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Datasheet for the decision of 6 April 2022

Case Number: T 0046/20 - 3.3.07

Application Number: 12765216.2

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Language of the proceedings: EN

Title of invention:
LYOPHILIZED PREPARATION OF BOTULINUM TOXIN

Patent Proprietor:
Medy-Tox Inc.

Opponent:
IPSEN PHARMA S.A.S.

Headword:
Lyophilized preparation of botulinum toxin / MEDY-TOX

Relevant legal provisions:
EPC Art. 83, 54, 56

Keyword:
Sufficiency of disclosure - (yes)
Novelty - (yes)
Inventive step - (yes)

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Case Number: T 0046/20 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 6 April 2022

Appellant: (Opponent)	IPSEN PHARMA S.A.S. 65, Quai Georges Gorse 92100 Boulogne-Billancourt (FR)
Representative:	Plasseraud IP 66, rue de la Chaussée d'Antin 75440 Paris Cedex 09 (FR)
Respondent: (Patent Proprietor)	Medy-Tox Inc. 78 Gak-ri 1-gil Ochang-eup Cheongwon-gun, Chungchongbuk-do 363-885 (KR)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 7 November 2019 rejecting the opposition filed against European patent No. 2692350 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	J. Lécaillon
	L. Basterreix

Summary of Facts and Submissions

I. European patent EP 2 692 350 was granted on the basis of 12 claims. The independent claim of the patent as granted read as follows:

"1. A pharmaceutical lyophilized preparation comprising:

botulinum toxin, polysorbate, and methionine; and one or more components selected from the group consisting of sugar, sugar alcohol, and an ionic compound;
wherein the preparation is free of an animal protein stabilizer."

II. An opposition was filed against the patent on the grounds that its subject-matter lacked novelty and inventive step and it was not sufficiently disclosed.

III. The opposition division took the decision to reject the opposition.

IV. The decision of the opposition division, posted on 7 November 2019, cited *inter alia* the following documents:

D1: US 2003/0118598 A1
D4: WO 2006/005910 A2

V. The opposition division decided in particular as follows:

(a) The subject-matter of the granted patent was sufficiently disclosed. In particular the stability

effect was not part of the claims, so that its achievement was not an issue of sufficiency of disclosure.

(b) The subject-matter of the granted claims was novel. In particular, to arrive at the presently claimed subject-matter, individual passages of D1 would have to be selected and combined. Such a combination was not directly and unambiguously disclosed.

(c) D4 was the closest prior art. The subject-matter claimed differed from example 1 of D4 in that the composition further contained methionine. None of D1, D3 or D5 suggested to add methionine to the composition of example 1 of D4 to solve the objective technical problem of providing a lyophilised preparation comprising botulinum toxin with improved stability on long-term storage at high temperatures.

VI. The opponent (appellant) lodged an appeal against the above decision of the opposition division.

VII. With its reply to the appellant's statement setting out the grounds of appeal the patent proprietor (respondent) defended its case on the basis of the patent as granted as the main request, and on the basis of auxiliary requests 1, 2, 2*, 3A, 3B, 3B*, 4A, 4B, 4B*, 5A, 5B, 5B* and 6. These auxiliary requests were filed during first instance proceedings on 3 September 2019 and 20 September 2019 and resubmitted with the reply to the statement setting out the grounds of appeal.

VIII. Oral proceedings were held by videoconference on 6 April 2022. In the course of the oral proceedings, the respondent withdrew all requests but auxiliary request 6, which became the new main and sole request.

IX. The content of the claims upon which the present decision is based can be illustrated as follows:

The independent claim of the main request read as follows:

"1. A pharmaceutical lyophilized preparation consisting of:

botulinum toxin, polysorbate, and methionine; and one or more components selected from the group consisting of sugar, sugar alcohol, and an ionic compound, wherein the sugar when present is included in an amount of 0.1 to 50 mg with respect to 100 units of the botulinum toxin, wherein the sugar alcohol when present is included in an amount of 0.1 to 50 mg with respect to 100 units of the botulinum toxin, wherein the ionic compound when present is included in an amount of 0.1 to 10 mg with respect to 100 units of the botulinum toxin, and wherein the polysorbate is included in an amount of 0.01 to 2 mg with respect to 100 units of the botulinum toxin;
wherein the preparation is free of an animal protein stabilizer."

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

XI. The respondent requested that a patent be granted on the basis of the new main request which was filed as

auxiliary request 6 with the reply to the statement setting out the grounds of appeal.

XII. The arguments of the appellant, as far as relevant for the present decision, can be summarised as follows:

(a) The botulinum toxin stability described in the patent in suit could only be achieved under specific conditions, in particular specific amounts of components, which led to a lack of sufficiency of disclosure.

(b) A lack of novelty arose over D1, namely over the disclosure of formulations B, C, E and F (see table 1, example 3) combined with the disclosure of methionine as most preferred stabilizer in paragraph [0185].

(c) The addition of methionine to the composition of example 1 of the closest prior art D4 was obvious.

XIII. The arguments of the respondent, as far as relevant for the present decision, can be summarised as follows:

(a) The main request met the requirements of Articles 123(2) and 123(3) EPC.

(b) The main request fulfilled the requirements of Article 83 EPC. In particular, the claims of the main request incorporated the amounts of the various components which were described as being preferred for the achievement of the toxin stability.

(c) The subject-matter of the claims of the main request was novel over D1, since D1 did not

directly and unambiguously disclose the combination of the specific compositions of the examples with any further excipient, in particular methionine.

(d) The appellant did not contest the inventiveness of the present main request, which involved an inventive step.

Reasons for the Decision

Main request (former auxiliary request 6)

1. Amendments

The subject-matter claimed in the main request (former auxiliary request 6) is disclosed in the original claims and the original description. Furthermore the scope of the claims was limited compared to the one of the granted claims. The appellant did not raise any objection under Articles 123(2) and 123(3) EPC. The Board considers that the requirements of Articles 123(2) and 123(3) EPC are fulfilled.

2. Sufficiency of disclosure

2.1 The objection of lack of sufficiency of disclosure of the appellant (initially raised in the context of the claims as granted, *i.e.* the former main request) concerned the fact that according to the description of the patent specific conditions, in particular specific amounts of components, were required to achieve the botulinum toxin stability described in the patent in suit.

2.2 As stated by the respondent in the written proceedings, the present claims have been limited to the

corresponding amounts of components identified as being preferred to achieve the described botulinum toxin stability. This was not contested by the appellant. Independently of the relevance of the achievement of a non-claimed technical effect for the issue of sufficiency of disclosure, the objection of the appellant does therefore not apply to the present amended claims.

2.3 Accordingly, the main request (former auxiliary request 6) meets the requirements of Article 83 EPC.

3. Novelty

3.1 During appeal proceedings the appellant objected to the novelty over D1 based on the disclosure of formulations B, C, E and F (see table 1, example 3) combined with the disclosure of methionine as most preferred stabilizer in paragraph [0185]. According to the appellant, each of the stabilising agents described in D1 (*i.e.* recombinant human serum albumin, polysaccharide and amino acid) acted through different mechanisms and could thus be combined. The combination of stabilising agents would furthermore be described as a possible option in paragraph [0152] due to the use of the terms "and/or". Consequently, there would be no reasons preventing the skilled person from combining the previous two embodiments (specific examples and preferred amino acid), thus anticipating the present compositions.

3.2 The formulations B, C, E and F of example 3 of D1 contain a botulinum toxin, recombinant human serum albumin (rHSA), polysorbate and an ionic compound but lack methionine. D1 does indeed generally disclose the use of rHSA, polysaccharide and amino acids (preferably

methionine, see [0185]) to replace human serum albumin as stabiliser for botulinum toxin (see paragraph [0152]). There is however no clear and unmistakable teaching to combine the specific formulations B, C, E or F with paragraph [0185] disclosing methionine as preferred amino acid. These specific formulations are indeed disclosed as final complete formulations (see biological evaluation of these formulations in Table 2 of D1), which do not require any further modification.

Moreover it appears clear from the overall description of D1, and in particular from paragraphs [0153] and [0175], that rHSA, on the one hand, and a polysaccharide and/or an amino acid on the other hand constitute separate embodiments. In this context the single sentence of paragraph [0152] referred to by the appellant, which may suggest that the combination of (a) rHSA and (b) a polysaccharide and/or an amino acid is envisaged, cannot be considered in isolation from the remaining parts of the description. Consequently D1 does not directly and unambiguously disclose a composition comprising rHSA and methionine, let alone the addition of methionine to the specific formulations B, C, E and F.

3.3 Regarding the argument of the appellant that there would be no reasons preventing the skilled person from combining different passages of D1, the Board notes that this criterion is not pertinent in the present case. As explained above (see point 3.2), the embodiments combined by the appellant are individual separate embodiments not linked to each other in any manner. The formulations B, C, E and F are representative of the embodiment in which rHSA is used as stabiliser. It is therefore not representative of the alternative general embodiment relating to the use

of an amino acid as stabiliser. The passage of the Case Law of the Boards of Appeal referred to by the appellant (see Case Law of the Boards of Appeal, 9th Edition 2019, I.C.4.2, fifth paragraph) addresses the combination of an example with a general embodiment of the description wherein the example was representative of, or in line with, said general embodiment. It does therefore not apply to the present case. On the contrary the criterion of a clear teaching towards the combination of separate passages, as developed in the paragraphs of the Case Law of the Boards of Appeal, 9th Edition 2019, I.C.4.2 immediately preceding the passage cited by the appellant, applies and is not fulfilled (see point 3.2).

3.4 Accordingly, the main request (former auxiliary request 6) complies with the requirements of Article 54 EPC.

4. Inventive step

4.1 As confirmed by the appellant during the oral proceedings, its argumentation regarding the issue of inventive step (initially raised in the context of the claims as granted, *i.e.* the former main request) concerned only the addition of methionine to the composition of example 1 of the closest prior art D4, which contains a botulinum toxin, polysorbate, a sugar, an ionic compound, and histidine.

4.2 The claims of the present main request (filed as auxiliary request 6) have however been limited to compositions which do not contain *inter alia* histidine. The absence of histidine constitutes thus a further distinguishing feature *versus* the closest prior art. During oral proceedings, the appellant confirmed that

it had no arguments concerning this distinguishing feature.

4.3 In the absence of any explanation substantiating why the skilled person would have removed histidine from the closest prior art composition, the present compositions are considered to involve an inventive step.

4.4 As a result, the main request (former auxiliary request 6) fulfills the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The case is remitted to the opposition division with the order to maintain the patent on the basis of the claims of the new main request which was filed as auxiliary request 6 with the reply to the statement setting out the grounds of appeal, and a description to be adapted thereto.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated