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Datasheet for the decision of 2 February 2016

Case Number: T 1036/11 - 3.3.04

Application Number: 04019048.0

Publication Number: 1488803

IPC: A61K38/48, A61P21/02

Language of the proceedings: EN

Title of invention:
Neurotoxic component of botulinum toxins for treating cervical dystonia

Patent Proprietors:
Allergan, Inc.
Merz Pharma GmbH & Co. KGaA

Opponent:
Solstice Neurosciences, Inc. (opposition withdrawn)

Headword:
Neurotoxic component/ALLERGAN

Relevant legal provisions:
EPC Art. 76(1)

Keyword:
Divisional application - added subject-matter (yes)

This datasheet is not part of the Decision.
It can be changed at any time and without notice.

Decisions cited:
G 0001/06, T 1972/10

Catchword:

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Case Number: T 1036/11 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 2 February 2016

Appellant: (Patent Proprietor 1)	Allergan, Inc. 2525 Dupont Drive Irvine, CA 92612 (US)
Appellant: (Patent Proprietor 2)	Merz Pharma GmbH & Co. KGaA Eckenheimer Landstrasse 100 60318 Frankfurt Main (DE)
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 20 December 2010 revoking European patent No. 1488803 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	R. Morawetz
	L. Bühler

Summary of Facts and Submissions

I. The appeal of the patent proprietors ("appellants") lies against the decision of the opposition division to revoke European patent No. EP 1 488 803, entitled "Neurotoxic component of botulinum toxins for treating cervical dystonia".

II. The following documents are referred to in the decision:

D1 WO95/17904

D2 EP 1 005 867 A2

D3 EP 1 366 770 A2

D5 Moyer E. and P.E. Setler, Botulinum toxin type B: experimental and clinical experience, in: "Therapy with botulinum toxin", Jankovic J. and M. Hallet (Eds.), New York, Marcel Dekker (1994), pages 71-85

D6 Jankovic J. and M.F. Brin, The New England Journal of Medicine (1991), vol. 324, pages 1186-1194

D13 Declaration of Dr. K.R. Aoki dated 22 September 2010

D14 Declaration of Dr. M.F. Brin dated 10 September 2010

D15 Declaration of Dr. L.A. Smith dated 10 September 2010

III. The present patent is based upon European patent application No. 04019048.0, which is a divisional

application of European patent application No. 03015589.9 (parent application, document D3), which is itself a divisional of European patent application No. 99203920.6 (grand parent application, document D2), which is itself a divisional of European patent application No. 95906674.7 (root application, document D1).

IV. An opposition had been filed on the ground *inter alia* of Article 100(c) EPC in conjunction with Article 76(1) EPC. After the opponent had withdrawn its opposition on 17 November 2010, the opposition division continued the proceedings of its own motion. In the decision under appeal the opposition division dealt with a single request, all auxiliary requests having been withdrawn. It decided that there was no basis in any of the preceding applications for claiming the second medical use of the neurotoxic component of Botulinum toxin, and that therefore the requirements of Article 76(1) EPC were not met.

V. With their statement of grounds of appeal the appellants - who are the sole party to the appeal proceedings - filed a main request and auxiliary requests I to V. These were said to be the same requests as those filed in the first instance proceedings.

VI. The board issued a communication giving its preliminary opinion on the requests on file. The board also remarked on some discrepancies it had noted between the main requests as submitted with the statement of grounds of appeal and as filed in the first instance proceedings.

VII. During oral proceedings held before the board on 2 February 2016 the appellants confirmed that the main request was identical to the main request before the

opposition division. They withdrew auxiliary requests I to V.

Claim 1 of the main request reads:

"1. Use of the neurotoxic component of Botulinum toxin for the manufacture of a medicament for treatment of cervical dystonia, with the proviso that the treatment does not comprise

(i) administering to the patient a therapeutically effective amount of botulinum toxin of a selected serotype until the patient experiences loss of clinical response to the administered botulinum toxin and thereafter administering to the patient another botulinum toxin of a different serotype being administered in therapeutically effective amounts, wherein at least one of the above botulinum toxins is in the form of the neurotoxic component; or
(ii) administering to the patient a therapeutically effective amount of a combination of at least two neurotoxins selected from a group consisting of botulinum toxin types A, B, C, D, E, F and G, an amount of each selected neurotoxin being further selected to control a duration of therapeutic activity of the administered combination, wherein at least one of the above botulinum toxins is in the form of the neurotoxic component."

At the end of the oral proceedings the chairwoman announced the board's decision.

VIII. The arguments of the appellants can be summarised as follows:

Main (sole) request

Articles 100(c) and 76(1) EPC: claim 1

The critical issue was whether document D1 disclosed the medical use of the neurotoxic component - which was the active part of the neurotoxin complex without the accompanying non-active proteins - on its own. Document D1 clearly disclosed that the use of the neurotoxic component was part of the invention. Thus it disclosed in the first paragraph on page 1 that the invention related to methods of treating various disorders and conditions with Botulinum toxins.

Pages 2 and 3 of document D1 went on to explain what Botulinum toxins were, and which toxins could be used in the context of the invention. It was clear from the final sentence of the second complete paragraph on page 3 that the neurotoxic component could be used in the invention, in either the single chain or dichain form.

Where document D1 referred to "Botulinum toxins" or "toxins" in general, the skilled reader therefore understood this to mean the whole group of toxins, including the sub-groups of different serotypes (A, B, C, etc.) and the sub-groups of different toxin forms (complex, single chain neurotoxic component, dichain neurotoxic component etc.).

The skilled reader of document D1 would be aware that before the priority date of the patent the term "Botulinum toxin" did not refer exclusively to the

complex but was also used in the art to refer to the neurotoxic component only; see document D5 on page 72, last sentence of first paragraph and first sentence of third paragraph and document D6 on page 1186, left hand column, second paragraph.

Declaration D13 by one of the patent's co-inventors explained that it was the inventors' understanding that the active entity in a Botulinum toxin-containing composition was the neurotoxic component, sometimes referred to as "toxin" for short. As explained in declaration D13, the inventors had established that the neurotoxic component in either its single or dichain form had therapeutic value and could be formulated as a stable preparation, contrary to the prevailing view in the field. There was the clear intention to use the neurotoxic component for therapeutic purposes and thus it was expressly stated that it had utility within the method of the invention. Declarations D14 and D15 confirmed that this was fully derivable from the patent.

IX. The appellants requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request.

Reasons for the Decision

Main (sole) request

Articles 100(c) and 76(1) EPC: claim 1

1. Article 76(1), second sentence, EPC provides that a European divisional application may be filed only in respect of subject-matter which does not extend beyond the content of the earlier application as filed.

2. It is established case law of the Boards of Appeal that, in order to determine whether or not a divisional application extends beyond the content of the earlier application as filed, the same principles are to be applied as when determining whether or not an amendment offends against Article 123(2) EPC. Thus, the subject-matter of the divisional application must be directly and unambiguously derivable from the earlier application as filed (see Case Law of the Boards of Appeal of the EPO, 7th edition, 2013, section II.F.1.1). In the case of a sequence of applications consisting of a root (originating) application followed by divisional applications, each divided from its predecessor, for a divisional application of that sequence to comply with Article 76(1), second sentence, EPC it is a necessary and sufficient condition that anything disclosed in it must be directly and unambiguously derivable from what is disclosed in each of the preceding applications as filed (see G 1/06, OJ 2008, 307, headnote).

3. Claim 1 relates to the use of the neurotoxic component of Botulinum toxin for the manufacture of a medicament for the treatment of cervical dystonia. It was uncontested that the neurotoxic component referred to in claim 1 is understood to be the active part of the neurotoxin complex without the accompanying non-active proteins.

4. The issue to be decided in the present case is whether or not the claimed use of the neurotoxic component of Botulinum toxin is disclosed in each of the preceding applications as filed, i.e. documents D1, D2 and D3 (see G 1/06, *supra*). Thus, if it is not disclosed in one of them, e.g. in the root application (document D1), there is no need to consider the disclosures of the

other preceding applications.

5. Document D1 discloses "methods for treating various disorders and conditions, with Botulinum toxins" (see page 1, lines 7 to 9). According to page 2, lines 24 to 33 of document D1 "The term Botulinum toxin is a generic term embracing the family of toxins produced by the anaerobic bacterium *Clostridium botulinum* and, to date, seven immunologically distinct neurotoxins have been identified. These have been given the designations A, B, C, D, E, F and G. For further information concerning the properties of the various Botulinum toxins, reference is made to the article by Jankovic and Brin, *The New England Journal of Medicine*, No. 17, 1990, pp. 1186-1194 ..." [note by the board: this is document D6 in the present proceedings].

6. In the following two paragraphs on page 3, lines 5 to 24, document D1 provides a description of the structure of the neurotoxic component of Botulinum toxin. This passage is set out below in full:

"The neurotoxic component of Botulinum toxin has a molecular weight of about 150 kilodaltons and is thought to comprise a short polypeptide chain of about 50 kD which is considered to be responsible for the toxic properties of the toxin, i.e., by interfering with the exocytosis of acetylcholine, by decreasing the frequency of acetylcholine release, and a larger polypeptide chain of about 100 kD which is believed to be necessary to enable the toxin to bind to the presynaptic membrane.

The "short" and "long" chains are linked together by means of a simple disulfide bridge. (It is noted that certain serotypes of Botulinum toxin, e.g., type E, may exist in the form of a single chain un-nicked protein,

as opposed to a dichain. The single chain form is less active but may be converted to the corresponding dichain by nicking with a protease, e.g., trypsin. Both the single and the dichain are useful in the method of the present invention.)"

7. The board is not persuaded that it is clear from the final sentence of the second complete paragraph on page 3 that the neurotoxic component of Botulinum toxin - without the accompanying non-active proteins - can be used in the invention. The sentence at issue needs to be considered in its context. It forms part of a bracketed passage consisting of three sentences (see point 6 above). This passage explains that certain serotypes of Botulinum toxin may exist in the form of a single chain as opposed to a dichain, that the single chain may be converted to the corresponding dichain, and that both the single and the dichain are useful in the method of the invention. The disclosure of the use of single and the dichain forms is thus made in the context of the Botulinum toxin, not in that of the neurotoxic component of Botulinum toxin. The use of the neurotoxic component of Botulinum toxin is thus not directly and unambiguously derivable from the passage on page 3 of document D1 (see also decision T 1972/10, reasons, point 21).

8. Therefore the appellants' argument that where document D1 refers to "Botulinum toxins" or "toxins" in general the skilled reader understands this to mean the different toxin forms, including complex, single chain neurotoxic component and dichain neurotoxic component, fails because it is based on the submission that document D1 discloses on page 3 that the use of the neurotoxic component is part of the invention.

9. The appellants further submitted that before the priority date of the patent the term "Botulinum toxin" did not refer exclusively to the complex but was also used in the art to refer to the neurotoxic component only, and that a skilled reader of document D1 would be aware of this. The board is not persuaded by this line of argument either.

10. Document D1 explains that "Botulinum toxin" is a generic term and refers the reader to document D6 for further information concerning the properties of the various Botulinum toxins (see point 5 above). Document D6 (see page 1186, left hand column, second paragraph) discloses that "the neurotoxic component of botulinum toxin (...) forms a complex with nontoxic proteins and hemagglutinin."

11. Document D5, also relied on by the appellants in this context, discloses (see page 72, first paragraph) that "Formation of an association complex with the nontoxin proteins appears to stabilize the activity of BTXs [Botulinum toxins], perhaps by helping to maintain a necessary secondary or tertiary structure (...). It is presumably for this reason that the only currently commercially available BTX for clinical use, type A, is formulated in the form of a toxin-hemagglutinin-containing nontoxin protein complex, rather than as a formulation of the pure toxin". Thus, also according to document D5, "Botulinum toxin" refers to the complex of neurotoxic component, non-toxic proteins and hemagglutinin while "pure toxin" is used for the neurotoxic component.

12. The board concludes that before the priority date of the patent the term "Botulinum toxin" had a defined meaning for the person skilled in the art and denoted the

complex of neurotoxic component, non-toxic proteins and hemagglutinin. There is also no indication in document D1 that this term had a meaning different from that prevailing in the art before the priority date (see also point 5 above). Accordingly, the board sees no reason why the skilled person reading document D1 should understand "Botulinum toxin" to mean anything but the complex.

13. The appellants' final argument, which is based on the submission that, contrary to the prevailing view at the time, the inventors had determined that the neurotoxic component could be formulated as a stable preparation in both single and dichain form, is not found persuasive either.

14. As set out above (see point 11), at the priority date of the patent the only commercially available Botulinum toxin for clinical use, type A, was formulated in the form of a complex. The notion that the neurotoxic component could be formulated as a stable preparation on its own is not disclosed in document D1 which is completely silent as regards the separation of the neurotoxic component from the accompanying non-active proteins present in the complex. The skilled person thus has no reason to understand a reference to "toxin" in document D1 to mean the neurotoxic component.

15. The board concludes from the above that the claimed use of the neurotoxic component of Botulinum toxin is not disclosed in document D1. Therefore the main request does not meet the requirements of Article 76(1), second sentence, EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated