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**Datasheet for the decision
of 26 October 2017**

Case Number: T 0246/16 - 3.3.07

Application Number: 10010686.3

Publication Number: 2269631

IPC: A61K38/48, A61K47/30,
A61K47/26, A61K9/00

Language of the proceedings: EN

Title of invention:

Pharmaceutical compositions comprising botulinum neurotoxin
for use in medicine and cosmetics

Patent Proprietor:

Ipsen Biopharm Limited

Opponent:

ALLERGAN, INC.

Headword:

Pharmaceutical compositions comprising botulinum neurotoxin
for use in medicine and cosmetics/Ipsen Biopharm Limited

Relevant legal provisions:

RPBA Art. 12(2), 13(3)
EPC Art. 100(b), 100(c), 56

Keyword:

Admission of new evidence - No
Admission of auxiliary request - Yes
Amendments - Yes
Inventive step - Yes

Decisions cited:

Catchword:



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Case Number: T 0246/16 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 26 October 2017

Appellant: ALLERGAN, INC.
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Decision under appeal: **Interlocutory decision of the Opposition**
Division of the European Patent Office posted on
1 December 2015 concerning maintenance of the
European Patent No. 2269631 in amended form.

Composition of the Board:

Chairman J. Riolo
Members: D. Boulois
P. Schmitz

Summary of Facts and Submissions

- I. European patent No. 2 269 631 was granted on the basis of a set of 11 claims.

Independent claim 1 as granted read as follows:

"1. A solid or liquid pharmaceutical composition consisting of:

- a) botulinum neurotoxin complex (type A, B, C, D, E, F or G) or high purity botulinum neurotoxin (type A, B, C, D, E, F, or G), and
 - b) a non-ionic surfactant as a stabilizing agent,
 - c) sodium chloride,
 - d) a buffer to maintain pH between 5.5 to 7.5,
 - e) a disaccharide,
 - f) and optionally water
- for use in therapy."

- II. An opposition was filed under Article 100 (a), (b) and (c) EPC on the grounds that its subject-matter lacked novelty and inventive step, the patent was not sufficiently disclosed, and its subject-matter extended beyond the content of the application as filed.

- III. The appeal by the opponent (hereinafter appellant) lies from the decision of the opposition division to maintain the patent in amended form. The decision was based on 2 sets of claims filed with letter of 17 September 2015 as main request and filed during the oral proceedings of 20 December 2015 as auxiliary request 1.

The subject-matter of claim 1 of auxiliary request 1 was identical to the subject-matter of claim 1 of the main request.

- IV. The documents cited during the opposition proceedings included the following:
- D1: Statement by Dr Richard submitted on March 13, 2011 in the US prosecution of the US counterpart of the Ipsen application
 - D2: WO2001/058472
 - D3: US 2003/118598
 - D4: Chi et al., Pharm. Res. 20(9), Sept. 2003
 - D5: Notice of opposition against EP 1 391 306 B1 filed by Ipsen Pharma S.A.S. April 29, 2014
 - D6: WO01/37656
 - D7: Österberg et al., Pharm. Res.14(7), p. 892-898, Jul. 1997
 - D8: Brin, Archives of Ophthalmology 121(11), p. 1661-1662, 2003

- V. According to the decision under appeal, the subject-matter of dependent claim 8 of the main request did not meet the requirements of Article 76(1) EPC.

The opposition division considered that auxiliary request 1 complied with Article 76(1) EPC, in view of the deletion of dependent claim 8.

The subject-matter of claim 1 of auxiliary request 1 was considered to be sufficiently disclosed in view of the functional limitation of the surfactant as being suitable for stabilization of the composition. This meant that any concentration of the surfactant which did not allow a stabilization of the claimed composition was excluded, this stabilisation effect being obtained at a concentration around or above the CMC, which could be determined by the skilled person.

As regards inventive step, document D2 was considered as closest prior art. It disclosed in example 5 a composition comprising all features of claim 1 except the presence of a non-ionic surfactant and of a disaccharide, and the further presence of hetastarch, which was excluded by the wording "consisting of" present in claim 1. There was no improved technical effect based on this difference, and the technical problem was the provision of an alternative composition for stabilizing botulinum toxin, or the provision of an alternative albumin-free botulinum toxin composition. The solution was not considered obvious.

VI. The opponent (hereafter called appellant) filed an appeal against said decision. With the statement setting out the grounds of appeal the appellant submitted a new item of evidence:
D15: Abstract of Eur. J. of Pharm. Sci., 2002, March, 15(2), 115-33.

VII. With a letter dated 29 August 2016, the patent proprietor (hereafter the respondent) filed a main request corresponding to the auxiliary request 1 considered to be allowable by the opposition division and auxiliary requests 1A, 1B, 2A, 2B, 3A, 3B, 4A, 4B, 5A, 5B, 6A and 6B.

The subject-matter of independent claim 1 and of the new independent claim 2 of auxiliary request 1A read as follows, difference(s) compared with claim 1 of auxiliary request 1 as considered to be allowable by the opposition division shown in bold:

"1. A ~~solid or~~ liquid pharmaceutical composition consisting of:

a) botulinum neurotoxin complex (type A, B, C, D, E, F or G) or high purity botulinum neurotoxin (type A, B, C, D, E, F, or G), and
b) a non-ionic surfactant as a stabilizing agent,
c) sodium chloride,
d) a buffer to maintain pH between 5.5 to 7.5,
e) a disaccharide,
f) and **optionally** water
for use in therapy."

"2. A solid ~~or liquid~~ pharmaceutical composition consisting of:

a) botulinum neurotoxin complex (type A, B, C, D, E, F or G) or high purity botulinum neurotoxin (type A, B, C, D, E, F, or G), and
b) a non-ionic surfactant as a stabilizing agent,
c) sodium chloride,
d) a buffer to maintain pH between 5.5 to 7.5,
e) a disaccharide,
~~f) and optionally water~~
for use in therapy."

VIII. With a letter dated 13 January 2017, the appellant requested that all auxiliary requests filed by the respondent not be admitted into the proceedings, and submitted new evidence:

D16: Annexes I-IV of marketing authorization of Botox

D17: Wikipedia extract for "Saline (medicine)".

IX. With a letter dated 17 March 2017, the respondent requested that D16 and D17 not be admitted into the proceedings and submitted as new evidence the complete serial article corresponding to D15:

D18: Eur. J. of Pharm. Sci., 2002, March, 15(2), 115-33

X. A communication from the Board dated 1 August 2017 was sent to the parties. In this it was stated in particular that the main request did not meet the requirements of Article 76(1) EPC. However the claimed invention appeared to be sufficiently disclosed, and the main request met the requirements of Article 56 EPC.

XI. With a letter dated 26 September 2017, the appellant filed new documents:

D19: US 2003/0224020

D20: Wikipedia page on Surfactants

D21: Chapter 23 of Interfacial Electrochemistry, Theory, Experiment, and Applications

D22: Handbook of Nonmedical Applications of Liposomes, Band 3

XII. Oral proceedings took place on 26 October 2017. During the oral proceedings the appellant withdrew the main request.

XIII. The arguments of the appellant may be summarised as follows:

Documents D19-D22 should be admitted into the proceedings, since they are prima facie highly relevant. D19 was cited in a parallel case, belonged to the same technical field, and could be seen as the closest prior art. This document was cited in a parallel case, and could not be cited earlier, since the appellant was not aware that a surfactant was used in the liposome compositions of D19.

All of the twelve Auxiliary Requests now filed by the patentee were new, and as such could have been filed in the first instance. As such, the Board had a discretion

under 12(4) RPBA to find all of these requests inadmissible.

Auxiliary request 1A did not meet the requirements of Article 76(1) and 123(2) EPC in view of the term "consisting of" and of the combination of features of claim 1.

As regards the term "consisting of" this term was introduced in claims 1, 2 and 10 of auxiliary request 1A to replace the term "comprising". Such an amendment was only allowable if there is "a direct and unambiguous implicit disclosure in the application as filed". It was crystal-clear from page 4 of the parent application as filed that there was a difference between "comprising", "consisting essentially of" and "consisting of", and that a disclosure of one of the compositions disclosed with said term "consisting of", "consisting essentially of" and "comprising" did not provide a basis for the others. Moreover, the selection of the term "consisting of" eliminated from the teaching some part of the original application. Finally, the examples of the parent application as filed did not consist of the components specified in claim 1 of the auxiliary request, and therefore did not provide basis for this amendment either.

The liquid pharmaceutical compositions in example 1 of the applications as filed had indeed also to include an unspecified solvent, in order for the lyophilization process described to be carried out. Examples 2 and 3 also required the presence of an unspecified solvent. The examples therefore could not be said to "consist" of the components specified in claim 1 of auxiliary request 1A, even when "water" is optionally present in the claimed composition.

To arrive at claim 1 of auxiliary request 1A from the parent application as filed, it was necessary to combine the following groups:

- i. claims 1, 3, 4, and 6,
- ii. restriction of the surfactant to a non-ionic surfactant from page 6, line 4,
- iii. optional inclusion of water from page 4, line 33,
- iv. the term "consisting of",
- v. the restriction of the subject-matter claimed to use in therapy. This combination was not disclosed in the parent application as filed as the skilled person had to make multiple selections.

The claimed invention was also not sufficiently disclosed. The concentration of the surfactant was not given in claims 1 or 2 of auxiliary request 1A, while this was seen as an essential feature. At concentrations lower than the CMC, not all of the interfaces will be saturated with surfactant, with the result that the botulinum toxin will begin to lose its three dimensional active conformation, and denature. This variant would therefore be incapable of stabilizing botulinum toxin composition. As the claims of Auxiliary Request 1A were not limited to a concentration of surfactant above the CMC, the opposed patent was invalid on grounds of insufficiency of disclosure.

As regards the claimed feature "a buffer to maintain pH between 5.5 to 7.0", the opposed patent is insufficiently disclosed because the skilled person is not given any guidance about how the pH of solid compositions is to be measured. The patent failed to provide any indication of a test method for determining the pH of the claimed solid pharmaceutical composition. Moreover, there were two different interpretations of the term buffer to maintain pH between 5.5 to 7.0. The

first is that the claimed composition had to comprise a buffer which is, if added in the correct amounts, capable of maintaining a pH in the range specified in the claim and the second interpretation was that the buffer must actually maintain the pH between 5.5 and 7.0 in the claimed pharmaceutical composition. Moreover, there was no teaching as to the nature of solvent to be used for the reconstitution of the solid composition and the pH depended in any case on the amount of water, which was not given.

As regards inventive step, D2 was the closest prior art. Example 5 of D2 explicitly disclosed features a), c), d), f) of claims 1 or 2. Therefore, the distinguishing features of the opposed patent over Example 5 of D2 were that the opposed claim 1 stipulated the presence of features b) and e) (a surfactant and a disaccharide) in the composition. As no effect was linked with these features, the technical problem was the provision of an alternative composition for stabilizing botulinum toxin. Moreover, D1 made obvious that the effect was linked with the concentration of the non-ionic surfactant which was not claimed. There was also no evidence in the opposed patent that the combination of the surfactant and disaccharide led to a combined technical effect. Therefore, the objective technical problem had to be considered to be an aggregation of two partial problems.

The use of a surfactant in a composition for stabilizing botulinum toxin was obvious in view of documents D2, D3, D4; D5-D8 were also cited in the written proceedings. D2 taught that surfactants may be used to reduce absorption (see D2, page 34, lines 19-20) and that reducing adhesion or adsorption of

botulinum toxin to surfaces increases stability (see page 25, lines 10-20). The skilled person would directly and unambiguously have derived from D2 that the addition of surfactant to botulinum toxin compositions was a conventional means for stabilizing botulinum toxin. D3 specifically referred to the preferred surfactant in the opposed patent, polysorbate 80 as a secondary stabilizer (see D3, par. [0114]). D4 provided a general teaching as to the use of a non-ionic surfactant to a protein solution, as it reduces absorption.

The inclusion of a disaccharide in a composition for stabilizing botulinum toxin was also obvious in view of D2 (see page 30, lines 30-33). D7 taught also that compositions comprising histidine, sodium chloride, polysorbate 80 and a disaccharide can be used to replace albumin in the stabilization of sensitive proteins.

XIV. The arguments of the respondent may be summarised as follows

Documents D19-D22 should not be admitted into the proceedings. They were filed very late, and their relevance could not be a criteria for admission; if admitted, the respondent would have to request a postponement of the oral proceedings, since he had not enough time to prepare a defence. D19 was a document cited in the opposition proceedings of 2015 of the parent patent application of the the contested patent, and the appellant had sufficient time to file it in the present proceedings.

As regards the amendment of the term "comprising" by "consisting of", it could not contravene Article 76(1)

or 123(2) EPC, since the claimed components were the only components present in the compositions, and the claimed subject-matter was clearly and unambiguously derivable from the parent application and the application as filed. Moreover, all the claimed features found a basis without the necessity to make any selection.

As regards sufficiency of disclosure, the non-ionic surfactant had to be in an amount sufficient to stabilize the botulinum toxin, and the skilled person had to be sure to work around or above the CMC of the surfactant; said CMC could have been measured easily. Moreover, the solid and liquid compositions of the invention were well-described in the application as filed, including in the examples, and hence the person skilled in the art was perfectly capable of reproducing such compositions.

As to inventive step, the compositions of claims 1 or 2 differed from those disclosed in D2 by the presence of a non-ionic surfactant, a disaccharide, and a buffer to maintain the pH between 5.5 to 7.5. The composition according to the invention contained a number of different components as indicated in the claims and the invention required the presence of each of these components. The appellant was artificially attempting to force the use of the "partial problem" approach.

The claimed solution could not be seen as obvious. D2 did not teach the use of a surfactant as a stabilizer of the botulinum toxin and specifically taught away from the use of disaccharides (please see page 11, lines 17-21; and page 26, lines 9 -11). D3 focused on recombinant human serum albumin and on its use in animals. D4 was a journal article which did not

make any mention whatsoever of botulinum toxin. D7 was related to compositions of factor VIII.

XV. Requests

The appellant (opponent) requested that the decision under appeal be set aside and that the patent be revoked. Additionally, it requested that the auxiliary requests filed with letter of 29 August 2016 not be admitted into the proceedings.

The respondent (patent proprietor) requested that decision under appeal be set aside and the patent be maintained on the basis of the set of claims of auxiliary request 1A (main request), or one of auxiliary requests 1B, 2A, 2B, 3A, 3B, 4A, 4B, 5A, 5B, 6A and 6B all filed with letter of 29 August 2016. Additionally, it requested that documents (16) and (17) filed with letter of 13 January 2017 and (19) to (22) filed with letter of 26 September 2017 not be admitted into the proceedings.

Reasons for the Decision

1. Admission of documents D19-D22 into the proceedings

According to Article 13(3) RPBA, amendments to a party's case sought to be made after oral proceedings have been arranged shall not be admitted if they raise issues which the Board or the other party cannot reasonably be expected to deal with without adjournment of the oral proceedings.

Documents D19-D22 have been filed shortly before the oral proceedings and after the sending of a

communication by the Board. Document D19 is presented as a new closest prior art in the assessment of inventive step and documents D20-D22 are filed in support of this objection. This request constitutes therefore a fresh case introduced at a very late stage of the proceedings; it furthermore raises points that the Board and the other party might not reasonably deal with without adjournment of the oral proceedings. Under these circumstances, the relevance of the document is not the decisive criterion.

Hence, the Board decides not to admit said documents D19-D22 into the proceedings (Article 13(3) RPBA).

2. Auxiliary request 1A (main request)

2.1 Admission into the proceedings

All auxiliary requests have been filed by the respondent in response to the statement of grounds of appeal, thus at the earliest stage of the appeal proceedings. Hence, the respondent's case was complete with its reply, and there is no reason not to admit auxiliary request 1A into the proceedings according to Article 12(2) RPBA.

As to the argument of the appellant that said auxiliary request could have been filed earlier during the opposition proceedings, this argument appears irrelevant since the patent was considered to be allowable in amended form by the opposition division and this request was then filed in reply to the appellant's appeal. There is thus no objective reason why the patentee should have been expected to file this request during the opposition proceedings. Thus Article 12(4) RPBA does not apply.

2.2 Article 76(1) EPC - Article 100(c) EPC

Objections have been raised under Article 76(1) and 100(c) EPC by the appellant against claims 1 and 2 of the main request with regard to the term "consisting of", as well as an undisclosed combination of features in claims 1 and 2.

2.2.1 Article 76(1) EPC

The description of the parent application

WO2006/005910 discloses on pages 7 and 8 "a solid or liquid pharmaceutical composition comprising:

(a) botulinum neurotoxin complex (type A, B, C, D, E, F or G) or high purity botulinum neurotoxin (type A, B, C, D, E, F or G),

(b) a surfactant,

(c) a crystalline agent,

(d) a buffer to maintain pH between 5.5 to 7.5.

Preferably, a disaccharide will also be included in the pharmaceutical compositions according to the present invention, especially when they are in a solid form".

The following passage on page 8 mentioned that "a solid pharmaceutical composition can be obtained by lyophilising a sterile water solution containing the components (a) to (d) as mentioned previously. A liquid pharmaceutical composition according to the invention will be obtained by mixing a solid (e.g. lyophilized) mixture of said components (a) to (d) with sterile water."

This passage of the description constitutes undeniably an explicit basis for a combination of all the features a)-f) of claim 1 and a)-e) of claim 2, with the

exception of the mention that the surfactant must be non-ionic and the restriction to a therapeutic use. The description does furthermore not disclose the presence of a further excipient or class of excipients and all examples are indisputably restricted to compositions comprising only features a)-f) when in liquid state of a)-e) when lyophilised, thus "consisting of" features a)-f) or a)-e).

As to the non-ionic character of the surfactant, the first paragraph of page 6 relates to said surfactant and on page 6, line 4, of the description of the parent application, it is mentioned that "preferably, the surfactant will be a non-ionic surfactant".

The restriction to a therapeutic use is also directly and unambiguously derivable from the teaching the parent application, which relates to a pharmaceutical composition and discloses diseases, conditions or syndromes to be treated on pages 10-13.

Thus, the presence of the combination of all features a)-f) of claim 1 and features a)-e) of claim 2 is disclosed directly and unambiguously in the parent application.

Even if the Board agrees with the appellant that the description of the parent application envisaged initially several types of alternative compositions, either "consisting essentially of a botulinum toxin and a surfactant, or "consisting essentially of a botulinum toxin, a surfactant and water" or simply "comprising a botulinum toxin and a surfactant", as disclosed on page 4 of the parent application, it remains that the choice of one alternative at the expense of the others cannot constitute a violation of Article 76(1) EPC, in view of

the suppression of a part of the original teaching of an application, as argued by the appellant. An amendment infringes Article 76(1) EPC (or Article 123(2) EPC) only if the subject-matter **remaining in the claim** is not, be it explicitly or implicitly, directly and unambiguously disclosed to the skilled person using common general knowledge, in the parent application (or in the application as filed in the case of Article 123(2) EPC).

2.2.2 Article 100(c) EPC

The passages corresponding to pages 7,8, page 6 and 10-13 of the parent application mentioned above in paragraph 2.2.1 are to be found *verbatim* on respectively page 5, page 4 and pages 6-8 of the application as filed. The requirements of Article 100(c) EPC are therefore met for the same reasons as Article 76(1) EPC above.

2.3 Article 100(b) EPC

A lack of sufficient disclosure of the claimed invention was objected by the appellant as specifically to the question of the concentration of the non-ionic surfactant in claim 1, and as to the the presence of a "buffer to maintain pH between 5.5 to 7.5" in a solid composition.

2.3.1 The compositions of claims 1 and 2 refer to the presence of a "non-ionic surfactant as a stabilizing agent". The description of the application as filed mentions that the "concentration of the surfactant will be from above the critical micellar concentration to a concentration of 1% v/v" and also gives a certain number of possible alternative surfactant to be used,

preferably polysorbate 80 (see description of the specification par. [0024]).

The skilled person would therefore have no difficulty to determine the necessary concentration of the surfactant in the composition. The critical micellar concentration (CMC) is indeed a standard known characteristic of a surfactant, in particular for usual surfactants such as polysorbate 80. Moreover, if, as argued by the appellant, different methods of measurement could give different results for some surfactant, the skilled person would still be in a position to determine a stabilizing concentration value over said measured CMC values.

- 2.3.2 As to the presence of a "buffer able to maintain pH between 5.5 and 7.5" in a solid composition, the skilled person would understand that the buffer is present in the solid composition in an amount such that a pH between 5.5 and 7.5 is obtained when reconstituted and that the amount of water, or of a mixed solvent system comprising necessarily water, necessary for reconstitution, should be adapted to the use. This is explicitly reflected by the teaching of example 1 of the specification, which describes the lyophilisation of a specific aqueous composition and the storage of the obtained lyophilized dry composition.

In any case, if a large amount is used for the reconstitution of the liquid composition, the pH will anyway tend to the value 7.0, which belongs to the claimed range of 5.5 to 7.5.

- 2.3.3 Hence, in view of points 2.3.1 and 2.3.2 above, and since claims 1 and 2 relate to a composition as such,

the skilled person would not have any difficulty in preparing the claimed compositions.

The patent discloses therefore the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

2.4 Article 56 EPC - Inventive step

2.4.1 The present invention aims to find alternative stabilising agents to albumin by using another stabilising agent, in pharmaceutical compositions containing as active principle a botulinum toxin (see specification par. [0001] and [0003]).

2.4.2 Document D2 was considered as closest prior art by the appellant and by the opposition division in its decision. The Board sees no reason to choose a different approach.

D2 discloses compositions stabilized by a polysaccharide, and more particularly in example 5 a composition comprising a botulinum toxin, hetastarch, histidine, sodium chloride and water. This document does not disclose the presence of a non-ionic surfactant or a disaccharide, and uses as stabilizing agent a hetastarch.

2.4.3 According to the appellant, the problem is the provision of an alternative composition for stabilization of botulinum toxin.

2.4.4 As a solution to this alleged problem, claims 1 and 2 of auxiliary request 1A propose a composition comprising a non-ionic surfactant as stabilizing agent, a disaccharide and which does not comprise hetastarch.

2.4.5 In view of the results of example 1 of the contested patent, the Board sees no reason to question the stabilising effect of the claimed compositions.

The Board can in particular not follow the appellant's arguments as to the lack of plausibility of the effect, in view of the absence of the concentration feature of the non-ionic surfactant in claims 1 and 2. Both claims refer indeed to the presence of "a non-ionic surfactant as a stabilizing agent", a functional feature which implies that said non-ionic surfactant must be present at an effective concentration.

2.4.6 It remains to be determined whether the solution was obvious to the person skilled in the art.

(a) D2 does not suggest or teach the replacement of the polysaccharide stabilizing agent by any other stabilizing agent, even less by a non-ionic surfactant, and does even not suggest or teach the addition of a non-ionic surfactant to the disclosed compositions.

Surfactants are mentioned on page 34 of D2 as possible additional components of the disclosed compositions to reduce adsorption, but without reference to the non-ionic nature of the surfactants. There is also no link or possible technical association between said passage and the disclosure of example 5.

The presence of a disaccharide as the polysaccharide stabilizing agent is also explicitly excluded in D2. A first passage on page 19, lines 4-6 gives indeed the meaning of "polysaccharide" in D2, namely a polymer of more than two saccharide molecules. The description on page 26 excludes

furthermore from the scope of the invention disaccharides oligosaccharides with a molecular weight of less than 20 kD. This is reinforced by the technical discussion over the background prior art on pages 11 and 12 of D2, which mentions some disaccharides such as cellobiose or glucose as unsuitable as a toxin stabilizer.

(b) D3 mentions the use of the non-ionic surfactant polysorbate as secondary stabilizing agent for the botulinum toxin in addition to a stabilizer which can be a protein or a polysaccharide, such as albumin, gelatin, collagen and hetastarch (see par. [0114]); even if it is mentioned that said secondary stabilizer "may be used alone or in combination with primary stabilizers", D3 does not provide any composition with such a secondary stabilizer alone. A specific composition comprising albumin as main stabilizer and polysorbate 80 as secondary stabilizer is disclosed in the presence of further secondary stabilizers, namely zinc chloride, sodium caprylate and N-acetyl tryptophan (see D3 par. [0114] and [0172]). This document emphasizes also particularly the difficulty to find an appropriate stabilizing agent for the botulinum toxin in view of its physico-chemical particularities (see par. [0052]-[0058]) and does not suggest at all the use of disaccharides in compositions of botulinum toxin.

(c) D4 is a general review on protein stability which mentions the use of non-ionic surfactants in particular for inhibiting aggregation (see page 1328). This document does not suggest the use of a non-ionic surfactant for complex proteins such as toxins.

- (d) D7 teaches the use of polysorbate 80, L-Histidine, calcium chloride and sucrose for stabilizing a formulation of Factor VIII; sucrose is used as a non-crystallising compound and the function of the polysorbate is not specifically given. The structure of Factor VIII is however too remote to find an incentive to use the same composition with the botulinum toxin.
- (e) The other cited documents are not more relevant for assessing the obviousness of the solution:
- (i) D5 is an opposition communication from an opponent in the opposition proceedings against EP 1 391 306 B1 which discusses the relevance of document D6.
 - (ii) D6 relates to the use of a preservation mixture for sensitive biological products, viruses, bacteria and cells by a composition mono-, di- or oligosaccharides. This document does not relate to the botulinum toxin or to the use of surfacants.
 - (iii) D8 relates to the use of albumin for stabilizing botulinum toxin. There is no mention of a surfactant or a disaccharide in this document.

There is thus no cited document which discloses or suggest the use of a non-ionic surfactant in combination with botulinum toxin and in the absence of a protein or polysaccharide stabilizer, even less a document suggesting or disclosing the use of a disaccharide in combination with a non-ionic surfactant.

2.4.7 The claimed solution is thus a non-obvious alternative and auxiliary request 1A meets the requirements of Article 56 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 with the order to maintain the patent on the basis of the set of claims of auxiliary request 1A filed with letter of 29 August 2016 (which is now the main request) and a description to be adapted.

The Registrar:

The Chairman:



S. Fabiani

J. Riolo

Decision electronically authenticated