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**Datasheet for the decision
of 20 May 2014**

Case Number: T 2350/10 - 3.3.02

Application Number: 04713111.5

Publication Number: 1597584

IPC: G01N33/68, G01N33/94, G01N33/50

Language of the proceedings: EN

Title of invention:
QUANTIFICATION OF BOTULINUM TOXIN

Patent Proprietor:
Ipsen Biopharm Limited

Opponent:
Merz Pharma GmbH & Co. KGaA

Headword:
Quantification of Botulinum Toxin/IPSEN

Relevant legal provisions:
EPC Art. 123(2)

Keyword:
Amendments - added subject-matter (yes)

Decisions cited:
G 0004/92, T 0263/05, T 0789/89

Catchword:



**Beschwerdekammern
Boards of Appeal
Chambres de recours**

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Case Number: T 2350/10 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 20 May 2014

Appellant: Ipsen Biopharm Limited
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted on 28 September
2010 revoking European patent No. 1597584
pursuant to Article 101(3) (b) EPC.

Composition of the Board:

Chairman H. Kellner
Members: T. Sommerfeld
D. Prietzel-Funk

Summary of Facts and Submissions

- I. European patent 1597584, based on application 04713111.5 and published as international application WO2004/074838, was granted with 14 claims.
- II. The published international application (hereinafter, the original application) comprised 24 claims, of which independent claim 1 read as follows:

"1. A method for determining the quantity of a pre-synaptic neuromuscular blocking substance in a sample which comprises the following steps:

- (i) determining the minimum voltage V_m needed to induce the contraction of muscle tissue, said muscle tissue being connected to an electrical stimulator through a motor nerve;
- (ii) adding the sample containing the pre-synaptic neuromuscular blocking substance;
- (iii) electrically stimulating, at a voltage at least equal to V_m , the muscle tissue at certain time intervals;
- (iv) comparing the effect induced by the sample to the effect induced by a reference substance and thereby determining the quantity of the pre-synaptic neuromuscular blocking substance in the sample."

Claim 1 of the granted patent differs from original claim 1 by the following amendments (additions underlined, deletions struck through):

"1. An ex vivo method for determining the quantity of a pre-synaptic neuromuscular blocking substance in a sample which comprises the following steps:

(i) selecting a muscle tissue capable of being electrically stimulated below 10V to induce the contraction of the muscle tissue, and determining the minimum voltage V_m needed to induce the contraction of the muscle tissue, said muscle tissue being connected to an electrical stimulator through a motor nerve;
(ii) adding the sample containing the pre-synaptic neuromuscular blocking substance;
(iii) electrically stimulating, at a voltage at least equal to V_m , the muscle tissue at certain time intervals by train pulse electrical stimulations which comprise stimulations lasting a time t_s separated from each other by periods lasting a time t_p during which no stimulation is exerted, wherein the time t_s is from 50 μ s to 500 ms, the time t_p is from 0.1 to 10 s and the ratio t_s/t_p is from 1:2 to 1:50 000;
(iv) comparing the effect induced by the sample to the effect induced by a reference substance and thereby determining the quantity of the pre-synaptic neuromuscular blocking substance in the sample."

III. An opposition was filed against the granted patent, the opponent requesting revocation of the patent in its entirety on the grounds of lack of novelty and inventive step (Articles 54(2) and 56 EPC and Article 100(a) EPC), lack of sufficiency of disclosure (Article 100(b) EPC) and added subject-matter (Article 100(c) EPC).

IV. During the proceedings before the opposition division, the patent proprietor requested that the opposition be rejected and the patent maintained as granted (**main request**) or, alternatively, according to the first, second or third auxiliary requests, all filed during oral proceedings before the opposition division.

Claim 1 of the first, second and third auxiliary requests differs from claim 1 of the main request mainly in step (i), as follows:

"...

(i) selecting a motor nerve of a muscle tissue capable of being electrically stimulated below 10V to induce the contraction of the muscle tissue, and determining the minimum voltage V_m needed to induce the contraction of the muscle tissue, said muscle tissue being connected to an electrical stimulator through a the motor nerve; ..."

(first auxiliary request)

"...

(i) selecting a ~~muscle tissue~~ rib cage intercostal nerve capable of being electrically stimulated below 10V to induce the contraction of the rib cage muscle tissue, and determining the minimum voltage V_m needed to induce the contraction of the muscle tissue, said rib cage muscle tissue being connected to an electrical stimulator through ~~a motor~~ the intercostal nerve;

...

(iii) electrically stimulating, at a voltage at least equal to V_m , the rib cage muscle tissue ..."

(second auxiliary request)

"...

(i) selecting a rib cage muscle tissue capable of being electrically stimulated below 10V through its intercostal nerve to induce the contraction of the muscle tissue, and determining the minimum voltage V_m needed to induce the contraction of the muscle tissue,

said muscle tissue being connected to an electrical stimulator through ~~a motor~~ the intercostal nerve; ..."
(third auxiliary request)

- V. By decision pronounced at oral proceedings on 15 September 2010 and posted on 28 September 2010, the opposition division revoked the patent under Article 101(2) and 101(3)(b) EPC.

The opposition division decided that all claim sets on file contravened Article 123(2) EPC, while the first and the second auxiliary requests also contravened Article 123(3) EPC.

- VI. The patent proprietor (appellant) lodged an appeal against that decision. With the statement of the grounds of appeal, the appellant requested that the decision of the opposition division be set aside and that the patent be maintained as granted, or according to the first, second or third auxiliary requests, all of which had served as a basis for the decision of the opposition division and were again filed with the grounds of appeal. Alternatively, the case should be remitted to the first instance for further prosecution.
- VII. The opponent did not submit any substantive reply to the grounds of appeal, but instead, with letter dated 14 April 2011, withdrew its opposition.
- VIII. Summons for oral proceedings before the board were issued.

As an annex to the summons to oral proceedings, the board issued a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA). In said communication the board

summarised the situation and expressed a detailed negative opinion on all requests on file in relation to Article 123(2) EPC and on the first and second auxiliary requests in relation to Article 123(3) EPC.

- IX. With letter dated 22 April 2014, the appellant submitted a new auxiliary request 4 and provided arguments in reply to the board's comments.

Claim 1 of **auxiliary request 4** differs from claim 1 as granted in that the muscle and nerve were further defined:

"...

(i) selecting a rib cage muscle tissue which is a piece of rib muscle obtained from a mouse or a rat capable of being electrically stimulated below 10V through its intercostal nerve to induce the contraction of the muscle tissue, and determining the minimum voltage V_m needed to induce the contraction of muscle tissue, said muscle tissue being connected to an electrical stimulator through ~~a motor~~ the intercostal nerve; ..."

- X. Oral proceedings before the board took place on 20 May 2014. At the end of oral proceedings the decision of the board was announced.

- XI. The appellant's arguments, in so far as relevant for the present decision, may be summarised as follows:

Main request - Article 123(2) EPC

Claim 1 was based on original claims 1 and 14. While indeed the disputed feature "selecting a muscle tissue" was not specifically disclosed in the general description, it could be directly and unambiguously

derived from original claim 1 in combination with Example 3, in particular page 13, lines 1 to 10 of the original application, and in addition from Example 1, page 10, second full paragraph. The general disclosure of the invention repeatedly referred to "muscle tissue" (e.g. page 2, lines 20, 22 and 29; page 3, third to seventh paragraphs; page 4, second last paragraph). Claim 1 of the original application disclosed the determination of the minimum voltage V_m needed to induce the contraction of muscle tissue, and further added that said muscle tissue was connected to an electrical stimulator through a motor nerve. It was clear from the disclosure on page 13, lines 1 to 10, that the term "stimulation" could refer both to the nerve and the muscle, given that whilst the nerve was directly connected to the stimulator the muscle would be stimulated, through the nerve, to contract. It was well known that a muscle tissue could only be electrically stimulated to produce contraction through a motor nerve of the muscle tissue. According to the passage on page 13, the skilled person first selected a nerve, then checked whether the voltage requirement applied, and once it arrived at the right selection it would then dissect the muscle tissue comprising the nerve, i.e. the 2-rib section containing the dissected nerve. In the context of the claimed method, when selecting a nerve, one necessarily had to select a muscle tissue as well.

First auxiliary request - Article 123(2) EPC

Claim 1 had a basis in original claims 1 and 14 in combination with the disclosure on page 10, lines 2 to 18, and page 13, lines 1 to 10. According to the disclosure of Examples 1 and 3, a nerve was dissected and tested to determine whether the minimum voltage V_m

required to induce muscle contraction was below 10V; if stimulation could not be achieved below 10V, another nerve was dissected (page 10, lines 9 to 18, and page 13, lines 2 to 8 of the original application). Although the disputed feature had been taken from examples, these could be seen as just further explanation of the invention.

Second auxiliary request - Article 123(2) EPC

The further limitations of claim 1 found their basis in page 12, lines 14 to 19, and page 13, lines 1 to 10. Examples 1 and 3 specifically disclosed selecting a rib cage intercostal nerve and inducing a contraction of the muscle tissue containing said nerve by stimulating said nerve and determining the minimum voltage V_m needed.

Third auxiliary request - Article 123(2) EPC

Claim 1 had a basis in original claim 1 in combination with the disclosure on page 12, lines 14 to 19, and page 13, lines 1 to 10.

Fourth auxiliary request - Article 123(2) EPC

Claim 1 corresponded to the combination of claims 1 and 14 of the third auxiliary request, the introduced amendment finding its basis in page 4, lines 21 to 22 of the original application. Although the examples disclosed other features as well, only those which were also part of the general disclosure were to be considered as essential to the invention.

XII. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of the claims according to the main request or according to one of the first, second or third auxiliary requests, filed with the grounds of appeal, or according to the fourth auxiliary request, filed with letter of 22 April 2014. Alternatively it requested that the decision be set aside and the case remitted to the first instance for further prosecution.

Reasons for the Decision

1. The appeal is admissible.
2. During the present appeal proceedings, the sole opponent, who in the present case would be respondent, has withdrawn its opposition.

Withdrawal of the opposition by the opponent who is not appellant does not affect the appeal proceedings, in so far as the board has to re-examine the substance of the opposition division's decision. The board can set the appealed decision aside and maintain the patent as requested by the appellant only if the specification meets the requirements of the EPC; thereby account can be taken of arguments and evidence cited by the opponent before the opposition was withdrawn (decision T 263/05 of 28 June 2007, OJ EPO 2008, 329). However, withdrawal of an opposition by the respondent means that the respondent ceases to be party to the appeal proceedings in respect of the substantive issues; he remains party to them only as regards apportionment of costs (T 789/89, OJ EPO 1994, 482). Since in the present case no issue of apportionment of costs has

been raised, the opponent is no longer a party to the proceedings.

3. Main request (claims as granted): Added subject-matter

3.1 According to Article 123(2) EPC, the European patent application or European patent may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed.

An amendment is considered unallowable under Article 123(2) EPC if it results in the skilled person being presented with information which is not directly and unambiguously derivable from that presented by the application as filed, account being taken of matter which is implicit to a person skilled in the art.

3.2 The original application does not disclose the step of selecting a muscle tissue capable of being electrically stimulated at 10V. The passage on page 13, lines 1 to 10, does not disclose selecting a muscle tissue, but instead selecting a nerve which is capable of inducing stimulation at a voltage below 10V: the muscle tissue is still the same, only the nerves are tested until an appropriate one is found and selected. The same is also true in relation to Example 1, see in particular page 10, lines 14 to 18. Hence, these passages cannot be seen as providing a basis for the disputed feature, because selecting one nerve (from a nerve bundle of a muscle tissue) is not the same as selecting one muscle tissue (from among other muscle tissues).

3.3 The appellant's argument that it is clear from page 13, lines 1 to 10, that the term "stimulation" could refer both to the nerve and to the muscle cannot be followed: while it is apparent from this passage that nerve

stimulation results in muscle contraction, what is selected according to this passage are still nerves and not muscle tissues. The board accepts that it is common general knowledge that a muscle tissue can only be electrically stimulated to produce contraction through a motor nerve of the muscle tissue, but notes that this is not the issue at stake: the fact is that the mentioned passages of the description all disclose selection of a motor nerve rather than of a muscle tissue.

3.4 Likewise the references to muscle tissue in the general part of the original description (page 2, lines 20, 22 and 29; page 3, third to seventh paragraphs; page 4, second last paragraph) cannot provide a basis either, as they only indicate that muscle tissue is to be used in the method of the invention and how it should be prepared. They do not disclose at all that a given muscle tissue is to be selected on the basis of a given stimulation threshold.

3.5 The appellant further pointed to the passage on page 13, lines 8 to 10 of the original application, disclosing that once an appropriate nerve is identified, the corresponding 2-rib section of the half rib cage is then isolated from the rest of the muscle tissue. Again the board notes that, while indeed a given muscle tissue is to be isolated, the method as disclosed in the example still involves nerve selection and not muscle tissue selection.

4. First auxiliary request: Added subject-matter

4.1 In this request, claim 1 has been amended in relation to claim 1 as granted in that step (i) of the method

consists of selecting a motor nerve of a muscle tissue rather than of selecting a muscle tissue.

4.2 In relation to this amendment, the board concludes that, while the passages indicated by the appellant as a basis for the amendment (page 10, lines 2 to 18, and page 13, lines 1 to 10 of the original application) do indeed disclose the feature "selecting a motor nerve of a muscle tissue capable of being electrically stimulated below 10V to induce the contraction of the muscle tissue", this is in the context of specific examples: these examples refer to a particular animal model (Wistar rats), to a specific muscle tissue (namely rib cage muscle tissue), to specific nerves (intercostal nerves), and to specific stimulation conditions. It cannot be concluded from the examples or from the general disclosure of the patent that exactly the same minimum voltage of 10V would be required for other animal models, different muscle tissues and nerves, and other stimulation conditions.

4.3 Accordingly, the board comes to the conclusion that there is no basis in the original application for this combination of features in the general context of claim 1. The first auxiliary request thus does not fulfil the requirements of Article 123(2) EPC.

5. Second auxiliary request: Added subject-matter

5.1 The second auxiliary request is further limited to rib cage intercostal nerves and rib cage muscle tissue.

5.2 Again the board considers that the indicated passages on page 12, lines 14 to 19, and page 13, lines 1 to 10, do not constitute a basis for the combination of these features, taken from examples, with the other features

of claim 1. As such the board comes to the conclusion that the second auxiliary request also does not fulfil the requirements of Article 123(2) EPC.

6. Third auxiliary request: Added subject-matter

6.1 Claim 1 of this request differs from granted claim 1 in that the muscle tissue is further defined as rib cage muscle tissue which is stimulated by its intercostal nerve.

6.2 For the same reasons as given above for the main request, the board concludes that this claim contravenes Article 123(2) EPC, in so far as none of the passages indicated by the appellant (page 12, lines 14 to 19, and page 13, lines 1 to 10) discloses selection of muscle tissue as claimed, but rather selection of nerves.

7. Fourth auxiliary request: Added subject-matter

7.1 Claim 1 of this request differs from claim 1 of the third auxiliary request in that the muscle tissue is further defined as being obtained from a mouse or rat.

7.2 The board agrees that the added feature is disclosed on page 4, lines 21 and 22 of the original application, but considers that this is not a suitable basis for the combination of this feature with the other features of claim 1, for the same reasons as given above in relation to the third auxiliary request. Hence, the board concludes that the fourth auxiliary request also contravenes the requirements of Article 123(2) EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



N. Maslin

H. Kellner

Decision electronically authenticated