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**Datasheet for the decision  
of 15 May 2012**

**Case Number:** T 0611/08 - 3.3.04  
**Application Number:** 00203421.3  
**Publication Number:** 1103267  
**IPC:** A61K 38/16, A61P 29/02  
**Language of the proceedings:** EN

**Title of invention:**

Botulinum toxins for treating pain associated with muscle disorders

**Patentee:**

ALLERGAN, INC.

**Opponents:**

IPSEN PHARMA S.A.S.  
Revanche Therapeutics, Inc.

**Headword:**

Botulinum toxins/ALLERGAN INC.

**Relevant legal provisions:**

EPC Art. 123(2)

**Relevant legal provisions (EPC 1973):**

-

**Keyword:**

"Main request and 1<sup>st</sup> to 6<sup>th</sup> auxiliary requests: added subject-matter (yes)"

**Decisions cited:**

-

**Catchword:**

-



Case Number: T 0611/08 - 3.3.04

**DECISION**  
of the Technical Board of Appeal 3.3.04  
of 15 May 2012

**Appellant:** IPSEN PHARMA S.A.S.  
(Opponent 01) 65, Quai Georges Gorse  
FR-92100 Boulogne-Billancourt (FR)

**Representative:** Heinemann, Monica  
Abitz & Partner  
Patentanwälte  
Postfach 86 01 09  
D-81628 München (DE)

**Respondent:** ALLERGAN, INC.  
(Patent Proprietor) 2525 Dupont Drive  
Irvine CA 92612 (US)

**Representative:** HOFFMANN EITLE  
Patent- und Rechtsanwälte  
Arabellastraße 4  
D-81925 München (DE)

**Party as of right:** Revance therapeutics, Inc.  
(Opponent 02) 2400 Bayshore Parkway, Suite 100  
Mountain View, CA 94043 (US)

**Representative:** Ruffles, Graham Keith  
Marks & Clerk LLP  
62-68 Hills Road  
Cambridge CB2 1LA (UK)

**Decision under appeal:** Interlocutory decision of the Opposition  
Division of the European Patent Office posted  
15 January 2008 concerning maintenance of  
European patent No. 1103267 in amended form.

**Composition of the Board:**

**Chairman:** C. Rennie-Smith  
**Members:** R. Gramaglia  
R. Morawetz

## Summary of Facts and Submissions

- I. The present European patent No. 1 103 267 having the title "Botulinum toxins for treating pain associated with muscle disorders" is based on European patent application No. 00 203 421.3, which is a divisional application of the earlier European patent application No. 95 906 674.7 (published as WO 95/17904 and EP 0 737 074).
- II. Notices of opposition were filed by opponents 01 and 02 requesting the revocation of the European patent on the grounds of Article 100(a) and (b) EPC on the grounds that the claims did not fulfil the requirements of Articles 54, 56 and 83 EPC.
- III. The opposition division came to the conclusion that granted claim 1 lacked novelty, whereas the subject-matter of the claims of the first auxiliary request then on file was found to meet the requirements of the EPC.
- IV. Claim 1 of the first auxiliary request as accepted by the opposition division (now main request before the board) read as follows:
- "1. The use of from 50 to 300 units of a botulinum toxin for the manufacture of a medicament for treating pain associated with a muscle disorder, whereby the muscle disorder is a hand, wrist, forearm or leg spasticity condition secondary to a stroke or a cerebral vascular event."

Claims 2 to 4 were directed to specific embodiments of the use according to claim 1.

V. The opposition division inter alia held that claim 1 of this request fulfilled the requirements of Article 123(2) EPC because the new features ("from 50 to 300 units" and "whereby the muscle disorder is a hand, wrist, forearm or leg spasticity condition secondary to a stroke or a cerebral vascular event") in claim 1 had a basis in Example 9 (paragraph [0062]) of the published "A1" application as filed.

VI. The appellant (opponent O1) filed an appeal against the decision of the opposition division. In reply thereto, the respondent (patentee) submitted with letter dated 23 December 2010 new claims in form of a first auxiliary request, of which claim 1 read as follows:

"1. The use of from 50 to 300 units of a botulinum toxin for the manufacture of a medicament for treating pain associated with a muscle disorder, whereby the muscle disorder is a hand, wrist, forearm or leg spasticity condition secondary to a stroke or a cerebral vascular event, wherein the medicament is for administration in the major muscles involved in severe closing of hand and curling of wrist or forearm or the muscles involved in closing the legs."

VII. Opponent O2 is a party as of right, but it did not take part in the appeal proceedings.

VIII. With letter dated 16 April 2012, the respondent filed further auxiliary requests 2<sup>nd</sup> to 6<sup>th</sup>.

Claim 1 of the 2<sup>nd</sup> auxiliary request read as follows:

"1. The use of from 50 to 300 units of a botulinum toxin for the manufacture of a medicament for treating pain associated with a muscle disorder, the muscle disorder being a hand, wrist and forearm spasticity condition secondary to a stroke or a cerebral vascular event, or a leg spasticity condition secondary to a stroke or a cerebral vascular event;  
wherein the medicament is for administration by injection into the major muscles involved in severe closing of the hand and curling of the wrist and forearm, or the muscles involved in closing the legs."

Claim 1 of the 3<sup>rd</sup> auxiliary request read as follows:

"1. The use of from 50 to 300 units of a botulinum toxin for the manufacture of a medicament for treating pain associated with a muscle disorder, the muscle disorder being a hand, wrist and forearm spasticity condition secondary to a stroke or a cerebral vascular event, or a leg spasticity condition secondary to a stroke or a cerebral vascular event;  
wherein the medicament is for administration by injection into the major muscles involved in severe closing of the hand and curling of the wrist and forearm, or the muscles involved in closing the legs;  
and wherein one unit of the botulin toxin is the equivalent amount of the toxin which kills 50% of a group of 18 to 20 female Swiss-Webster mice weighing about 20 g each."

Claim 1 of the 4<sup>th</sup> auxiliary request read as follows:

"1. The use of from 50 to 300 units of a botulinum toxin type A for the manufacture of a medicament for treating pain associated with a muscle disorder, the muscle disorder being a hand, wrist and forearm spasticity condition secondary to a stroke or a cerebral vascular event, or a leg spasticity condition secondary to a stroke or a cerebral vascular event; wherein the medicament is for administration to a human male by injection into the major muscles involved in severe closing of the hand and curling of the wrist and forearm, or the muscles involved in closing the legs."

Claim 1 of the 5<sup>th</sup> auxiliary request read as follows:

"1. The use of from 50 to 300 units of a botulinum toxin type A for the manufacture of a medicament for treating pain associated with a muscle disorder, the muscle disorder being a hand, wrist and forearm spasticity condition secondary to a stroke or a cerebral vascular event, or a leg spasticity condition secondary to a stroke or a cerebral vascular event; wherein the medicament is for administration to a human male by injection into the major muscles involved in severe closing of the hand and curling of the wrist and forearm, or the muscles involved in closing the legs;  
and

wherein one unit of the botulin toxin is the equivalent amount of the toxin which kills 50% of a group of 18 to 20 female Swiss-Webster mice weighing about 20 g each."

Claim 1 of the 6<sup>th</sup> auxiliary request read as follows:

"1. The use of from 50 to 300 units of a botulinum toxin type A for the manufacture of a medicament for treating pain associated with a muscle disorder, the muscle disorder being a hand, wrist, forearm or leg spasticity condition secondary to a stroke; wherein the medicament is for administration by injection into the major muscles involved in severe closing of the hand and curling of the wrist or forearm, or the muscles involved in closing the legs; and wherein one unit of the botulin toxin is the equivalent amount of the toxin which kills 50% of a group of 18 to 20 female Swiss-Webster mice weighing about 20 g each."

- IX. Oral proceedings were held on 15 May 2012, during which the respondent filed a new main request and new auxiliary requests 1 to 6, all of which were successively withdrawn.
- X. The submissions by the appellant (opponent O1), insofar as they are relevant to the present decision, can be summarized as follows:

*Main Request*

- Claim 1 represented an unallowable generalisation of Example 9 (paragraph [62]) of the published "A1" application, because the differences listed below, between claim 1 and said example, had an influence on the dose:

- (i) The age of seventy years is specified in the example, while omitted in claim 1;

- (ii) In the example, the muscle spasms were characterized as being severe and causing closing of hand and curling of wrist and forearm or the muscles involved in the closing of legs, while in claim 1 no degree of severity and no specific spastic symptom was indicated;
- (iii) The patient of the example suffered from more than one spastic muscle while according to claim 1, the muscles disorders of the hand, wrist, forearm or leg were linked by "or", indicating that only one muscle disorder at a time was considered;
- (iv) The example was not limited to the treatment of pain since it stated that the patient experienced relief of symptoms of severe closing of hand and curling of wrist and forearm or the muscles involved in the closing of legs upon administration of 50 to 300 units of botulinum toxin.

*1<sup>st</sup> Auxiliary Request*

- Claim 1 of this request referred to the "major muscles involved in severe closing of hand and curling of the wrist or forearm", contrary to the supporting wording in Example 9.



XI. The submissions by the respondent (patentee) can be summarized as follows:

*Main Request*

- The patient of Example 9 of the published "A1" application was merely an illustration of the utility of botulinum toxin when treating pain. This utility was not limited to male patients at the age of 70.
- The claimed treatment was about the treatment of pain caused by certain spasticity conditions specified in claim 1. These spasticity conditions were derivable from Example 9, which was not confined to the treatment of specific muscles of each of the hand, wrist, forearm or legs. The patient could suffer from a spastic condition of just one of these body parts (e.g. the hand).
- There was no need to stipulate "severe closing of the hand" in claim 1, as disclosed in Example 9 because the treatment of muscle spasms was a separate effect, and present claim 1 was not directed to the treatment of muscle spasms.
- The control of pain was mentioned not only in the title of Example 9, but also throughout the application as filed (see e.g. paragraph [0026] of the published "A1" application).

*1<sup>st</sup> Auxiliary Request*

- Claim 1 of this request was based on claim 1 of the main request, with the specification that the medicament is "for administration in the major muscles involved in severe closing of hand and curling of wrist or forearm or the muscles involved in closing the legs". This feature was based on page 8, lines 16-18 of the published "A1" application.

*2<sup>nd</sup> Auxiliary Request*

- Claim 1 of the 2<sup>nd</sup> Auxiliary Request included restricted definitions of the treated spasticity condition, the route of administration (injection) and the muscles into which the botulinum toxin was administered. These amendments were based on Example 9 (paragraph [62]) of the published "A1" application.

*3<sup>rd</sup> Auxiliary Request*

- Claim 1 of the 3<sup>rd</sup> Auxiliary Request differed from Claim 1 of the 2<sup>nd</sup> Auxiliary Request in that it defined the method for measuring the potency of the botulinum toxin set out on page 4 (paragraph [25]) of the published "A1" application.

*4<sup>th</sup> Auxiliary Request*

- Claim 1 of the 4<sup>th</sup> Auxiliary Request differed from Claim 1 of the 2<sup>nd</sup> Auxiliary Request in that the botulinum toxin was restricted to being type A toxin and the patient was a human male (see Example 9

(paragraph [62]) and claim 17 of the published "A1" application). Moreover claims 2 and 3 of the 2<sup>nd</sup> Auxiliary Request were no longer present in this request.

*5<sup>th</sup> Auxiliary Request*

- Claim 1 of the 5<sup>th</sup> Auxiliary Request supplemented Claim 1 of the 4<sup>th</sup> Auxiliary Request by the potency measurement method defined in claim 1 of the 3<sup>rd</sup> Auxiliary Request.

*6<sup>th</sup> Auxiliary Request*

- Claim 1 of the 6<sup>th</sup> Auxiliary Request represented a restriction of claim 1 of the 1<sup>st</sup> Auxiliary Request in that the reference to a cerebral vascular event had been deleted and the botulinum toxin was restricted to being type A toxin. Claim 1 of the 6<sup>th</sup> Auxiliary Request also defined the potency measurement method recited in claim 1 of the 3<sup>rd</sup> and 5<sup>th</sup> Auxiliary Requests. Claim 2 of the 6<sup>th</sup> Auxiliary Request defined the patient as being a human male based on Example 9 (paragraph [62]) of the published "A1" application.

XII. The appellant (opponent 01) requested that the decision under appeal be set aside and that the European patent No. 0 754 059 be revoked.

The respondent (patentee) requested as main request that the appeal be dismissed, or that the decision under appeal be set aside and the patent be maintained on the basis of the claims of the first auxiliary

request filed with letter dated 23 December 2010, or on the basis of the claims of one of auxiliary requests 2<sup>nd</sup> to 6<sup>th</sup> filed with letter dated 16 April 2012.

## **Reasons for the Decision**

### *Main Request*

#### *Article 123(2) EPC*

1. Article 123(2) EPC prohibits amendments generating "subject-matter which extends beyond the content of the application as filed". In order to determine whether or not the subject-matter of an amended claim satisfies this requirement it has to be examined whether that amended claim comprises technical information which a skilled person would not have objectively and unambiguously derived from the application as filed. It was agreed that the published "A1" application represented the application as filed.
2. Claim 1 of the main request differs from claim 1 as filed by the inclusion of a dosage interval ("from 50 to 300 units") and by the definition of the muscle disorder as being "a hand, wrist, forearm or leg spasticity condition secondary to a stroke or a cerebral vascular event".
3. The opposition division concluded that these new features in claim 1 of this request had a basis in the example described on page 8, lines 10 to 20 of the published "A1" application, which reads as follows:

"Example 9

The use of Botulinum toxin Type A-G in the Treatment of Muscle Spasms and Control of Pain Associated with Muscle Spasms in Spasticity Conditions Secondary to Stroke, Traumatic Brain or Spinal Chord Injury

[0062] A male, age 70, post-stroke or cerebral vascular event, is injected with 50 to 300 units of Botulinum toxin in the major muscles involved in severe closing of hand and curling of wrist and forearm or the muscles involved in the closing of the legs such that the patient and attendant have difficulty with hygiene. Relief of these symptoms occurs in 7 to 21 days."

4. However, the appellant maintains that the differences (i) to (iv) (see paragraph X supra) between claim 1 and Example 9 (paragraph [62]) of the published "A1" application have an influence on the dose of botulinum toxin to be administered. Hence, the interval "50 to 300 units" (Example 9) cannot be generalised, as done in present claim 1.
  
5. The board observes that the Example described on page 8, lines 10 to 20 of the published "A1" application (see point 3 supra) relates to the treatment of **both** the pain associated with muscle spasms (originating from spasticity conditions secondary to stroke, traumatic brain or spinal chord injury) **and** the muscle spasms themselves (see the title of the example and lines 18-19 of page 8, where it is stated that the "relief of these symptoms occurs in 7 to 21 days").

Therefore, the board agrees with the appellant's view that this example is not limited to the treatment of pain only. Example 9, in the board's view, is indeed akin to Example 7 of the published "A1" application, which also deals with the treatment of both pain and spasms (see the wording "relief of pain associated with muscle spasms, possible reduction of jaw clenching occurs in about 1-3 days").

6. Once it has been established that Example 9 on page 8, lines 10 to 20 of the published "A1" application is not limited to the treatment of pain, the question arises whether or not treating pain only (claim 1) requires the same dose of botulinum toxin as treating both pain and spasms (the example of the published "A1" application).
  
7. In connection with this, the respondent has always insisted on the differences existing between the treatment of pain and the treatment of spasms (submission dated 3 April 2006, page 4, lines 3-4: "Treatment of pain does not necessarily involve a treatment of the muscle disorder *per se*"; submission dated 23 December 2010, page 3, lines 2-4: "As the claim is about the treatment of pain, the severity of the closure of the hand is obviously not relevant"; submission of 16 April 2012, page 3, last paragraph: "The treatment of muscle spasms is a separate effect"; submissions during the oral proceedings before the board: "The severity of spasms does not correlate 1:1 to the severity of pain" and "Severity of pain and not of spasm is relevant for the dose to be administered").

8. The board notes that this respondent's view is in keeping with paragraph [0026] of the published "A1" application, according to which a smaller dose (up to 50 U) of botulinum toxin may be used for the relief of pain.
  
9. In view of the foregoing, the board must conclude that the dosage of "50 to 300 units" (Example 9 of the published "A1" application) was meant for the treatment of both severe muscle spasticity conditions and pain, not for the treatment of pain alone (present claim 1). Hence, the technical feature in present claim 1 that "50 to 300 units" botulinum toxin should be used for the treatment of pain only cannot be derived directly and unambiguously from the application as filed and the subject-matter of claim 1 of the main request does not satisfy the requirements of Article 123(2) EPC.

*1<sup>st</sup> to 6<sup>th</sup> Auxiliary Requests*

10. The conclusion of point 9 supra extends to claim 1 of all the Auxiliary Requests, since they all require that 50 to 300 units botulinum toxin be used for the treatment of pain only.
  
11. For each of the above reasons neither of the respondent's requests satisfies the requirements of Article 123(2) EPC. Therefore neither request is allowable.

**Order**

**For these reasons it is decided that:**

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:

B. Atienza Vivanco

C. Rennie-Smith