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Datasheet for the decision of 7 September 2023

Case Number: T 0718/21 - 3.3.08

Application Number: 13733838.0

Publication Number: 2800973

IPC: G01N33/542, C12Q1/37, G01N33/569, G01N33/58

Language of the proceedings: EN

Title of invention:
Methods and compounds for increasing sensitivity of botulinum assays

Patent Proprietor:
Biomadison, Inc.

Opponent:
Merz Pharma GmbH & Co. KGaA

Headword:
Methods for increasing sensitivity of botulinum assays/ BIOMADISON

Relevant legal provisions:
EPC Art. 123(2)
RPBA 2020 Art. 13(2)

Keyword:
Amendments - added subject-matter (yes)
Amendment after summons - exceptional circumstances (no)

Decisions cited:
G 0002/10, J 0014/19, T 0914/18

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Case Number: T 0718/21 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 7 September 2023

Appellant: (Opponent)	Merz Pharma GmbH & Co. KGaA Eckenheimer Landstrasse 100 60318 Frankfurt/Main (DE)
Representative:	Altmann Stößel Dick Patentanwälte PartG mbB Theodor-Heuss-Anlage 2 68165 Mannheim (DE)
Respondent: (Patent Proprietor)	Biomadison, Inc. 1568 Luneta Drive Del Mar, CA 92014 (US)
Representative:	Zaccaro, Elisabetta Notarbartolo & Gervasi S.p.A. Viale Achille Papa, 30 20149 Milano (IT)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 7 April 2021 concerning maintenance of the European Patent No. 2800973 in amended form**

Composition of the Board:

Chairwoman	T. Sommerfeld
Members:	R. Morawetz
	D. Rogers

Summary of Facts and Submissions

I. European patent No. 2 800 973 ("the patent") is based on European patent application No. 13 733 838.0 which was filed as an international patent application published as WO 2013/103737 ("the application as filed"). The patent is entitled "*Methods and compounds for increasing sensitivity of botulinum assays*".

Claim 1 as granted reads as follows:

"1. A method of detecting presence of a Botulinum toxin, comprising:
providing an assay with a cell having (a) a molecule with cleavage site that interacts with a portion of the Botulinum toxin and (b) a reporter that provides an observable signal upon cleavage of the molecule at the cleavage site induced by Botulinum toxin, wherein the reporter comprises a fluorescent protein; and
incubating the cell in a culture media that contains an isoquinolynyl compound effective to increase sensitivity of the assay by at least 0.5 log relative to a baseline sensitivity provided by the assay utilizing incubation in the absence of said compound;
treating the cell with an amount of the Botulinum toxin, then sensing the signal, and correlating the signal with presence or absence of the Botulinum toxin, wherein said compound is effective to both inhibit PKC and to induce neurite formation."

II. One opposition was filed against the granted patent. The patent was opposed under Article 100(a) EPC on the ground of lack of inventive step (Article 56 EPC) and under Article 100(b) and (c) EPC.

III. By an interlocutory decision, the opposition division decided that the patent in amended form on the basis of the set of claims of the main request, submitted by letter dated 28 April 2020, and the invention to which it relates met the requirements of the EPC.

IV. The opponent (appellant) filed notice of appeal against the opposition division's decision.

V. In the statement setting out the grounds of appeal the appellant maintained *inter alia* its added matter objection against claim 1 of the set of claims found allowable by the opposition division.

VI. In reply to the statement of grounds of appeal, the patent proprietor (respondent) maintained the set of claims found allowable by the opposition division as its sole claim request (main request) and provided its observations concerning the objections raised by the appellant, including the added matter objection.

VII. The board scheduled oral proceedings in accordance with the parties' requests and subsequently issued a communication under Article 15(1) RPBA, in which it indicated that, on a preliminary basis, it agreed with the appellant that claim 1 of the main request contravened Article 123(2) EPC.

VIII. By letter dated 1 August 2023, the respondent submitted sets of claims of auxiliary requests 1 to 6 and four new documents: Felipo V. *et al.*, J. Biol. Chem. 265, 1990, 9599-9601 (document D53); Critchfield J.W. *et al.*, Antiviral Chemistry & Chemotherapy 10, 1999, 275-284 (document D54); Hagiwara M. *et al.*, Mol. Pharmacol. 32, 1987, 7-12 (document D55) and US 2003/176423 A1 (document D56). With a further

letter, dated 31 August 2023, the respondent submitted a set of claims of auxiliary request 7.

Claim 1 of the main request is identical to claim 1 as granted.

Claim 1 of auxiliary request 1 is based on claim 1 of the main request, amended to specify that the Botulinum toxin is serotype A Botulinum toxin (BoNT/A).

Claim 1 of auxiliary request 2 is based on claim 1 of the main request, amended to specify that the isoquinolynyl compound is 1-(5- isoquinolinyl-sulfonyl)-2-methylpiperazine dichloride (H7).

Claim 1 of auxiliary request 3 combines the amendments of claim 1 of auxiliary requests 1 and 2.

Claim 1 of auxiliary request 4 is based on claim 1 of the main request, amended to specify that the cell is of a BoCell™ model cell line.

Claim 1 of auxiliary request 5 combines the amendments of claim 1 of auxiliary requests 1 and 4.

Claim 1 of auxiliary request 6 combines the amendments of claim 1 of auxiliary requests 2 and 4.

Claim 1 of auxiliary request 7 combines the amendments of claim 1 of auxiliary requests 1, 2 and 4.

IX. Oral proceedings before the board took place as scheduled. At the end of the oral proceedings the Chairwoman announced the board's decision.

X. The appellant's arguments relevant to the decision are summarised below.

Admittance and consideration of documents D53 to D56 (Article 13(2) RPBA)

There was no reason which would have prevented the respondent's filing of documents D53 to D56 in reply to the appeal.

That the position taken by the board differed from the contested decision was not an exceptional circumstance within the meaning of Article 13(2) RPBA.

Main request
Amendments (Articles 100(c) and 123(2) EPC) - claim 1

The feature "*wherein said compound is effective to both inhibit PKC and to induce neurite formation*" found no basis in paragraphs [0052], [0053], [0056], and page 13, lines 5 to 6, item 3, of the application as filed.

Paragraphs [0050] to [0051] of the application as filed related to a specific embodiment and paragraph [0052] explained the likely mechanisms underlying the increase in sensitivity to BoNT/A seen with H7 in the BoCell™ model. There existed a structural and functional relationship between PKC inhibition, neurite induction, the BoCells, H7 and BoNT/A.

The skilled person would not derive from paragraphs [0051, [0052], [0059] and Figure 1, read in the context of the application as filed as a whole, that "*to both inhibit PKC and to induce neurite formation*" were characteristics of a compound that ensured an increase in sensitivity to any BoNT in any cell.

Admittance and consideration of auxiliary requests 1 to 7 (Article 13(2) RPBA)

There was no reason whatsoever which would have prevented the respondent from submitting the claims of auxiliary requests 1 to 7 as fallback positions in reply to the appeal.

That the position taken by the board differed from the contested decision was not an exceptional circumstance within the meaning of Article 13(2) RPBA.

Pursuing auxiliary requests 1 to 7 at this stage in the appeal proceedings did not simplify the proceedings or enhance procedural economy. The set of claims of auxiliary requests 1 to 7 did not overcome the issues raised by the board and the appellant, they contravened Article 123(2) EPC and were not *prima facie* allowable.

XI. The respondent's arguments relevant to the decision are summarised below.

Admittance and consideration of documents D53 to D56 (Article 13(2) RPBA)

Document D53 had been cited in paragraph [0052] of the application and was therefore to be considered incorporated in the application as filed.

The respondent had been forced to file documents D53 to D56 so late because it was taken by surprise by the board's preliminary opinion regarding added matter in claim 1 of the main request.

The feature "*wherein said compound is effective to both inhibit PKC and induce neurite formation*" had been

introduced during examination. During the opposition procedure, the appellant objected to it using substantially the same arguments as in the appeal proceedings and the opposition division concluded that the feature met the requirements of Article 123(2) EPC. There was therefore no reason why the EPO should have changed its mind. That the board agreed with the appellant and dissented from the two preceding opinions of the examining and opposition divisions was therefore a new and unforeseen development of the case giving rise to exceptional circumstances according to Article 13(2) RPBA.

Main request
Amendments (Articles 100(c) and 123(2) EPC) - claim 1

Paragraphs [0050], [0051] and [0052] of the application as filed related to embodiments wherein BoNT/A was used as BoNT. However, it was immediately and unambiguously clear for a skilled person that the observations of paragraph [0053] represented a principle interpretation of the results, regardless of which BoNT was used, and regardless of what working cell type was used in the assay.

The skilled person knew that the inhibition of PKC by the isoquinolynyl compound was independent of presence or absence of a specific BoNT (e.g. the presence of BoNT/A). The same was true for the function of the compound on neurite formation.

Reading paragraph [0053] of the application as filed in the context of paragraphs [0036], [0043], [0051], [0052], [0056], [0059] and Figure 1 allowed a generalisation to any BoNT and all cells.

The H7 treatment was a pre-treatment (paragraph [0051]), the skilled person therefore understood that the effect of H7 was independent of the BoNT which was used thereafter.

The application as filed indicated that other BoNTs were contemplated (paragraph [0036]) and that many cell lines were suitable as host cells (paragraph [0043]).

From paragraphs [0052], [0059] and Figure 1 of the application as filed the skilled person understood that any compound that inhibited PKC and induced neurite formation could be used.

Admittance and consideration of auxiliary requests 1 to 7 (Article 13(2) RPBA)

The amendments proposed in auxiliary requests 1 to 7 were mere restrictions of the claimed subject-matter and they did not constitute an amendment of the respondent's appeal case within the meaning of Article 13 RPBA (T 914/18).

The appellant's arguments in the grounds of appeal were the same as submitted during opposition proceedings. There had been therefore no reason to submit any fall back positions in reply to the appeal.

Auxiliary requests 1 to 7 should be admitted and were justified by the fact that the respondent was faced with an exceptional circumstance in accordance with Article 13(2) RPBA, for the same reasons given for the admission of documents D53 to D56.

The amendments proposed in auxiliary requests 1 to 7 reduced the complexity of the proceedings by

eliminating matters in dispute and were thus in line with the principle of procedural economy.

XII. The appellant requested to set aside the decision under appeal and to revoke the patent. The appellant further requested that auxiliary requests 1 to 7 and documents D53 to D56 not be admitted into the proceedings.

The respondent requested, as a main request, that the appeal be dismissed (the patent be maintained on the basis of the claims found allowable by the opposition division), or alternatively, that the decision under appeal be set aside and the patent be maintained upon the basis of one of auxiliary requests 1 to 7. The respondent further requested that documents D53 to D56 be admitted into the proceedings.

Reasons for the Decision

Admittance and consideration of documents D53 to D56 (Article 13(2) RPBA)

1. In reaction to the board's communication pursuant to Article 15(1) RPBA, the respondent submitted documents D53 to D56 as evidence of the common general knowledge of the skilled person at the time of filing of the application. The appellant requested that these documents not be admitted into the appeal proceedings because they constituted an amendment to the respondent's appeal case and there were no exceptional circumstances.

2. The reference point for examining whether there is an amendment of a party's appeal case in accordance with Article 13(2) RPBA is the statement of grounds of

appeal or the reply.

3. In its reply the respondent did not rely on the skilled person's common general knowledge let alone a document representing the skilled person's common general knowledge at the filing date of the application. In this context the board notes that the mere fact that a document is referred to in the application as filed - here document D53 in paragraph [0052] - does not mean that the contents of this document form part of the respondent's reply. The respondent's reliance on documents D53 to D56 therefore constitutes an amendment of its appeal case.

4. Pursuant to Article 13(2) RPBA, any amendment to a party's appeal case after notification of a summons to oral proceedings is, as a rule, not to be taken into account unless there are exceptional circumstances justified with cogent reasons by the party concerned.

5. Exceptional circumstances are new or unforeseen developments in the appeal proceedings which lie outside the sphere of influence of the party affected by them, such as new objections raised by the board or by another party (see Case Law of the Boards of Appeal, 10th edition 2022, ("CLBA"), V.A.4.5.1).

6. For the following reasons, the board was not persuaded that the respondent's justification (see section XI. above) for filing documents D53 to D56 only after the board provided its preliminary opinion was indicative of exceptional circumstances within the meaning of Article 13(2) RPBA.

7. The objection of added matter as regards the feature "*wherein said compound is effective to both inhibit PKC*

and induce neurite formation" in claim 1 of the main request does not stem from the board. It had been raised by the opponent during the opposition proceedings and it was repeated in the appeal proceedings in the appellant's grounds of appeal. In its reply to the appeal, the respondent provided its observations concerning this objection.

8. The respondent had to expect that with respect to the added matter objection in question, the board would accept either the argument of the appellant or that of the respondent. As it turned out, in its preliminary opinion the board agreed with the appellant's objection of added matter, one of the possible outcomes. The board's preliminary opinion therefore did not create extraordinary circumstances within the meaning of Article 13(2) RPBA (see also CLBA, V.A.4.5.4a and V.A.4.5.6c).

9. That the respondent was for the first time faced with an objection under Art 123(2) EPC by a department of the EPO and that the board's position differed from the contested decision although the appellant had used substantially the same arguments in the opposition and the appeal proceedings is not a cogent reason justifying an exceptional circumstance within the meaning of Article 13(2) RPBA.

10. Opposition appeal proceedings are separate and independent from opposition proceedings. Their purpose is to give the losing party a possibility to challenge the opposition division's decision on its merits. The board has the power and the obligation to review the impugned decision and to give a judicial decision upon its correctness. It would not be in conformity with the purpose of appeal proceedings if the board could not

deviate from the decision taken by the opposition division, i.e. were to be bound by it, in the absence of new arguments on appeal. To the contrary, in view of the primary object of the appeal proceedings to review the decision under appeal in a judicial manner, a party's appeal case must as a matter of fact be directed to the requests, facts, objections, arguments and evidence on which the decision under appeal was based (Article 12(2) RPBA). The respondent's understanding that absent any new argument by the appellant the board could not deviate from the impugned decision was thus unfounded.

11. The board concludes from the above that the respondent's surprise cannot be objectively justified as resulting from a new and unforeseeable development in the appeal proceedings within the meaning of Article 13(2) RPBA, and is merely subjective. It is therefore not a justification for not filing documents D53 to D56 in reply to the statement of grounds of appeal, when the respondent should have made its appeal case (Article 12(3) RPBA).

12. Since documents D53 to D56 constitute an amendment of the respondent's case, and since the respondent has not demonstrated cogent reasons justifying exceptional circumstances, the board decided not to admit these documents into the appeal proceedings.

Main request

Amendments (Articles 100(c) and 123(2) EPC) - claim 1

13. Claim 1 of the main request is identical to claim 1 as granted and reads as follows:

"1. A method of detecting presence of a Botulinum toxin, comprising:
providing an assay with a cell having (a) a molecule with cleavage site that interacts with a portion of the Botulinum toxin and (b) a reporter that provides an observable signal upon cleavage of the molecule at the cleavage site induced by Botulinum toxin, wherein the reporter comprises a fluorescent protein; and
incubating the cell in a culture media that contains an isoquinolynyl compound effective to increase sensitivity of the assay by at least 0.5 log relative to a baseline sensitivity provided by the assay utilizing incubation in the absence of said compound;
treating the cell with an amount of the Botulinum toxin, then sensing the signal, and correlating the signal with presence or absence of the Botulinum toxin, wherein said compound is effective to both inhibit PKC and to induce neurite formation."

14. Claim 1 of the main request is based on claim 1 as filed. During examination, the isoquinolynyl compound had been further characterised by the feature "*wherein said compound is effective to both inhibit PKC and to induce neurite formation*". The opposition division held that paragraphs [0052], [0053], [0056], and page 13, lines 5-6, item 3 of the application as filed provided a basis for this amendment. This is disputed by the appellant.

15. It is established case law of the boards of appeal that the standard for assessing compliance with the requirements of Article 123(2) EPC is the standard set out in decision G 2/10 (OJ EPO 2012, 376, Reasons 4.3). Amendments are only permitted within the limits of what a skilled person would derive directly and unambiguously, using common general knowledge, and seen

objectively and relative to the date of filing, from the whole of the application as filed. After the amendment, the skilled person may not be presented with new technical information (ibid., Reasons 4.5.1).

16. Paragraph [0053] of the application as filed, which was held by the opposition division to provide a "general statement" which formed the basis for the amendment at issue reads as follows: "*It is thus contemplated that inhibition of specific PKC isoforms with selective isoquinolynyl analogues and other drugs may infer similar increases in BoNT/A sensitivity in established model cell lines by inducing neurite formation.*"

17. As noted by the appellant, paragraph [0053] of the application as filed refers to the "*inhibition of specific PKC isoforms*" with "*selective isoquinolynyl analogues*" and "*increases in BoNT/A sensitivity*" in "*established model cell lines*" while claim 1 of the main request refers generally to "*inhibit PKC*" and "*an isoquinolynyl compound*". Furthermore, paragraph [0053] does not mention any other BoNT serotypes while claim 1 relates to increases in sensitivity to "*Botulinum toxin*" in "*cells*" generally.

18. Contrary to what was held in the decision under appeal, the board considers that item 3 in paragraph [0056] of the application as filed does not extend the teaching of paragraph [0053] to other BoNT serotypes.

19. Paragraph [0056] reports that "*With H7 treatment, we get BoCell™ BoNT/A sensitivities after 24 hours of BoNT/A treatment that are equivalent to 72 hour BoNT/A treatments with our current assay conditions*" (page 12, last three lines) and "*Using H7 we can increase the sensitivity of the assay by 0.5 log - 1.0 log with a 48*

hour BoNT/A treatment compared to our current assay conditions" (page 13, lines 1 to 3).

20. As noted by the appellant, paragraph [0056] of the application as filed thus refers specifically to the isoquinolynyl compound H7, to BoNT/A and to BoCell™ cells and lists possible technological advantages of H7. Furthermore, contrary to what was held in the decision under appeal, item 3 of paragraph [0056] does not "unequivocally" state that H7 treatment will result in increased neuronal cell sensitivity to other BoNT serotypes. Instead, item 3 read in the context of paragraph [0056] discloses that "*Increase neuronal cell sensitivity to other BoNT serotypes*" is one of the possible technological advantages of H7 treatment - not of treatment with isoquinolynyl compounds generally - that the inventors are "*currently testing*" (see page 13, lines 5 to 6). As the results of these tests are not disclosed in the application as filed, the skilled person reading paragraph [0056] of the application as filed does not derive directly and unambiguously from it that the teaching of paragraph [0053] of the application as filed regarding "*increases in BoNT/A sensitivity*" is generally applicable, i.e. to all BoNT serotypes.

21. The board furthermore considers that paragraph [0052] of the application as filed does not ascribe the effect of isoquinolynyl compound H7 to PKC inhibition in general, contrary to what was held in the decision under appeal.

22. As noted by the appellant, paragraph [0052] of the application as filed discusses the effect of a specific isoquinolynyl compound, H7, in the context of a specific type of cell, neuroblastoma cells and

furthermore discloses that there is a functional and structural relationship between pretreatment with H7 and the increased sensitivity of the BoCell™ assay, which was not seen with other known neuronal cell differentiators or with drugs previously shown to induce neurite formation (see last two sentences of paragraph [0052] on page 11). Paragraph [0052] therefore does not disclose any effects of isoquinolynyl compounds in general and accordingly provides no basis for generalising the specific disclosure of paragraph [0053] either.

23. Furthermore, as also correctly noted by the appellant, the opposition division's argument that the appellant had failed to prove that specific PKC isoforms "are essential" is not persuasive. The relevant standard for the assessment of the allowability of amendments is the standard set out in point 15. above and the so-called essentiality test can not take the place of the standard set out in G 2/10. In the more recent, and now well-established, case law of the boards of appeal the essentiality test is no longer considered appropriate (see CLBA, II.E.1.4.4c).

24. The board concludes from points 16. to 23. above that the opposition division's assessment as regards added matter with respect to the feature "*wherein said compound is effective to both inhibit PKC and to induce neurite formation*" was not correct.

25. For the reasons set out below, none of the respondent's arguments in support of allowability of the amendment at issue were considered persuasive.

26. The respondent's main argument was that it is immediately and unambiguously clear for a skilled

person from the wording in paragraph [0053] that the observations of paragraph [0053] represent a principle interpretation of the results, which are suggested to represent the underlying, principle mechanism of the increase in sensitivity regardless of which BoNT is used, and regardless of what working cell type is used in the assay. In this discussion, the respondent quoted an abridged part of paragraph [0053], where a number of specific features were left out (see reply, section 1.2).

27. The respondent provided however no reasons as to why the skilled person reading paragraph [0053] of the application as filed would ignore the explicit reference to "*BoNT/A*" and "*established model cell lines*" made therein (see also point 16. above) which were simply omitted in the respondent's abridged reproduction of paragraph [0053] to support its submission that it would disclose a principle mechanism of the increase in sensitivity which would be independent of the BoNT's serotype and the cell type used in the assay.

28. Nor is it in the board's view self-evident that the skilled person reading paragraph [0053] of the application as filed in its context understands that the disclosed increase in sensitivity is independent of the BoNT's serotype to be detected and the cell type used in the assay. To the contrary, the skilled person immediately understands that the statement in paragraph [0053] is based on the disclosure of the preceding paragraphs [0050], [0051] and [0052]. Paragraphs [0050] and [0051] relate to a specific embodiment: the increase of sensitivity of the BoCell™ model cell line to BoNT/A by pretreatment of the cells with the isoquinolynyl compound H7, while paragraph

[0052] provides an explanation of the likely mechanism underlying the observed increase in sensitivity to BoNT/A and a summary of the results obtained in the experiment described in paragraph [0059] and Figure 1 of the application.

29. While the board acknowledges that paragraph [0053] of the application as filed provides an interpretation of paragraphs [0050] to [0052], it limits the possible generalisation of the results described in paragraphs [0050] to [0052] explicitly to "*increases in BoNT/A sensitivity in established model cell lines*" (see point 16. above) and nothing in the wording of paragraph [0053] suggests that the teaching can be further extended to BoNTs other than BoNT/A or cells other than established model cell lines.

30. The respondent's additional argument in this respect, namely that the skilled person was immediately and unambiguously aware of the fact that the underlying characteristics of the effective compound (to both inhibit PKC and to induce neurite formation) were also underlying characteristics of the compound in assays detecting other BoNTs than BoNT/A is not found persuasive either.

31. The line of argument is based on the following assertions:
(i) "[t]he skilled person knows that the inhibition of PKC by the isoquinolynyl compound is totally independent of presence or absence of a specific Botulinum Neurotoxin (e.g. the presence of Botulinum Neurotoxin A). The same is true for the function of the compound neurite formation [sic]." and
(ii) "[s]ince the increase in sensitivity – in accordance with the teaching of e.g. original claim 1 –

functions with all Botulinum Neurotoxins in general, the skilled person, in view of paragraph [0053], unambiguously derives that these characteristics (to both inhibit PKC and to induce neurite formation) of the effective compound are the important characteristics which assure functioning of the compound not only in BoNT/A assays but also in assays with other Botulinum neurotoxins." (see reply, section 1.2, last paragraph on page 3 and line 1 on page 4)

32. The first assertion ignores that the application as filed discloses that there exists a structural and functional relationship between the increase in sensitivity of specific cells to BoNT/A and the induction of neurite formation by the inhibition of specific PKC isoforms in these cells by specific isoquinolynyl compounds (see paragraphs [0051], [0052] and [0053] of the application as filed and points 22. and 28. above).

33. The second assertion is based on the respondent's interpretation of paragraph [0053] of the application as filed, which interpretation is not accepted by the board (see points 27. and 28. above).

34. The respondent's final argument that reading paragraph [0053] of the application as filed in the context of the disclosure in paragraphs [0036], [0043], [0050] to [0052], [0056], Figure 1 and paragraph [0059] allowed a generalisation to any BoNT and all cells is not found persuasive either.

35. With respect to the respondent's reliance on paragraph [0051] of the application as filed, the board reiterates that the application as filed not only discloses that there exists a functional and structural

relationship between H7 pretreatment and increased sensitivity to BoNT/A seen in the BoCell™ Assay (see point 32. above) but also that it needs to be tested whether the effect seen with H7 pre-treatment can be seen at all with other BoNT serotypes (see point 20. above). The skilled person would therefore not derive directly and unambiguously from the disclosure of H7 pre-treatment in paragraph [0051] of the application as filed, read in the context of the whole of the application as filed, that the effect seen in the BoCell™ Assay is independent of the BoNT used, i.e. BoNT/A.

36. With respect to the respondent's reliance on paragraphs [0052], [0059] and Figure 1 the board notes that the experiment described in paragraph [0059] of the application as filed, the results of which are depicted in Figure 1, discloses that pretreatment with H7, but with none of the other compounds known to induce neurite formation, leads to an increase of sensitivity of BoCells to BoNT/A. These results were summarised in paragraph [0052] of the application as filed and, as set out above (see points 28. and 29.), they have already been interpreted in paragraph [0053] of the application as filed. Here, the generalisation has been limited to the "*inhibition of specific PKC isoforms*" with *"selective isoquinolynyl analogues"* and "*increases in BoNT/A sensitivity in established model cell lines*" (see also points 16. and 17. above).

37. The board therefore agrees with the appellant that the skilled person would not derive directly and unambiguously from paragraphs [0052], [0059] and Figure 1 of the application as filed, read in the context of the whole of the application as filed, that "*to both inhibit PKC and to induce neurite formation*"

were characteristics of a compound that ensured an increase in sensitivity to any BoNT in any cell.

38. In sum, the board concludes from the above that the skilled person would not derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing from paragraph [0053] of the application as filed when read in the context of the application as filed as a whole, that "*to both inhibit PKC and to induce neurite formation*" are disclosed in the application as filed as being the underlying characteristics which ensure functioning of an effective isoquinolynyl compound not only in BoNT/A assays but also in assays with other BoNTs and in any cell.

39. The board therefore agrees with the appellant that the amendment in claim 1 of the main request to further characterise the "*compound effective to increase sensitivity of the assay by at least 0.5 log*" by the expression "*wherein said compound is effective to both inhibit PKC and to induce neurite formation*" presents the skilled person with new technical information.

40. Claim 1 of the main request therefore contravenes Article 123(2) EPC.

Admittance and consideration of auxiliary requests 1 to 7 (Article 13(2) RPBA)

41. In reaction to the board's communication pursuant to Article 15(1) RPBA the respondent submitted auxiliary requests 1 to 7. The appellant requested that these claim requests not be admitted into the appeal proceedings.

42. As mentioned above (see point 2.), the reference point for examining whether there is an amendment of a party's case in accordance with Article 13(2) RPBA is the grounds of appeal or the reply. In its reply, the respondent relied on the main request and filed no fall back positions.

43. By submitting auxiliary requests 1 to 7, the respondent, for the first time on appeal, pursued claim requests that restricted the claimed subject-matter to BoNT/A, and/or the H7 isoquinolynyl compound, and/or the BoCell™ model cell line (see section VIII. above). The amendments in auxiliary requests 1 to 7 therefore constitute an amendment to the respondent's appeal case within the meaning of Article 13 RPBA (see also J 14/19, Reasons 1.1 to 1.5). Since the amendments at issue are not a deletion of an alternative or of a dependent claim, as was the case in T 914/18, the respondent's reference to T 914/18 does not help its case.

44. The respondent's main justification for exceptional circumstances within the meaning of Article 13(2) RPBA was the same as the one submitted in the context of admission of documents D53 to D56 (see section XI. above) and it failed for the same reason as set out above (see points 7. to 11.).

45. While exceptional circumstances within the meaning of Article 13(2) RPBA have been acknowledged in the case law of the boards if the admittance of amendments to a party's appeal case was not detrimental to the procedural economy of the appeal proceedings (see CLBA, V.A.4.5.1), in the case at hand, admittance would have been inconsistent with the requirement of procedural

economy of the appeal proceedings.

46. When filing auxiliary requests 1 to 7 the respondent indicated the basis in the application as filed for the individual features added to claim 1 of the main request. It did however not indicate the basis for the resulting claimed combination of features or provide any argument as to why all the objections as to added matter raised by the appellant against claim 1 of the main request no longer applied to claim 1 of auxiliary requests 1 to 7. For this reason alone, the new claim requests were therefore not *prima facie* clearly allowable and required more discussion and the respondent's submission that these requests would "reduce the complexity of the proceedings, by eliminating the matters in dispute" was unfounded.

47. The board therefore decided not to admit auxiliary requests 1 to 7 into the appeal proceedings.

Conclusion

48. The main request is not allowable and auxiliary requests 1 to 7 were not admitted into the appeal proceedings. Therefore, the patent cannot be maintained in amended form and must be revoked.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

L. Malécot-Grob T. Sommerfeld

Decision electronically authenticated