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Datasheet for the decision of 24 November 2022

Case Number: T 0229/20 - 3.3.07

Application Number: 11767935.7

Publication Number: 2627318

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Language of the proceedings: EN

Title of invention:
FORMULATION SUITABLE FOR STABILIZING PROTEINS, WHICH IS FREE OF MAMMALIAN EXCIPIENTS

Patent Proprietor:
Merz Pharma GmbH & Co. KGaA

Opponent:
ALLERGAN, INC.

Headword:
Stabilizing proteins/MERZ

Relevant legal provisions:
EPC Art. 123(2), 83, 56
RPBA 2020 Art. 12(2)

Keyword:

Amendments - allowable (yes)
Sufficiency of disclosure - (yes)
Inventive step - non-obvious alternative
primary object of appeal proceedings to review decision - appeal case directed to arguments on which decision was based (no)

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Case Number: T 0229/20 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 24 November 2022

Appellant: (Patent Proprietor)	Merz Pharma GmbH & Co. KGaA Eckenheimer Landstrasse 100 60318 Frankfurt am Main (DE)
Representative:	Ricker, Mathias Wallinger Ricker Schlotter Tostmann Patent- und Rechtsanwälte Partnerschaft mbB Zweibrückenstrasse 5-7 80331 München (DE)
Appellant: (Opponent)	ALLERGAN, INC. 2525 Dupont Drive Irvine CA 92612 (US)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 3 December 2019 concerning maintenance of the European Patent No. 2627318 in amended form.**

Composition of the Board:

Chairman	A. Usuelli
Members:	M. Steendijk
	A. Jimenez

Summary of Facts and Submissions

I. European patent 2 627 318 ("the patent") was granted on the basis of fourteen claims.

Claim 1 as granted related to:

> "A composition comprising
> (a) a pharmaceutically active protein, peptide or mixture thereof,
> (b) a mixture of a hydrophilic polymer and a non-ionic detergent, wherein the non-ionic detergent is present in said composition in an amount of between 0.2 and 0.01 mg/g, and the weight ratio of hydrophilic polymer to non-ionic detergent is from 18:1 to 22:1 (wt-%), and
> (c) a mixture of a polyalcohol and a sugar, wherein the weight ratio of polyalcohol to sugar is from 2:1 to 5:1 (wt-%),
> wherein the composition is free of animal or human serum albumin, gelatine, amino acids selected from histidine, lysine and methionine, and/or immunoglobulins."

Claim 2 as granted defined:

> "A composition comprising
> (i) a pharmaceutically active protein, peptide or mixture thereof,
> (ii) a mixture of a hydrophilic polymer and a non-ionic detergent, wherein the non-ionic detergent is present in said composition in an amount of between 0.2 and 0.01 mg/g, and the weight ratio of hydrophilic polymer to non-ionic detergent is from 2:1 to 30:1 (wt-%), and

(iii) a sugar, wherein no polyalcohol is present and the composition is free of animal or human serum albumin, gelatine, amino acids selected from histidine, lysine and methionine, and/or immunoglobulins, and wherein the composition is not a composition comprising ≤ 1.6 ng neurotoxic component of Botulinum toxin, 1.0 mg of hyaluronic acid, 10.0 mg of sucrose and 0.2 mg of polysorbate 80."

Claims 13 and 14 as granted related to the use of a formulation for stabilizing pharmaceutically active proteins, peptides or mixtures thereof, wherein the formulation is respectively defined in accordance with claims 1 and 2 as granted

II. The patent was opposed on the grounds that its subject-matter lacked inventive step, that the claimed invention was not sufficiently disclosed and that the patent comprised subject-matter extending beyond the content of the application as filed.

The patent proprietor and the opponent filed appeals against the interlocutory decision of the opposition division that the patent as amended in accordance with auxiliary request 2 as filed during the oral proceedings held on 27 September 2019, met the requirements of the EPC.

The decision was based on the patent as granted (main request), auxiliary request 1 filed as auxiliary request 3 on 2 October 2018 and auxiliary request 2 filed during the oral proceedings.

In its decision the opposition division cited *inter alia* the following documents:

D1: WO 2007/041664 A1
D2: WO 2006/079722 A2
D3: WO 2006/062875 A1
D4: EP 2248518 A1
D5: WO 2010/090677 A1
D6: WO 2006 020208 A2

The opposition division arrived at the following conclusions:

(a) The claims as granted did not comprise subject-matter extending beyond the content of the earlier application as filed.

The patent as granted sufficiently disclosed the claimed invention.

Document D2, which related to the stabilisation of proteins, represented a suitable starting point for the assessment of inventive step. The subject-matter of claim 2 as granted differed from the compositions of document D2 in the lower weight ratio of the hydrophilic polymer to the non-ionic detergent. In the absence of data showing any special effect of this difference the problem to be solved was the provision of an alternative composition capable of stabilizing protein. In view of document D5, which related to stabilized Botulinum toxin compositions, the defined lower ratio was arbitrary and did therefore not involve an inventive step.

(b) The composition of claim 2 of auxiliary request 1, which defined the ratio of the hydrophilic polymer to the non-ionic detergent more narrowly (between 2:1 and 10:1), lacked an inventive step for the

same reason as the composition of claim 2 as granted.

(c) Auxiliary request 2, in which claims 2 and 14 as granted were deleted and claim 1 as granted was amended to define a composition comprising Botulinum toxin as the pharmaceutically active protein, did not contravene the provisions of Articles 83 and 123(2) EPC.

Document D5 represented the most relevant prior art. Within document D5 the formulations of Table 8 (page 97 line 5 and page 98 line 9) having three excipients in common with the composition of claim 1 of auxiliary request 2 represented the closest prior art. The difference between the claimed composition and this prior art concerned the presence of the hydrophilic polymer and the reduced amount of the non-ionic detergent (between 0.2 and 0.01 mg/g instead of 200 mg/g). In the absence of evidence of an effect linked to this difference the problem to be solved was the provision of an alternative stable formulation of Botulinum toxin. Neither document D5 alone nor document D5 in combination with any general knowledge suggested as solution the replacement of a large amount of non-ionic detergent by a mixture comprising a hydrophilic polymer in a ratio to the non-ionic detergent of 18:1 to 22:1.

The subject-matter of auxiliary request 2 therefore involved and inventive step.

III. In support of arguments regarding the ground of lack of sufficient disclosure the appellant-opponent filed with

the statement of grounds of appeal the following documents:

D9: BioImpacts, 2011, 1(1), 23-30
D10: Advanced Drug Delivery Reviews, 2006, 58(14), 1523-1531

and referred to the US Food and Drug Administration IIG database under the link:

"https://www.accessdata.fda.gov/scripts/cder/iig/index.cfm".

IV. With the statement of grounds of appeal the appellant-patent proprietor maintained its main request relating to the patent as granted.

V. The Board invited the parties to attend oral proceedings on 17 November 2022.

In its communication pursuant to Article 15(1) RPBA the Board indicated that it did not intend to admit the appellant-opponent's new submissions regarding the ground of lack of sufficient disclosure. Regarding the requirement of inventive step the Board questioned whether the skilled person would have expected that protein stabilisation would be achieved upon reduction of the content of the hydrophile polymer in a composition as described in document D2 to the weight ratio with respect to the detergent as defined in the claims as granted.

VI. With the letter of 4 November 2022 the appellant-opponent withdrew its request for oral proceedings and announced not to attend the oral proceedings scheduled for 17 November 2022.

The oral proceedings were cancelled with the Boards communication of 10 November 2022.

VII. The arguments of the appellant-patent proprietor relevant to the present decision are summarized as follows:

- Basis for the amendments

  The opposition division correctly found that claims 1 and 2 as granted were adequately based on claims 1 and 2 as originally filed in combination with claim 7 and paragraphs [0017] and [0031] of the application as filed.

- Sufficiency

  The opposition division had correctly concluded that the appellant-opponent had not raised serious doubts based on verifiable facts that the stabilization demonstrated in the examples of the patent with respect to Botulinum toxin could not be achieved with respect to pharmaceutical proteins and peptides in general as defined in the claims of the patent. The additional arguments regarding potential issues with specific excipients were raised for the first time during the appeal proceedings and should not be admitted.

- Inventive step

  The difference between the claimed subject-matter of the patent as granted and the most relevant formulation described in document D2, the PVP/ Sucrose/Tween 80 comprising composition ("PSW")

presented on page 11, Table I, concerned the lower weight ratio of the hydrophilic polymer to the non-ionic detergent (in claim 2 as granted between 2:1 and 30:1 instead of 200:1 in document D2). The patent demonstrated that the claimed composition allows for preservation of 90% of functional activity after 12 months storage using reduced amounts of hydrophilic polymer. Document D5 described compositions with substantially higher amounts of hydrophilic polymer and provided no suggestion towards the compositions defined in the claims as granted.

VIII. The arguments of the appellant-opponent relevant to the present decision are summarized as follows:

- Basis for the amendments

The application as filed disclosed in paragraph [0017] that the formulation was free of stabilizing proteins, whilst the feature in claims 1 and 2 as granted, that the composition is "free of animal or human serum albumin (...) immunoglobulins", excludes these specified ingredients irrespective of any stabilizing effect.

The application as filed disclosed the defined weight ratios between the hydrophilic polymer and the detergents of the composition in general, whereas claims 1 and 2 as granted relate the defined ratios specifically to the non-ionic detergent only.

The application as filed did not disclose the embodiment of original claim 7 in combination with the features of paragraphs [0017] and [0031].

- Sufficiency

It had not been demonstrated that proteins or peptides of any kind could be stabilized with the excipients as defined in claims 13 and 14 as granted. Such stabilisation depended on a variety of factors, including the nature of the protein or peptide and the suitability of the excipients. The relevance of such factors was evident from documents D1, D4, D5 and D6. Moreover, documents D9 and D10 as well as references in the US Food and Drug Administration IIG database demonstrated that a variety of excipients covered by the claims are toxic and not suitable for use in pharmacy. It therefore required undue burden to carry out the defined stabilisations within the whole scope of the claims.

- Inventive step

The subject-matter of claim 2 as granted differed from the closest compositions described in document D5 (page 86, Table 6, compositions 5-8) in the lower amount of non-ionic detergent (0.01-0.2 mg/g instead of 5-12 mg/g). The subject-matter of claim 1 as granted differed from the closest compositions described in document D5 in the lower amount of detergent (0.01-0.2 mg/g instead of 3 mg/g) and the presence of a polyalcohol and a sugar as components (see D5, page 77, Table 4, composition 19) or in the defined amount of the non-ionic detergent and the presence of a hydrophilic polymer in a defined weight-ratio with respect to the detergent (see D5, page 97, Table 8, fifth composition).

It was not credible that a stabilizing effect is achieved over the whole scope of the claim. The patent actually presented stability tests only for lyophilized compositions, which do not fulfill all features of claim 2 as granted. Starting from document D5 the objective technical problem should therefore be formulated as the provision of a mere alternative composition. The defined amount of non-ionic detergent was obvious as solution in view of document D5 itself, which describes in paragraph [0091] a surfactant amount of 0.01% (w/v), which corresponds to 0.1 mg/g, as useful. Moreover, the skilled person would be aware from document D2 (page 11, Table 1) that a surfactant amount of 0.02% (0.2 mg/g) was conventional in stabilized protein compositions. The use of a polyalcohol and a sugar was also entirely conventional as evidenced by documents D2 and D5.

The subject-matter of claim 2 as granted differed from the "PSW" composition described document D2 (page 11, Table 1) in the lower weight ratio for the hydrophilic polymer with respect to the non-ionic detergent (2:1 to 30:1 instead of 200:1). The subject-matter of claim 1 as granted additionally differed from this prior art in the presence of the polyalcohol. In the absence of any unexpected effect the technical problem could only concern the provision of an alternative product. In view of documents D1, D3 and D5 the weight ratio between the hydrophilic polymer and the non-ionic surfactant defined in the claims as granted was entirely conventional.

The subject-matter of claim 2 as granted differed from the compositions with sucrose, PVP and

poloxamer described in document D1 (see Table 6) in the defined amount of non-ionic detergent and the weight ratio of the detergent with respect to the hydrophilic polymer. In the absence of any particular effect the claimed subject-matter represented a mere alternative which was obvious in view of the prior art.

IX. The appellant-patent proprietor requested that the decision under appeal be set aside and that the patent be maintained as granted.

The appellant-patent proprietor requested in this context that the arguments on insufficient disclosure regarding the suitability of specific excipients raised for the first time in the appellant-opponent's statement of grounds of appeal be disregarded.

X. The appellant-opponent requested that the decision under appeal be set aside and that the patent be revoked in its entirety.

The appellant-opponent requested in this context that new arguments and evidence on insufficient disclosure be admitted. Moreover, the appellant-opponent requested that the arguments on inventive step regarding protein integrity and reduction of polymer amount raised for the first time in the appellant-patent proprietor's statement of grounds of appeal be disregarded.

Reasons for the Decision

Main request, patent as granted

1. Added subject-matter

1.1 Claim 1 as originally filed defines:

"A formulation free of proteins comprising
(a) a mixture of a hydrophilic polymer and a non-ionic detergent, wherein the weight ratio between the hydrophilic polymer and the detergent is from 18:1 to 22:1 (wt-%),
(b) a mixture of a polyalcohol and a sugar, wherein the weight ratio of polyalcohol to sugar is from 2:1 to 5:1 (wt-%),
c) and wherein the non-ionic detergent is present in said fonnulation in an amount between 0.2 and 0.01 mg/g."

Claim 2 as originally filed defines:

"A formulation free of comprising
(d) a mixture of a hydrophilic polymer and a non-ionic detergent, wherein the weight ratio between the hydrophilic polymer and the detergent is from 2:1 to 30:1 (wt-%), and wherein the non-ionic detergent is present in said formulation in an amount between 0.2 and 0.01 mg/g;
(e) a sugar; and
(f) wherein no polyalcohol is present."

As explained in the decision under appeal (see page 5, lines 21-23) and not contested by the parties claim 2

as originally filed should be read to define a formulation free of proteins.

Claim 7 as originally filed defines a composition comprising the formulation according to any of the preceding claims, which further comprises a pharmaceutically active peptide, a protein or a mixture thereof.

Paragraph [0017] of the application as filed presents the following explanations as to the term "free of ..." used in original claims 1 and 2:

> "The term "free of proteins" hereinunder refers to a formulation which is free of any protein and/or peptide which is not the pharmaceutical active protein, peptide or mixture of thereof. In particular it is meant that the formulation is free of stabilizing proteins such as animal or human serum albumin (HSA), gelatine, amino acids such as histidine, lysine, methionine and/or immunoglobulins." [underlining by the Board]

Paragraph [0031] of the application as filed specifically discloses the proviso of granted claim 2 in an embodiment of a formulation as defined in claim 2 as originally filed.

1.2 As pointed out in the decision under appeal (see pages 5-6 section A.1.3) the features of claim 1 as granted derive from claims 1 and 7 in combination with paragraph [0017] of the application as filed and the features of claim 2 as granted derive from original claims 2 and 7 in combination with paragraphs [0017] and [0031] of the application as filed.

The application as filed presents in paragraph [0017] the listed agents including animal or human serum albumin as examples of the "stabilizing proteins" which the defined formulations are defined to be free of. Contrary to the appellant-opponent's argument the Board therefore considers that the feature "free of..." in the granted claims relates to a group of agents which is per definition included in the term "stabilizing proteins" as used in paragraph [0017] in the application as filed.

The Board further agrees with the decision under appeal (see page 5 paragraph 3) that no added matter results from the definition of the ratio between the hydrophilic polymer and the non-ionic detergent in the claims as granted, because "**the** detergent" in original claim 1 under (a) and in original claim 2 under (d) finds its only antecedent in the terms "a non-ionic detergent".

The Board observes that paragraph [0017] of the application as filed presents an explanation of the meaning of the term "free of proteins" in original claims 1 and 2 and therein specifically points to the embodiment of original claim 7 involving a pharmaceutically active protein or peptide. The Board therefore also agrees with the decision under appeal (see page 5 paragraphs 8-9) that the combination of features from original claim 7 and paragraphs [0017] and [0031] does not give rise to subject-matter which had not been originally disclosed.

1.3 Accordingly, the Board concludes that the patent as granted does not comprise subject-matter extending beyond the content of the application as originally filed.

2. Sufficiency

2.1 The appellant-opponent contested the finding in the decision under appeal that it had not discharged the burden of proof regarding the ground of lack of sufficient disclosure.

2.2 With the statement of grounds of appeal the appellant-opponent filed documents D9 and D10 and referred to the US Food and Drug Administration IIG database to support the argument that claim 11 of the request upheld by the opposition division does not meet the requirement of sufficient disclosure, because certain excipients are not suitable for the purpose of preparing pharmaceutical compositions, including compositions for administration by injection, as tought in the patent. According to the appellant-opponent documents D1 and D6 further demonstrated that certain types of sugar, such as cellobiose, are unsuitable as Botulinum toxin stabilisers. Moreover documents D4 and D5 demonstrated that the weight ratio between the hydrophilic polymer and the detergent required for stabilization of Botulinum toxin depends on the specific components used. Document D5 further showed that Botulinum toxin is highly sensitive to factors such as the pH and the nature of the used buffer (see statement of grounds of appeal, pages 6-12, section 5).

The appellant-opponent justified the filing of the new facts, arguments and documents in view of the conclusion in the decision under appeal (see page 6 section A.2.3) that the appellant-opponent had not discharged the burden of proof on insufficiency (see statement of grounds of appeal pages 6-12 section 5).

The Board observes that the appellant-opponent had argued before the opposition division that claims 13-14 as granted did not meet the requirement of sufficiency of disclosure, because these claims relate to the stabilisation of pharmaceutically active proteins or peptides in general, whereas it was well known that different proteins have significantly different stability profiles (see notice of opposition page 6 section 6; see letter of 23 July 2010 page 3 section 3; see minutes of the oral proceedings of 27 July 2019 bridging section pages 1-2). In fact, the appellant-opponent had not maintained the objection of lack of sufficient disclosure against claim 11 of the auxiliary request upheld by the opposition division, which was limited to the stabilisation of Botulinium toxin (see minutes of the oral proceedings of 27 July 2019 page final sentence; see also decision under appeal, page 15, section C.3).

Accordingly, the appellant-opponent's objection concerning the suitability of the excipients for the purpose of preparing pharmaceutical compositions or stabilizing Botulinum toxin do not address the considerations which led to the decision under appeal, but rather change the dimension of the objection to the extent that it confronts the appellant-patent proprietor and the Board with a fresh case. The Board does therefore not admit these new facts, arguments and evidence into the appeal proceedings under Articles 12(2), 12(4) and 12(6) RPBA 2020.

2.3 The appellant-opponent further maintained that different proteins have different stability profiles and that from the examples in the patent relating to the stabilization of Botulinum toxin no conclusions can be drawn regarding the stabilization of

pharmaceutically active proteins and peptides in general. According to the appellant-opponent the examples in the patent did actually not even demonstrate the stabilization in the claimed compositions, because the tested compositions in the patent were lyophilised and therefore comprised higher concentrations of the excipients than the compositions as claimed.

The Board agrees with the finding in the decision under appeal (see page 6, section A.2) that the appellant-opponent has not supported its contention that the experimental results reported in the patent regarding Botulinum toxin cannot be extrapolated to other proteins with any verifiable facts. In this context the Board observes that example 1 of the patent (see paragraphs [0141]-[0143] and figure 1) demonstrates the stability of a lyophilized composition, in which the relative amount of the non-ionic detergent may indeed surpass the 0.2 mg/g as defined in the claim due to solvent removal. However, as observed in the decision under appeal (see page 18 paragraph 8) example 1 still demonstrates that a composition as defined in the claims leads after solvent removal to a stable lyophilised Botulinum toxin formulation and can thus be used for the purpose of stabilization as defined in claims 13 and 14.

2.4 Accordingly, the Board concludes that the patent as granted fulfills the requirement of sufficient disclosure of the claimed invention.

3. Inventive step

3.1 The compositions of claims 1 and 2 as granted comprise in addition to the pharmaceutically active protein or

peptide a mixture of a hydrophilic polymer and a non-ionic detergent as well as a sugar. The claims define a specific concentration range of 0.01-0.2 mg/g for the non-ionic detergent. Due to the defined weight ratios of the hydrophilic polymer in relation to the detergent the claims also require specific concentration ranges for the hydrophilic polymer. In accordance with the broad definition of the ratio in claim 2 as granted (2:1 to 30:1) the concentration of the hydrophilic polymer ranges from 0.02-6 mg/g. The narrowly defined concentration of claim 1 as granted falls within this range. Claim 1 as granted further defines the presence of a polyalcohol in a defined weight ratio to the sugar, whereas claim 2 as granted excludes the presence of a polyalcohol.

3.2 Document D2 describes stabilized compositions for *Clostridium difficile* toxin, including a "PSW" composition comprising the hydrophile polymer PVP, the sugar sucrose and the non-ionic detergent Tween 80 which the appellant-opponent relied upon as suitable starting point. This "PSW" composition differs from the compositions of claims 1 and 2 as granted in the higher content of the hydrophile polymer, namely 40 g/L corresponding to 40 mg/g instead of the maximum of 6 mg/g as defined in the claims as granted.

Document D5 describes a variety of stabilized compositions for Botulinum toxin, including the following compositions specifically relied upon by the appellant-opponent:

- compositions comprising 20-24 mg/mL of the sugar sucrose, **20 mg/mL of the hydrophile polymer** PVP and **5 mg/mL of the non-ionic detergent** Poloxamer-188 (see D5, page 86, Table 6, compositions 5-8)

- a composition containing **60 mg/mL of the hydrophile polymer** PEG-3350 and **3 mg/mL of the non-ionic detergent** Poloxamer-188 (see D5, page 77, Table 4, composition 19)

- a composition comprising 15 mg/mL sucrose, 45 mg/mL of the polyalcohol mannitol and 0.2 mL/mL of the non-ionic detergent Polysorbate 20 (see D5, page 97, Table 8, composition 5); in line with the finding in the decision under appeal (see page 18 lines 2-3) 0.2 mL/mL approximately corresponds to an amount as high as **200 mg/g for the detergent**.

Document D1 describes stabilized Botulinum toxin formulations comprising 20 mg sucrose, **20 mg of the hydrophile polymer** PVP and **20 mg of the non-ionic detergent** poloxamer (see D1, page 42,Table 6).

The indicated compositions from documents D5 and D1 thus differ from the compositions defined in the claims as granted in the substantially higher content of the non-ionic detergent and the hydrophile polymer and their ratio or the drastically higher content of the ionic detergent in the absence of a hydrophile polymer.

3.3 The patent reports in its experimental section (see pages 14-15, examples 1 and 2 with reference to figures 1 and 2) that compositions in accordance with claims 1 and 2 which are lyophilized show stability over 12 months storage.

The appellant-opponent argued that the patent only demonstrated stability for lyophilized compositions not covered by the claims and that the stability profiles of proteins depend on the nature of the protein and the

excipients. In its view it was therefore not credible that a stabilizing effect is achieved over the whole scope of the claim.

As explained in section 2.3 the Board considers that the patent substantiates in the experimental section that exemplified compositions covered by the claims allow for the preparation of stable lyophilised Botulinum toxin formulations.

In line with the finding in the decision under appeal (see page 18, final paragraph) the Board further agrees that, in the absence of substantiated arguments from the appellant-opponent to the contrary, this effect may be considered representative for the whole scope of the claims.

In this context the Board notes that document D1 (see page 17, lines 4-5) and document D6 (see paragraph [0013] only mention that the disaccharide cellobiose had in previous compositions not been found effective for stabilizing Botulinum. Moreover, document D4 (page 13, examples 1-4) and document D5 (see page 99, Table 188) merely report the use of different amounts for different surfactants in stabilized botulin toxin compositions. Document D5 further shows that in certain compositions (see D5, page 78) the stability of Botulinum compositions also depends on the pH and the nature of the buffer. However, such information does not affect the teaching in the patent regarding the stabilizing effect of the compositions as defined in the claims as granted, which are concerned with particular new combinations of the defined excipients.

In line with the finding in the decision under appeal (see page 9, lines 4-6) the Board therefore considers

that the problem to be solved may be formulated as the provision of an alternative composition for stabilizing a pharmaceutically active protein or peptide.

3.4 For the assessment of inventive step of claims 1 and 2 as granted it is therefore decisive whether or not the skilled person would have expected that the protein stabilisation in the compositions as described in documents D5, D2 or D1 would be retained in compositions as defined in claims 1 and 2 as granted.

The Board observes that according to the appellant-opponent it is evident from document D5 that protein compositions such as Botulinum toxin are highly sensitive and that the stability of such compositions depends on a variety of factors (see statement of grounds of appeal, page 8). This sensitivity is confirmed by the results from example 1 of the patent, which show that a change in the ratio between the hydrophilic polymer and the detergent already affects the stability of the resulting formulation. In view of this sensitivity it would not have been obvious to the skilled person that the compositions with the reduced detergent concentration and the changed content of hydrophile polymer as defined in the claims of the patent represent a solution to the problem of providing an alternative composition for stabilizing a pharmaceutically active protein or peptide.

3.5 Accordingly, the Board concludes that the patent as granted fulfills the requirement of inventive step.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is maintained as granted.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated