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Datasheet for the decision of 8 August 2024

Case Number: T 1402/22 - 3.3.04

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Language of the proceedings: EN

Title of invention:
Stabilized non-protein clostridial toxin compositions

Patent Proprietor:
Allergan, Inc.

Opponent:
IPSEN PHARMA S.A.S.

Relevant legal provisions:
RPBA 2020 Art. 13(2)
EPC Art. 56

Keyword:
Amendment after notification of Art. 15(1) RPBA communication - exceptional circumstances (no)
Inventive step - (yes)

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Case Number: T 1402/22 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 8 August 2024

Appellant: (Opponent)	IPSEN PHARMA S.A.S. 65, Quai Georges Gorse 92100 Boulogne-Billancourt (FR)
Representative:	Plasseraud IP 104 rue de Richelieu CS 92104 75080 Paris Cedex 02 (FR)
Respondent: (Patent Proprietor)	Allergan, Inc. 2525 Dupont Drive Irvine, California 92612 (US)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 28 March 2022 rejecting the opposition filed against European patent No. 3 432 916 pursuant to Article 101(2) EPC**

Composition of the Board:

Chairman	B. Rutz
Members:	R. Hauss
	L. Bühler

Summary of Facts and Submissions

I. European patent No. 3 432 916 (the patent in suit) was granted with a set of 20 claims. Independent claim 1 reads as follows:

1. A pharmaceutical composition comprising:

(i) a Clostridial toxin active ingredient;

(ii) a tonicity agent;

(iii) a poloxamer and/or a polysorbate; and

(iv) an antioxidant, wherein

the antioxidant comprises one or more of methionine and N-Acetyl-cysteine, and wherein

the antioxidant further comprises ethylene diamine tetraacetic acid sodium salt (EDTA) or an EDTA analog.

II. The patent in suit was opposed under Article 100(a) and (b) EPC on the grounds that the claimed subject-matter lacked novelty and inventive step and was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

III. The patent proprietor requested that the opposition be rejected (main request). It also submitted five amended claim requests as auxiliary requests 1 to 5 (clean copies filed by letter dated 28 October 2020).

IV. The documents cited in the proceedings before the opposition division included the following:

D2: AU 2009339292 B2

D3: US 2007/0134199 A1

D4: EP 2 692 350 A2

D10: EP 3 436 054 B1

V. The decision under appeal is the opposition division's decision rejecting the opposition, announced on 12 January 2022 and posted on 28 March 2022.

VI. The following was found in the decision under appeal.

(a) The subject-matter of the claims as granted met the requirements of novelty and sufficiency of disclosure (Articles 100(a), 52(1) and 54 EPC; Article 100(b) EPC).

(b) Document D4 was considered to be the closest prior art. Starting from the disclosure of document D4, the claimed subject-matter was held to involve an inventive step.

(c) The opposition division did not assess inventive step starting from the disclosure of document D3, which had been proposed by the opponent as an alternative starting point, under the rationale that D3 was not the closest prior art and that it would have been chosen as the starting point for assessing inventive step only with hindsight.

VII. The opponent (appellant) filed an appeal against this decision.

VIII. In its statement setting out the grounds of appeal, the appellant argued, *inter alia*, that the claimed subject-matter lacked an inventive step starting from the disclosure of document D3.

The composition defined in claim 1 as granted differed from those described in D3 by including methionine and/or N-acetyl cysteine. In the absence of comparative evidence of a specific technical effect, the objective technical problem had to be defined as the provision of an alternative to the compositions of D3. The appellant then went on to explain why, in its opinion,

the person skilled in the art would have found it obvious to add methionine to the pharmaceutical compositions of D3 (see the statement setting out the grounds of appeal, introductory part of section 2 on pages 7 and 8, and points 2.1 to 2.4).

IX. With its reply to the appeal, the patent proprietor (respondent) requested as its main request that the patent be maintained as granted (i.e. that the appeal be dismissed). The respondent also maintained auxiliary requests 1 to 5 filed in the proceedings before the opposition division and submitted further sets of amended claims as auxiliary requests 6 to 17.

In point 3.3.2 of its submission, the respondent pointed out that the appellant's arguments about the assessment of inventive step starting from the disclosure of D3 addressed only the embodiment comprising methionine but did not substantiate the objection against the alternative embodiment of claim 1 that comprised N-acetyl cysteine rather than methionine as the mandatory antioxidant component.

X. In a further written submission dated 10 October 2023, the appellant did not comment on the issue of obviousness of the N-acetyl cysteine embodiment starting from the disclosure of document D3. In its comments on the auxiliary requests, the appellant stated that, *inter alia*, auxiliary request 2 lacked an inventive step for the same reasons as the main request.

XI. In a communication under Article 15(1) RPBA issued in preparation for oral proceedings and advising the parties of its preliminary opinion, the board mentioned that, in accordance with the appellant's objections, documents D3 and/or D4 would be considered as starting

points for the assessment of inventive step (see points 1.1 and 3.3 of the board's communication).

XII. Oral proceedings before the board were held on 8 August 2024. The parties presented arguments on whether the subject-matter of the main request and auxiliary request 2 involved an inventive step starting from the disclosure of document D3.

In the context of the debate on the main request, the board did not admit a new line of argument of the appellant that addressed the claim embodiment comprising N-acetyl cysteine. As a consequence, the debate on auxiliary request 2 was also restricted to the embodiment comprising methionine.

After deliberation, the board arrived at the conclusion that, starting from the disclosure of document D3, the subject-matter of auxiliary request 2 (methionine embodiment) involved an inventive step.

The appellant stated that it had no further objection against auxiliary request 2 in relation to inventive step or any other provision of the EPC. The respondent withdrew its main request and auxiliary request 1.

XIII. Claim 1 of auxiliary request 2 reads as follows

1. A pharmaceutical composition comprising:

(i) a Clostridial toxin active ingredient;

(ii) a tonicity agent;

(iii) poloxamer 188; and

(iv) an antioxidant, wherein

the antioxidant comprises one or more of methionine and N-Acetyl-cysteine, and wherein

the antioxidant further comprises ethylene diamine tetraacetic acid sodium salt (EDTA).

XIV. Auxiliary request 2 contains 16 claims. Claims 2 to 11 are product claims dependent on claim 1. Claims 12 to 16 are independent claims. Claim 12 relates to the pharmaceutical composition according to any previous claim for a first medical use, claims 13 to 15 relate to different second-medical-use applications, and claim 16 relates to a cosmetic method. These uses and method all involve administering the composition according to any of claims 1 to 11 to a subject in need thereof.

XV. The appellant's arguments relevant to the present decision may be summarised as follows.

The composition defined in claim 1 of auxiliary request 2 differed from stabilised compositions disclosed in the examples of document D3, in particular Example 7, by including methionine and poloxamer 188.

The experimental data relied on by the respondent in support of the alleged technical effect of improved stabilisation were not based on protocols providing a correct comparison of the claimed subject-matter with the starting point in the prior art (i.e. D3).

Hence, it had not been conclusively shown that compositions according to claim 1, on account of including a distinguishing technical feature of claim 1, provided improved stability in comparison with stable compositions according to D3.

As a consequence, the objective technical problem was to provide an alternative composition.

Both methionine and poloxamer 188 were known as components suitable for pharmaceutical compositions with stabilised clostridial toxin. Moreover, poloxamer 188 was taught as a suitable surfactant in D3 itself and also in D2.

Thus, the person skilled in the art seeking to provide an alternative composition would not have needed inventive skill to arrive at compositions according to claim 1.

XVI. The respondent's arguments relevant to the present decision may be summarised as follows.

D3 did not represent the closest state of the art and should not be taken into account as a starting point for the assessment of inventive step.

If, nevertheless, inventive step were to be assessed starting from the disclosure of document D3, methionine and poloxamer 188 recited in claim 1 were components that each provided an unexpected improvement in stability in comparison with compositions containing polysorbate 20 as taught in document D3.

In the case of poloxamer 188, this was shown by the comparative data provided in Tables 6 and 8 of document D10.

The objective technical problem should, on account of these results, be formulated as the provision of a composition with improved high-temperature stability.

The prior art in D2 and D3 (relied on by the appellant) did not provide any motivation for the skilled person to use poloxamer 188 over polysorbate to attain improved stability. Only polysorbate was used in the practical examples described in D3. This showed a clear preference for polysorbate.

XVII. The appellant (opponent) requested that the decision under appeal be set aside and that the patent be revoked.

XVIII. The respondent (patent proprietor) requested that the patent be maintained in amended form on the basis of the claims of one of auxiliary requests 2 to 5, all filed by letter dated 28 October 2020, or on the basis of the claims of one of auxiliary requests 6 to 17, all filed with the reply to the appeal.

Reasons for the Decision

1. Non-admittance of a line of argument (Article 13(2) RPBA)

1.1 As set out above (see points VIII. to X.), it was only for the methionine embodiment of claim 1 that the appellant, in its written appeal submissions, provided a complete assessment of inventive step starting from the disclosure of document D3.

1.2 The objection against the N-acetyl cysteine embodiment was not adequately substantiated since the appellant did not provide any reasoning as to why, starting from the disclosure of document D3, this embodiment would have been obvious to the person skilled in the art.

1.3 Although the respondent pointed out the omission, the appellant did not provide this missing part of its reasoning in advance of the oral proceedings before the board (see points IX. and X. above).

1.4 The appellant's pertinent reasoning presented at the oral proceedings before the board is an amendment to the appellant's appeal case under Article 13(2) RPBA.

1.5 As no exceptional circumstances were invoked, the board did not admit the appellant's line of argument on inventive step, starting from the disclosure of D3, of the embodiment based on N-acetyl cysteine. This

decision, which was taken in the context of the debate on the main request, also applies to auxiliary request 2 for the same reasons.

2. Inventive step (Articles 100(a), 52(1) and 56 EPC)

Patent in suit

2.1 The patent in suit sets out that pharmaceutical compositions containing a protein active agent, such as a clostridial toxin, can be difficult to stabilise. Protein agents, typically present in such formulations in very low concentrations, are susceptible to degradation and have a tendency to adhere to solid surfaces such as container walls (see paragraphs [0003] to [0008] of the patent specification).

2.2 It was known to use proteins such as albumin as stabilisers. Due to certain disadvantages of stabilising excipients that are proteins, the patent in suit aims, however, to provide a pharmaceutical composition in which a clostridial toxin active agent (such as a botulinum toxin) is stabilised by a non-protein excipient (see paragraphs [0004] and [0010] of the patent specification).

2.3 Claim 1 of auxiliary request 2 relates to a pharmaceutical composition comprising (i) a clostridial toxin active ingredient, (ii) a tonicity agent, (iii) poloxamer 188, and (iv) an antioxidant comprising EDTA and one or both of methionine and N-acetyl cysteine.

2.4 The following assessment of inventive step is for the embodiment in which the antioxidant in feature (iv) comprises methionine.

Starting point in the prior art

2.5 The appellant's sole remaining objection is based on the assessment of inventive step starting from the disclosure of document D3, in particular Example 7 (see point XII. above and the minutes of the oral proceedings before the board, page 3).

2.6 The respondent argued that D3 did not represent the closest state of the art and should, therefore, not be taken into account as a starting point for the assessment of inventive step. If D3 were selected as the starting point, this would, moreover, involve hindsight, this not being a correct approach when assessing inventive step. These arguments were also adopted by the opposition division in the decision under appeal (Reasons 19.2).

2.7 Thus, the respondent's concern seems to be, on the one hand, that D3 as the starting point is too close to the claimed invention (selected with hindsight) and, on the other hand, that it is not close enough (not the closest prior art).

2.8 Both arguments are flawed. The following general considerations are relevant.

2.8.1 Inventive step can, in principle, be assessed starting from any prior-art disclosure.

Article 56 EPC provides that an invention (i.e. the claimed subject-matter under consideration) involves an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art. The state of the art is any prior disclosure that is eligible under Article 56 EPC, i.e. the entire state of the art as defined in Article 54(2) EPC, without any ranking or distinction.

Any such prior disclosure may be used as the starting point for the assessment of inventive step and also as supplementary prior art in alternative scenarios with different starting points.

Accordingly, and in line with the established case law of the boards, if inventive step is to be acknowledged, the claimed subject-matter must be inventive starting from any potential starting point in the prior art.

If inventive step is to be denied, the choice of the starting point needs no specific justification (see Case Law of the Boards of Appeal of the European Patent Office, 10th edn. 2022, I.D.3.1).

2.8.2 The selection of a starting point serves the purpose of assessing inventive step and is performed not by the person skilled in the art but by the body deciding on inventive step, which selects from the cited prior-art disclosures that are eligible under Article 56 EPC.

The usual approach is to select a starting point that relates to the same or a similar purpose or objective as the claimed invention and corresponds as closely as possible to it in terms of technical features, as this presents the most relevant challenge to be overcome. The test is to establish if the claimed subject-matter would have involved an inventive step even starting from such a particularly "promising" starting point.

Depending on the circumstances of the individual case, either only one starting point or several alternative starting points will have to be considered.

2.8.3 The practice of focusing on one among several potential starting points on the basis of its greater similarity to the claimed subject-matter and its intended purpose (the so-called closest prior art) is a matter of efficiency for the deciding body. It may avoid having

to perform a detailed assessment of inventive step also for numerous comparatively more remote alternative starting points, in cases where inventive step is to be ultimately acknowledged over all these starting points.

The consideration in such cases is that, because an inventive step can be acknowledged in a scenario starting from the closest prior art, it can also be acknowledged, for at least the same reasons, starting from the more remote alternative starting points. The reasoning addressing the alternative starting points must at least set out why this criterion is met in each case. If it is not met, the starting point in question has to be considered independently in a separate assessment.

2.8.4 Nonetheless, its comparative remoteness does not prohibit any prior disclosure's consideration as a starting point in a detailed assessment according to the problem-and-solution approach. If a chosen starting point is too remote from the claimed subject-matter in terms of structural features and purpose, the problem-and-solution approach will simply not result in a finding of obviousness.

2.8.5 In view of the similarity criterion (see point 2.8.2 above), the starting point is by necessity selected with knowledge of the claimed subject-matter. This does not introduce a hindsight bias because any prior-art disclosure can in any case legitimately be taken as the starting point, and the claimed subject-matter must be inventive starting from any potential starting point (see point 2.8.1 above).

2.8.6 It is only in the ensuing stages of the problem-and-solution approach that hindsight might be a concern.

The following requirements ensure that inventive step is assessed without hindsight.

- The technical problem is determined objectively, and its formulation must not contain elements of the solution.
- The question:

  "What teaching would the skilled person seeking to solve the objective technical problem have derived from the disclosure providing the starting point in combination with any supplementary prior-art disclosures?"

  must be answered from the skilled person's point of view before the effective date.

2.8.7 For these reasons, the argument that the consideration of any particular starting point in the assessment of inventive step would somehow be prohibited because its selection involved hindsight or because it was not identified as the "closest" prior art is without merit.

An opponent is in any case not obliged to justify its choice of a starting point in terms of being "closer" than another starting point (see point 2.8.1 above). What an opponent must show, however, is why the claimed subject-matter would have been obvious in an assessment developed from the chosen starting point. If the assessment of inventive step from a given starting point results in a finding of obviousness, this starting point is evidently close enough to the claimed invention to decide the question of inventive step.

2.9 In the case at hand, a choice between several documents does not arise since the appellant's sole objection is based on D3 as the starting point. In this situation, it is appropriate for the board to examine the

appellant's objection by assessing inventive step starting from the disclosure of D3.

In view of the considerations set out in points 2.8.2 to 2.8.3 above, it is also legitimate to base the assessment of inventive step on the embodiment in D3 which has the most technical features in common with the claimed subject-matter, namely Example 7, because this is the most relevant test for inventive step in comparison with potential approaches based on alternative possible starting points within D3.

2.10 Like the patent in suit, document D3 seeks to provide an alternative to human serum albumin ("HSA") as a stabiliser in pharmaceuticals containing a protein agent (see D3: paragraphs [0001] and [0012]). *Clostridium botulinum* neurotoxins are mentioned as a preferred example for a protein agent that is used at low concentrations and that requires a protecting agent (see D3: paragraphs [0011], [0027] and [0034] to [0037]).

2.11 The alternative stabilising agent proposed in D3 is a composition of low-molecular weight, non-peptidic substances (see D3: paragraph [0013]). This composition has the following constituents: a surface-active substance; a mixture of at least two amino acids, which are either Glu and Gln or Asp and Asn; a disaccharide; and EDTA (see D3: claims 1 to 3, paragraphs [0016] to [0022]).

2.12 Example 7 of D3 (see paragraph [0060]) discloses a stabilised composition comprising 1.26 ng/ml *Clostridium botulinum* neurotoxin type A as the protein agent in combination with sucrose, polysorbate 80, EDTA, and the amino acids Glu, Gln, Asp and Asn. After sterile filtration, lyophilisation and reconstitution, 96 wt% of the protein agent was recovered, and its

biological activity was tested and confirmed. The lyophilised product also remained stable upon storage (Example 8).

Objective technical problem and solution

2.13 Sucrose is a tonicity agent as defined in the patent in suit (see the patent in suit, page 7, lines 25 to 27). The composition of claim 1 of auxiliary request 2 (methionine option, see point 2.4 above) differs from the composition of Example 7 of D3 by the presence of poloxamer 188 and methionine.

2.14 According to the respondent, both technical features have the effect of improving the composition's stability. The respondent did not argue that the alleged technical effect was based on an interaction between these two compounds, and the board is not aware of any reason for assuming that such an interaction exists. Hence, the technical effects of methionine and poloxamer 188 can be considered separately.

2.15 In the case of methionine, no convincing evidence was presented that adding this compound would improve the stability of a composition as described in D3.

2.16 In support of the alleged technical effect in the case of poloxamer 188, the respondent relied on post-published evidence provided in document D10 (see D10: Table 6 and Table 8). This evidence was taken into consideration for the following reasons.

2.16.1 In its letter of 10 October 2023, the appellant interpreted Order No. 2 of decision G 2/21 of the Enlarged Board of Appeal (OJ EPO 2023, A85) as meaning that, as a pre-condition for post-published evidence to be taken into account, the technical effect in question should be "clearly and unambiguously derivable from the

teaching of the application as filed", in analogy to the standard applied to evaluation of extension of subject-matter or novelty. However, decision G 2/21 does not support the appellant's contention as no reference is made to this particularly strict standard (also known as the gold standard).

Indeed, at the oral proceedings before the board, the appellant did not pursue this issue but instead contested only the probative value of document D10 (see point 2.18 below).

2.16.2 In any case, the information in the application as filed allows the board to conclude that the purported technical effect was recognised and achieved in connection with the claimed subject-matter at the effective date.

It is the object of the claimed invention to provide non-protein stabilising excipients for clostridial toxin agents. The application as filed and the patent in suit teach that all components of the claimed non-protein excipient function to stabilise the clostridial toxin agent. This includes the surfactant. According to the description, excipient components which can be used in the claimed invention enable a therapeutically effective amount of the clostridial toxin to be recovered using these agents (see the application as filed, paragraphs [0009], [0057], [0058], [0062] and the patent in suit, paragraphs [0010], [0024], [0025] and [0029]).

While there is no direct comparison in the application as filed demonstrating superiority of poloxamer 188 over polysorbate (used in D3) in respect of their stabilising effects, the examples in the application as filed show a preference for poloxamer 188 in the presence of methionine. Moreover, all formulations

containing EDTA have poloxamer 188 as the surfactant (see formulations 26 and 27). Stable formulations containing poloxamer 188 and methionine are disclosed (see formulations 2, 12 and 20). The two formulations shown that contained methionine in association with polysorbate ("Tween 20®") were not particularly stable in comparison (Table 1: "Comparator 1", Table 2: "Comparator 3").

Since the original teaching on the surfactants concerns their stabilising effect and there is at least indirect evidence in the application as filed that superiority of poloxamer 188 over polysorbate had been recognised at the filing date, supplementary data on the stabilising effect can be taken into account where this is necessary for comparison with the starting point in the prior art.

2.17 D10 describes an experiment in which the impact of the surfactant was studied for botulinum toxin type A compositions comprising only a buffer and methionine (Table 8), and for compositions that additionally included the tonicity agent trehalose (Table 6). Either poloxamer 188 ("P188") or polysorbate 20 (Tween-20®, abbreviated as "Tw-20") was used as the surfactant. The potency of the formulations was tested by a cell-based potency assay ("CPBA") after filling the bulk solutions into glass vials (initial potency) and again after storage for one month at 40°C (Tables 6 and 8) and also after storage for one month at -70°C (Table 8). The results reported in D10 are reproduced below.

The conclusion reported in D10 is that the formulations comprising poloxamer 188 provided improved stability after storage at 40°C or -70°C for one month relative to the formulations containing polysorbate (see D10, paragraphs [0173] and [0174]).

Table 6: Liquid formulations

Formulation no.	Tre	Tw-20	P188	Met	Buffer	Storage time (Months)	Storage Temp.	CBPA (U/mL) Initial	CBPA (U/mL) 1 month
29	8	0	4	0.2	20 mM His pH 6.0	1	40°C	133	138
30*	8	0.04	0	0.2	20 mM His, pH 6.0	1	40°C	114	9

Tre = Trehalose; P-188 = Poloxamer-188; Tw-20 = Tween-20; Met = L-Methionine; His = L-Histidine.
CBPA gives the residual activity expressed in U/ml
*this formulation does not form part of the invention and is provided for information only

Table 8: Liquid formulations

Formulation No.	**Tre**	**Sucr**	**Tw-20**	**P188**	**Met**	**Buffer**	**Target potency (U/mL)**	**CBPA (U/ml) -70 °C**	**CBPA (U/ml) 40 °C,**
36*	0	0	0.04	0	0.2	20 mM His pH 6.0	100	25	1
37	0	0	0	4	0.2	20 mM His pH 6.0	100	105	72

Sucr = sucrose; Tre = Trehalose; P-188 = Poloxamer-188; Tw-20 = Tween-20; Met = L-Methionine; His = L-Histidine.
Initial = initial activity expressed in U/ml
Results after 1 month are the residual activity expressed in U/ml
*these formulations do not form part of the invention and are provided for information only

2.18 The appellant raised three objections to contest the probative value of the comparative tests described in D10.

(a) The first objection was that the surfactants had been used at different concentrations. While the poloxamer compositions contained 4% w/v of this surfactant, the polysorbate compositions only contained 0.04% w/v of surfactant. Thus, any difference in stability observed might be due to this difference in quantity rather than to the type of surfactant chosen.

(b) The second objection was that the formulations tested according to D10 were representative neither of compositions according to claim 1 nor

compositions according to Example 7 of D3 because they did not contain EDTA.

(c) The third objection was that formulations 36 and 37 in Table 8 did not contain a sugar/tonicity agent.

2.19 These objections cannot call the experiments' probative value into question for the following reasons.

(a) With regard to the first objection, the respondent explained that the suitable concentration ranges were different for each surfactant and that appropriate equivalent concentrations had been used. In the absence of any evidence that the polysorbate surfactant was used at an inadequate concentration, the appellant's objection remains speculative.

(b) The only difference between the samples that were compared in the experiments described in D10 is the choice of surfactant. The observed difference in stability can, therefore, in each case be attributed to the choice of surfactant, which is also the technical feature distinguishing the claimed compositions from the composition disclosed in D3.

The appellant did not object to the fact that comparative samples 30 and 36 of D10 used polysorbate 20 (used in numerous formulation examples of D3) instead of polysorbate 80 (used in Example 7 of D3). Thus, polysorbate 20 was considered representative of polysorbate surfactants as used in D3.

The appellant did not provide any reason why the outcome of the comparative tests should be different if both samples also contained EDTA. Without such a reason, the experiments can be

considered to represent a fair comparison between the compositions defined in claim 1 and the compositions in Example 7 of D3.

(c) The objection that some of the samples tested did not contain a tonicity agent is dismissed for analogous reasons. Moreover, this objection does not apply to all the comparative tests since formulations 29 and 30 shown in Table 6 did contain a tonicity agent (namely, trehalose).

2.20 For these reasons, it can be accepted that the choice of poloxamer 188 as the surfactant was shown to improve the stability of the compositions in comparison with compositions according to D3.

2.21 On this basis, the objective technical problem starting from the disclosure of Example 7 of D3 is to provide a pharmaceutical composition with a clostridial toxin active ingredient that has improved stability.

Obviousness of the solution

2.22 The cited state of the art does not provide any indication that the use of poloxamer 188 as the surfactant could result in a better stability of the formulations.

2.22.1 Document D3 mentions poloxamer 188 as a possible option for the choice of surfactant (see D3: claim 11 and paragraph [0030]) but does not teach that it is superior in terms of its stabilising effect. Rather, all formulation examples presented in D3 use polysorbate 20 or polysorbate 80.

2.22.2 Document D2, which also relates to clostridial toxin pharmaceutical compositions, mentions poloxamer 188 as a possible surfactant component (see, for instance, D2: paragraph [0089]), but again, without any teaching

on it giving superior stability. The only example of a surfactant component mentioned in the claims of D2 is polysorbate (see D2: claims 2, 7 and 14).

2.22.3 Thus, neither D3 nor D2 would have provided the person skilled in the art with the motivation to use poloxamer 188 over polysorbate to achieve better storage stability.

2.23 For these reasons, the subject-matter of claim 1 of auxiliary request 2 involves an inventive step within the meaning of Article 56 EPC.

2.24 The subject-matter of all other independent claims (claims 12 to 16) relates to the administration of the composition according to claim 1 (see point XIV. above). The dependent claims (claims 2 to 11) refer back to claim 1. As a consequence, the subject-matter of claims 2 to 16 involves an inventive step for the same reasons as set out for the subject-matter of claim 1.

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 with the following claims and a description to be possibly adapted thereto:

   Claims 1 to 16 of auxiliary request 2 filed on 28 October 2020 and maintained with the reply to the appeal.

The Registrar: The Chairman:

A. Vottner B. Rutz

Decision electronically authenticated