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**Datasheet for the decision  
of 11 September 2018**

**Case Number:** T 0059/16 - 3.3.07

**Application Number:** 06816283.3

**Publication Number:** 1931306

**IPC:** A61K9/00, A61K47/10, A61K47/26,  
A61K47/32, A61K38/48

**Language of the proceedings:** EN

**Title of invention:**  
NON-PROTEIN STABILIZED CLOSTRIDIAL TOXIN PHARMACEUTICAL  
COMPOSITIONS

**Patent Proprietor:**  
ALLERGAN, INC.

**Opponent:**  
IPSEN PHARMA S.A.S.

**Headword:**  
Clostridial toxin/ ALLERGAN

**Relevant legal provisions:**  
EPC Art. 100(c), 123(2), 100(b), 111(1)  
RPBA Art. 13(1), 13(3)

**Keyword:**

Grounds for opposition - added subject-matter (yes)  
Late-filed auxiliary request - admitted (yes)  
Auxiliary request - added subject-matter (no)  
Claims - clarity in opposition proceedings  
Sufficiency of disclosure - (yes)  
Appeal decision - remittal to the department of first instance  
(yes)

**Decisions cited:**

G 0003/14



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Case Number: T 0059/16 - 3.3.07

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.07**  
**of 11 September 2018**

**Appellant:** ALLERGAN, INC.  
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**Decision under appeal:** **Decision of the Opposition Division of the  
European Patent Office posted on 23 October 2015  
revoking European patent No. 1931306 pursuant to  
Article 101(3) (b) EPC.**

**Composition of the Board:**

**Chairwoman** P. Schmitz  
**Members:** A. Usuelli  
E. Duval

## Summary of Facts and Submissions

- I. The appeal by the patent proprietor (hereinafter: the appellant) lies against the decision of the opposition division posted on 23 October 2015 revoking European patent No. 1 931 306.

The decision was based on the patent as granted as main request, and on 30 auxiliary requests filed on 7 September 2015 (auxiliary requests 1A-8A, 1B-8B and 2-8), on 6 October 2015 (auxiliary requests 9, 9A, 9B, 10, 10A, 10B) and during the oral proceedings held on 7 November 2015 (auxiliary request 11).

Claim 1 of the patent read as follows:

"1. A lyophilized or vacuum dried pharmaceutical composition comprising:  
(a) a botulinum toxin, wherein the botulinum toxin is not stabilized by a protein excipient,  
(b) a polyvinylpyrrolidone, and;  
(c) a disaccharide,  
wherein the potency of the botulinum toxin after reconstitution is at least 40% of the theoretical maximum potency of the botulinum toxin prior to lyophilization."

- II. In the appealed decision the opposition division held that the features "after reconstitution" and "prior to lyophilisation" introduced in claim 1 of the patent were not disclosed in the original application in the context of a general method but they were part of a specific disclosure relating to example 2. The introduction of these features in claim 1 represented an intermediate generalisation. Accordingly, claim 1 did not comply with Article 123(2) EPC.

The auxiliary requests filed on 7 September 2015 and on 6 October 2015 were not admitted into the proceedings.

Claim 1 of auxiliary request 11 specified the conditions of storage and reconstitution of the lyophilized botulinum toxin. The opposition division held that this request complied with Articles 123(2) and (3) EPC. However, it considered that there were no examples in the description that could demonstrate that the compositions covered by auxiliary request 11 had the potency defined in the claims. Accordingly, it concluded that auxiliary request 11 did not comply with the requirement of sufficiency of disclosure.

III. With the statement setting out the grounds of appeal filed on 2 March 2016 the appellant defended the patent as granted as its main request and filed thirty auxiliary requests. By letter of 14 August 2014 it submitted 11 new auxiliary requests, partly replacing the requests filed with the grounds of appeal.

The relevant requests in the context of the present decision are the main request (patent as granted) and auxiliary request 1 filed on 14 August 2018.

Claim 1 of auxiliary request 1 differed from claim 1 of the patent in the introduction of the following feature at the end of the claim:

"...wherein the theoretical maximum potency of the botulinum toxin prior to lyophilization is determined prior to the incorporation of the botulinum toxin into the pharmaceutical composition."

IV. In the reply to the appeal of the patent proprietor submitted on 5 July 2016 and in a further letter filed

on 14 August 2018 the opponent (hereinafter: the respondent) expressed the view that the main request did not comply with the requirement of Article 123(2) EPC and requested the Board not to admit the auxiliary requests into the appeal proceedings.

V. Oral proceedings before the Board of appeal took place on 11 September 2018.

VI. The appellant's arguments, as far as they are relevant for the present decision can be summarised as follows:

(a) Main request

Claim 1 was based upon original claim 13. The features "after reconstitution" and "prior to lyophilization" had the scope of clarifying how the theoretical maximum potency was to be calculated and were implicit in original claim 13. It was clear to the skilled person that the potency was to be determined after the step of reconstitution since it was not possible to determine the potency of a powder. Furthermore, the skilled person knew that mixing the botulinum toxin with excipients had the effect of reducing the potency. This was also clear from the original description. Thus, it was evident to the skilled person that the theoretical maximum potency prior to lyophilization was the potency of the pure botulinum toxin, i.e. before its addition into the formulation. This was in line with the teaching of example 2.

(b) Auxiliary request 1

Auxiliary request 1 was filed in response to the new attack under Article 123(2) EPC raised by the respondent with the reply to the appeal. It did not

raise any new complex issues and was therefore admissible. Claim 1 of auxiliary request 1 specified the meaning of the feature "prior to lyophilization" by incorporating the definition disclosed on page 25 of the original application. Hence, auxiliary request 1 met the requirements of Article 123(2) EPC. Furthermore, the amendments introduced in this request did not raise any clarity issue.

Table 4 of the patent disclosed several botulinum compositions having the required level of potency and could be used by the skilled person as guidance for preparing other compositions included in claim 1. Hence, auxiliary request 1 met the requirement of sufficiency of disclosure.

VII. The respondent's arguments, as far as they are relevant for the present decision, can be summarised as follows

(a) Main request

Original claim 13 did not include the features "after reconstitution" and "prior to lyophilization". These features could not be extracted from the disclosure of page 36 since this page related to a specific example and described compositions that did not necessarily have the same potency as the compositions of claim 1. Nor could the features "after reconstitution" and "prior to lyophilization" be derived from the first paragraph of page 25 since this passage did not refer to a maximum potency. Furthermore, according to page 36 of the original application the expression "prior to lyophilization" indicated that the initial potency was measured before incorporation of the botulinum into the formulation. However, this information was not included in claim 1 as granted. Moreover, claim 1 did not

indicate whether the reconstitution was made right after the lyophilization or after a period of storage. In this respect the original application disclosed different options. Thus, claim 1 of the main request defined a new invention that was not disclosed in the original application.

(b) Auxiliary request 1

Auxiliary request 1 was filed only one month before the oral proceedings. This late filing was not justified. Moreover, auxiliary request 1 raised new issues and did not overcome the outstanding objections. Hence, this request should not be admitted into the appeal proceedings.

The original application disclosed nowhere the subject-matter of claim 1 of auxiliary request 1. The feature added at the end of the claim was disclosed in original page 25 in a different context. Indeed this passage did not relate to compositions having the same potency as the compositions of claim 1. Hence, claim 1 did not meet the requirements of Article 123(2) EPC. Furthermore, the subject-matter of claim 1 lacked clarity. For instance, the claim did not define precisely when the potency measurements and the step of reconstitution were to be made.

The requirement of sufficiency of disclosure was not met either. The patent did not provide any information as to the amount of excipients. Table 3 of the description showed that some botulinum compositions did not have a potency of at least 40% of the theoretical maximum potency despite the fact of containing polyvinylpyrrolidone and a disaccharide as required by claim 1. Thus, the skilled person had no guidance on



how to provide botulinum compositions having a potency within the range of claim 1.

VIII. The appellant requested that the decision under appeal be set aside and that the opposition be rejected, (i.e. that the patent be maintained as granted) or, alternatively, that the patent be maintained according to one of auxiliary requests 1 to 11, whereby auxiliary requests 1 to 10 additionally included an "A" and a "B" version and wherein auxiliary request 1 and the "B" requests were filed on 14 August 2018 and the remaining auxiliary requests were filed with the statement setting out the grounds of appeal. Furthermore, the appellant requested to remit the case, in the event that any issue that had not been addressed in the decision under appeal was to be resolved.

IX. The respondent requested that the appeal be dismissed. Moreover, the respondent requested that none of the auxiliary requests be admitted into the appeal proceedings.

## **Reasons for the Decision**

### Main request - patent as granted

1. Articles 100(c) and 123(2) EPC

1.1 Claim 1 specifies that "the potency of the botulinum toxin after reconstitution is at least 40% of the theoretical maximum potency of the botulinum toxin prior to lyophilization..." (emphasis added).

Original claim 13, from which the subject-matter of claim 1 of the patent derives, recites that "the

potency of the botulinum toxin is at least 40% of the theoretical maximum potency of the botulinum toxin".

- 1.2 The appellant submits that the introduction of the features "after reconstitution" and "prior to lyophilization", which are not present in original claim 13, merely clarifies how the percent potency is to be calculated. This however does not add any new information since it was already clear in the context of the original application that the potencies "after reconstitution" and "prior to lyophilization" are the potencies to be used to determine the percent potency (relative potency). Example 2 merely confirms the definition of relative potency used in claim 1.
- 1.3 The Board notes that in example 2 (page 36, lines 25 to 28 of the original application), it is explained that the potency of the botulinum toxin after reconstitution is expressed as a percent of the potency of the botulinum toxin before lyophilisation of the formulation. However, this passage is to be considered in the whole context of example 2 and in particular in relation with the 2nd paragraph on page 36, line 5 to 18. This paragraph explains that the formulations of examples 2 are prepared by adding the excipients to sterile water to form a solution and then adding 100 to 200 units of botulinum to the solution. It further specifies (lines 15 to 18) that "[t]he potency prior to lyophilization of the botulinum toxin used was determined by the mouse LD50 assay prior to the addition of the botulinum toxin to the solution..." (emphasis added).

Thus, this passage clearly indicates that the "potency of the botulinum toxin before lyophilisation" referred to on page 36, line 27 is actually the potency of the

botulinum before its addition to the other components of the solution. In other words, the "reference potency", (i.e. the potency used as "denominator" in the calculation of the percentage) is not the potency of the pharmaceutical composition measured before its lyophilisation. It is rather the initial potency of botulinum, measured before its incorporation into the pharmaceutical composition. This interpretation is in line with the passage of page 25 (lines 9 to 11) of the original description which indicates that upon reconstitution of a lyophilised or vacuum dried botulinum toxin the toxin present in the reconstituted solution has "greater than about 20% and up to about 100% of the potency or toxicity that the biologically active botulinum toxin had prior to being incorporated into the pharmaceutical composition" (emphasis added).

1.4 In the Board's view, in the context of claim 1 as granted the feature "prior to lyophilization" loses its original meaning, which can be derived from example 2 and from the general description. This is because some clarifications provided in the original description as to the meaning of the expression "prior to lyophilization" have not been incorporated in the claim. It follows that claim 1 as granted covers the situation in which the potency prior to lyophilization is determined just before the lyophilization when the botulinum toxin has already been incorporated into the pharmaceutical composition. The Board takes the view that this is actually the natural reading of claim 1. Accordingly, claim 1 provides a definition of the concept of relative potency which is different from the definition derivable from the application as filed.

1.5 In the appellant's view, the skilled person reading claim 1 as granted would understand that the potency

prior to lyophilization is the potency measured prior to incorporation of the botulinum toxin into the pharmaceutical composition. In its opinion it would be clear to him that the potency of the toxin may decrease during its incorporation into the pharmaceutical composition. Since claim 1 refers to the "theoretical maximum potency" prior to lyophilization this could only be read as the potency of the pure toxin, i.e. before its incorporation into the pharmaceutical composition.

In this regard the Board observes that nowhere in the original application the expression "theoretical maximum potency" is used to identify the potency of the pure botulinum toxin. The passages of page 25 (lines 9 to 11) and 36 (lines 15 to 18) which clarify that the potency prior to lyophilization is the potency of the pure botulin (see point 1.3 above) do not define this potency as the "theoretical maximum potency". Hence, in the Board's view the appellant's argument is not convincing.

- 1.6 In the light of the above considerations the Board concludes that claim 1 contains subject-matter which extends beyond the content of the application as filed. Consequently, the ground of opposition under Article 100(c) EPC prejudices the maintenance of the opposed patent.

#### Auxiliary request 1

#### 2. Admissibility

- 2.1 Auxiliary request 1 was filed by the appellant on 14 August 2018.

The amendments introduced in claim 1 of this request address (see point III above) the issue under Article 123(2) EPC concerning the feature "prior to lyophilization" discussed above in relation to the patent as granted. The Board agrees with the appellant that this issue was raised for the first time by the respondent with the reply to the appeal. The filing of auxiliary request 1 represents therefore a legitimate attempt from the side of the appellant to react to the new objection. Moreover, the Board considers that the amendment introduced in the claim does not increase its complexity. Accordingly, it should not be difficult for the respondent to deal with the new request.

2.2 Hence, the Board decides to admit auxiliary request 1 into the appeal proceedings (Article 13(1) and (3) RPBA).

3. Article 123(2) EPC

3.1 Like claim 1 of the patent, claim 1 of auxiliary request 1 derives from original claim 13. However, in comparison to the granted patent, auxiliary request 1 further specifies that the potency of the botulinum toxin prior to lyophilization is determined prior to its incorporation into the pharmaceutical composition.

This amendment finds its basis in example 2 on page 36, lines 15 to 19 and page 25, lines 10 and 11, of the original description. By effect of this amendment, the meaning of the feature "prior to lyophilization" is now consistent with its meaning in the original application.

In other words, the feature "the potency of the botulinum toxin is at least 40% of the theoretical

maximum potency of the botulinum toxin", included in original claim 13, has been amended in claim 1 of auxiliary request 1 to specify that the potency after reconstitution is expressed as a percent of the potency of the botulinum toxin prior to its incorporation into the pharmaceutical composition. This amendment reflects the meaning of the concept of percent potency as disclosed in the original description in particular in example 2.

Thus, the objection leading to the rejection of the main request is overcome.

- 3.2 The respondent argues that extracting some features from a specific example relating to specific formulations and incorporating them in the context of a claim concerning a broad family of formulations would offend against Article 123(2) EPC.

However, as explained above, the features introduced in claim 1 indicate how the percent potency is to be calculated. These features cannot be regarded as inextricably linked with the other features of example 2 such as the specific composition of the formulations tested. It would be meaningless to calculate the percent potency in different ways depending on the composition of the formulation tested.

Also the fact that some of the formulations tested in example 2 do not present a potency of at least 40%, as required by claim 1 of auxiliary request 1, is no valid reason to exclude the disclosure of this example as a basis for the amendments introduced in claim 1. Indeed, the way of calculating the percent potency is independent on the actual value of potency of the specific formulations tested.

- 3.3 The respondent further observes that claim 1 does not specify that the reconstitution is made right after the lyophilization, as disclosed on page 36, lines 33 of the original application.

In this regard it is noted that the passage of page 36, lines 25 to 27 of the original application, which is the passage explaining that the percent potency is the potency of the botulinum toxin after reconstitution expressed as a percent of the potency of the botulinum toxin before lyophilisation of the formulation, does not require that the reconstitution be made right after the lyophilization. Thus, the omission of the expression "right after" does not result in addition of subject-matter.

- 3.4 Accordingly, claim 1 of auxiliary request 1 meets the requirements of Article 123(2) EPC.

#### 4. Clarity

- 4.1 The respondent observes that claim 1 does not specify the precise conditions under which the measurements of potency are carried out. In its opinion this results in a lack of clarity of the claim.

- 4.2 The Board notes that information concerning the conditions for measuring the botulinum potency was not included in claim 1 of the patent either. Hence, the potential issues of clarity referred to by the respondent do not arise from amendments made after the granting of the patent. Therefore, in application of the principles affirmed in decision G 3/14 (OJ EPO 2015, A102), these objections as to lack of clarity

cannot be examined in the present opposition appeal proceedings.

4.3 As explained above, the amendments introduced in claim 1 of auxiliary request 1 specify how the percent potency is calculated. In the Board's view, no clarity issue arises out of these amendments.

5. Sufficiency of disclosure

5.1 The respondent's central argument with regard to the requirement of sufficiency of disclosure is that the skilled person has no guidance on how to provide botulinum compositions having a potency within the range of claim 1. In this regard it refers to Table 3 of the patent which shows that some botulinum compositions do not have a potency of at least 40% despite the fact of containing polyvinylpyrrolidone and a disaccharide as required by claim 1.

5.2 The Board notes that the description provides information as to the procedure for preparing the lyophilised formulations (see paragraphs [0106] and [0107]).

As correctly pointed out by the respondent, Table 3 of the patent discloses some botulinum formulations that do not present the minimum level of potency required by claim 1. However, Table 4 of the patent exemplifies at least seventeen botulinum toxin formulations containing polyvinylpyrrolidone and a disaccharide having a relative potency above 40% (see examples 1 to 17 in Table 4 and Table 6). In the Board's view, the skilled person could derive from the data on Table 4 relevant indications as to the suitable amounts of active ingredient and excipients. In this regard it is also



noted that the ingredients (a) to (c) of the formulations of claim 1 are narrowly defined and the preparation of the lyophilized product is based on standard procedures (see paragraph [0106]). Thus, even though some experimentation may be required to find the suitable proportions of ingredients there is no evidence that this would amount to an undue burden.

For the above reasons the Board concludes that the subject-matter of auxiliary request 1 meets the requirement of sufficiency of disclosure.

## 6. Remittal

6.1 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.

6.2 These observations fully apply to the present case. The decision of the opposition division is limited to the assessment of the requirements of Article 123(2) EPC and sufficiency of disclosure whereas the requirements of novelty and inventive step have not been dealt with.

Under these circumstances the Board considers it appropriate to remit the case to the opposition division for further prosecution (Article 111(1) EPC). This conclusion was agreed upon by the parties during the oral proceedings.

## 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 Chairwoman:



S. Lichtenvort

P. Schmitz

Decision electronically authenticated