1:25.

Claim 1 as granted differs from the disclosure on page 3 in specifying that:

a) the echinocandin compound is the specific molecule depicted in claim 1 (anidulafungin),

b) the surfactant is polysorbate 80, 40 or 20,

c) the bulking agent is mannitol, and

d) the composition further contains a buffer which is tartaric acid.

2.1.1 Feature a), the compound anidulafungin, is disclosed for instance on page 21. It is the compound prepared on page 25 and is the active ingredient of the 27 formulations described in Table 1. The parent application (and the application as originally filed) do not disclose any other specific molecule.

2.1.2 The selection of polysorbate 80, 40 or 20 as the surfactant (feature b) above) is supported by the disclosure on page 14, line 16. This passage indicates that several other substances can be used as surfactant. However, the list of preferred surfactants is quite short and includes, in addition to the polysorbates 80, 40 or 20, only one further item, namely poloxyethylene hydroxystearates, which is not included in any of the formulations specifically disclosed in the patent. In contrast, the polysorbates are present in the vast majority of these formulations.

2.1.3 Mannitol (feature c) above) is one of the four preferred bulking agents disclosed on page 17, lines 13 and 14. In the formulations disclosed in the

experimental part of the description, when a bulking agent is present this is always mannitol (see Tables 1 to 4).

2.1.4 Feature d), i.e. the use of tartaric acid as buffer is disclosed on page 16, line 26. In the same sentence it is stated that for freeze-dried formulations, the preferred buffer is tartaric acid.

2.2 The analysis made in point 2.1 above, shows that the selection of features a) to d) reflects the content of the preferred embodiments and of the examples of the original description. In other words, the skilled person reading the parent application would find, in the disclosure of the preferred embodiments and of the examples, a clear pointer towards the combination of ingredients recited in claim 1.

Thus, the subject-matter of claim 1 fulfils the requirements of Articles 76(1) and 123(2) EPC.

2.3 In point 6 of its decision, the opposition division considered that the insertion of the word "preferably" into paragraph [0054] of the description contravened the requirements of Article 123(2) EPC. In this regard the decision merely indicates that the contested word "was not present in the description as originally filed".

In its communication of 6 September 2019, the Board expressed the view that the insertion of the term "preferably" did not result in added subject-matter. This opinion was not disputed by the respondents. The Board concludes, therefore, that the insertion of the word "preferably" into paragraph [0054] of the

description does not offend the requirements of Articles 123(2) and 76(1) EPC.

3. Sufficiency of disclosure

3.1 During the proceedings before the opposition division respondent 3 submitted experimental reports D22 and D28. Each of these reports describes an attempt to produce a freeze-dried formulation according to claim 1 by using Method C disclosed in paragraph [0089] of the patent. The attempts failed because the first step of the procedure was unsuccessful, namely the dissolution of free-anidulafungin in an aqueous solution of polysorbate 80. On the basis of these experiments, the opposition division came to the conclusion that the procedure disclosed in Method C did not enable the skilled person to prepare the composition of example 13, i.e. a freeze-dried formulation included in claim 1. Accordingly, it decided that the requirement of sufficiency of disclosure was not met.

3.2 The results of the experiments carried out by the appellant (documents D52 and D54) diverge from those of respondent 3. In document D54 the first step of Method C has been replicated using free-anidulafungin or the complex of anidulafungin with fructose. In both cases the active ingredient is completely dissolved in the polysorbate 80 solutions.

Document D52 describes some tests carried out by the appellant in order to compare the solubility of the free-anidulafungin and of fructose complex. Table 1 of D52 shows that both substances can be dissolved at 25°C in several solvents including solutions of polysorbate 80. The data show minor differences in terms of solubility.



3.3 The Board is unable to identify any evident deficiency in one or more of the experimental reports that could explain the different results. Nor have the parties presented conclusive arguments in this regard. In the decision under appeal, the opposition division came to the conclusion that respondent 3 did not succeed in repeating the procedure of Method C because it used free-anidulafungin as the starting material. The inventors used the fructose complex instead, although this was not mentioned in the description of Method C.

This explanation is contradicted by the experiments filed by the appellant, which indicate that Method C can be carried out using either free-anidulafungin or its fructose complex.

3.4 In any case, the Board considers that even accepting that the protocol of the first step of Method C may not always result in dissolving the free-anidulafungin, this alone does not justify the conclusion that the requirement of sufficiency of disclosure is not met.

In the Board's view, the normal attitude of any researcher confronted with a problem when repeating the example of a patent would be to make some attempt to overcome this problem. This could be done for instance by looking for any relevant information in other parts of the patent or by using their own general knowledge. In this regard it is noted that the patent discloses in paragraph [0091] solubility studies which show that anidulafungin can be dissolved in solutions of polysorbate 80 at room temperature. In the Board's opinion, the skilled person encountering problems in dissolving a substance would not ignore a test concerning the solubility of this substance. These

solubility studies could suggest modifying the procedure of Method C, carried out at a temperature between 5°C and 15°C, by increasing the temperature. Indeed D52 shows that it is possible to solubilise anidulafungin (in free or complexed form) at 25°C in solutions of polysorbate 80. The patent also discloses in paragraphs [0087] and [0088] two further methods for preparing the pharmaceutical freeze-dried formulations containing anidulafungin. These methods do not concern the preparation of the formulation of claim 1 because a different buffer is used. Nevertheless, they show that a freeze-dried composition containing anidulafungin can also be prepared by methods that are slightly different from Method C, for instance because the pH is lower.

Furthermore, as observed by the appellant, in Method C specific amounts of ingredients are used. Also in this respect, the skilled person would see the possibility of bringing some changes that could potentially facilitate the dissolution of the active ingredient, such as a modification in the amount of polysorbate 80 and/or water.

- 3.5 The experiments disclosed in D22 and D28 do not go beyond the literal repetition of the procedure of Method C. In the Board's view, the skilled person seeking to reproduce an experimental procedure is willing to succeed in this objective. Accordingly, they are prepared to make some attempts to adjust said procedure, if this is necessary to overcome some difficulties. As explained above, in doing so they can take into account any relevant information disclosed in other parts of the document describing the procedure or they can refer to their common knowledge. A conclusion of insufficiency of disclosure is justified only if an undue burden is required to overcome these

difficulties. Hence, in the present case, this conclusion cannot be drawn on the basis of the experiments disclosed in D22 and D28, since no attempt whatsoever has been made to adjust the procedure of Method C in order to solubilise the active ingredient.

3.6 Therefore, the Board concludes that the patent meets the requirements of sufficiency of disclosure.

4. Remittal

4.1 The primary function of an appeal is to consider whether the decision issued by the first-instance department is correct. Hence, a case is normally remitted if essential questions regarding the patentability of the claimed subject-matter have not yet been examined and decided by the department of first instance.

In particular, remittal is considered by the boards in cases where a first-instance department issues a decision against a party solely upon some issues which are decisive for the case, and leaves other essential issues outstanding. If, following appeal proceedings, the appeal on the particular issues addressed is allowed, the case is normally remitted to the first-instance department for consideration of the undecided issues (Article 111(1) EPC).

4.2 The observations above apply in full to the present case, since the opposition division considered only the grounds of opposition pursuant to Article 100(b) and 100(c) EPC, without deciding on any other issue.

Under these circumstances, the Board considers it appropriate to remit the case to the opposition division for further prosecution (Article 111(1) EPC).

## 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

E. Duval

Decision electronically authenticated