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Datasheet for the decision of 1 December 2021

Case Number: T 1229/17 - 3.3.01

Application Number: 09733444.5

Publication Number: 2277050

IPC: G01N33/68, C07K14/00

Language of the proceedings: EN

Title of invention:
ANALYSIS OF AMINO ACID COPOLYMER COMPOSITIONS

Patent Proprietor:
Momenta Pharmaceuticals, Inc.

Opponents:
Actavis Group ehf
Guardian IP Consulting I/S
Generics [UK] Ltd (trading as Mylan)

Headword:
Analysis of glatiramer acetate batches/MOMENTA

Relevant legal provisions:
RPBA Art. 12(4)
RPBA 2020 Art. 13(1), 13(2)
EPC R. 80
EPC Art. 84, 123(2), 123(3), 56

Keyword:
Late-filed evidence
Amendment occasioned by ground for opposition - (yes)
Claims - clarity (yes)
Amendments - allowable (yes) extension beyond the content of the patent (no)
Inventive step - (no) MR: effect not made credible within the whole scope of claim; (yes) AR1

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 1229/17 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 1 December 2021

Appellant I: (Patent Proprietor)	Momenta Pharmaceuticals, Inc. 301 Binney Street Cambridge, MA 02142 (US)
Representative:	Potter Clarkson The Belgrave Centre Talbot Street Nottingham NG1 5GG (GB)
Appellant II: (Opponent 2)	Guardian IP Consulting I/S Diplomvej, Building 381 2800 Kgs. Lyngby (DK)
Representative:	Prins, Hendrik Willem Arnold & Siedsma Bezuidenhoutseweg 57 2594 AC The Hague (NL)
Appellant III: (Opponent 3)	Generics [UK] Ltd (trading as Mylan) Albany Gate Darkes Lane Potters Bar Hertfordshire EN6 1 AG (GB)
Representative:	Gill Jennings & Every LLP The Broadgate Tower 20 Primrose Street London EC2A 2ES (GB)
No longer party: (Opponent 1)	Actavis Group ehf - opposition withdrawn -
Representative:	

Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 27 March 2017 concerning maintenance of the European Patent No. 2277050 in amended form**

Composition of the Board:

Chairwoman M. Pregetter
Members: T. Sommerfeld
L. Bühler

Summary of Facts and Submissions

I. European patent No. 2277050 is based on application No. 09733444.5, which was filed as an international application and published as WO 2009/129018. The patent is entitled "Analysis of amino acid copolymer compositions" and was granted with 12 claims.

II. Three oppositions were filed against the granted patent, with all opponents requesting that the patent be revoked 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); during opposition proceedings, opponent 1 withdrew its opposition.

III. By an interlocutory decision announced at oral proceedings, the opposition division decided that the patent could be maintained as amended on the basis of the second auxiliary request filed during oral proceedings (Articles 101(3)(a) and 106(2) EPC).

The opposition division considered that the set of claims according to the main request (claims as granted) complied with Article 54 EPC but that claim 7 contravened Article 123(2) EPC, claims 11 and 12 contravened Article 83 EPC and claims 1 to 7 contravened Article 56 EPC. It also held that the claims according to the first auxiliary request complied with Article 83 EPC but not with Article 56 EPC. The claims of the second auxiliary request were considered to comply with the EPC requirements, in particular Rule 80 EPC and Articles 84, 123(2) and (3)

and 56 EPC. The opposition division also decided to admit documents D32 to D34 into the proceedings.

IV. All parties lodged an appeal against the opposition division's decision.

V. With its statement of grounds of appeal, the patent proprietor (appellant I) requested that the patent be maintained as granted (main request) or, alternatively, on the basis of auxiliary requests 1 to 4, all filed with the grounds of appeal.

Auxiliary requests 1 and 2 were identical, respectively, to the first and second auxiliary requests decided upon by the opposition division.

VI. With their statements of grounds of appeal, both opponent 2 (appellant II) and opponent 3 (appellant III) requested that the decision be set aside and the patent revoked in its entirety. Appellant III also filed new documents, D35 to D37, and requested that they be admitted into the proceedings.

VII. With its reply to appellant I's grounds of appeal, appellant II requested that document D25 and auxiliary requests 3 and 4 not be admitted into the proceedings.

VIII. With its reply to the opponents' grounds of appeal, appellant I submitted new documents, D38 and D39, and requested that they be admitted into the proceedings.

IX. Appellant II submitted a further letter, requesting that document D39 not be admitted into the proceedings. It also filed a new document, D40 (hereinafter D40-O2), and requested that it be admitted into the proceedings.

X. With a further letter, appellant III submitted a new document D40 (hereinafter D40-O3).

XI. Summons for oral proceedings before the board were issued. In the communication pursuant to Article 15(1) RPBA, the board provided a preliminary opinion concerning some issues, in particular admission of requests and documents.

XII. By letter dated 21 September 2021, appellant III withdrew its request for oral proceedings and gave notice that it would not be attending oral proceedings.

XIII. By further letters, appellants I and II submitted new documents, D41 (appellant I), D42 and D43 (appellant II).

XIV. Oral proceedings before the board took place by videoconference, with the parties' agreement.

At the oral proceedings, appellant I withdrew its main request and auxiliary requests 3 and 4. Hence, the previous auxiliary requests 1 and 2 became the main request and auxiliary request 1, respectively. At the end of the oral proceedings the chair announced the board's decision.

Claims 1 and 2 of the **main request** read as follows:

"1. A method of selecting a batch of a composition comprising glatiramer acetate, the method comprising:

providing a batch of a composition comprising glatiramer acetate;

measuring the amount of pyro-glutamate (pyro-Glu) in the batch; and

selecting the batch if the amount of pyro-Glu in the batch is 2000-7000 ppm,
thereby selecting a batch of a composition comprising glatiramer acetate."

"2. A method of preparing a pharmaceutical composition comprising glatiramer acetate, the method comprising:
providing a batch of a composition comprising glatiramer acetate,
measuring the amount of pyro-Glu in the batch;
selecting the batch for use in the preparation of a pharmaceutical composition if the amount of pyro-Glu in the batch is within a predetermined range; and
preparing a pharmaceutical composition comprising at least a portion of the selected batch,
wherein the concentration of pyro-Glu in the selected batch is 2000-7000 ppm."

Claims 1 and 2 of **auxiliary request 1** differ from claims 1 and 2 of the main request, respectively, in that the expression "a batch of a composition comprising glatiramer acetate" was replaced with simply "a batch of glatiramer acetate".

Independent claims 6, 7 and 8 of auxiliary request 1 are identical, respectively, to claims 8, 9 and 10 as granted and read:

"6. A method for preparing a pharmaceutical composition comprising glatiramer acetate, comprising:
polymerizing N-carboxy anhydrides of L-alanine, benzyl-protected L-glutamic acid, trifluoroacetic acid (TFA) protected L-lysine and L-tyrosine to generate a protected copolymer;

treating the protected copolymer to partially depolymerize the protected copolymer and deprotect benzyl protected groups and deprotecting TFA-protected lysines to generate glatiramer acetate;
purifying the glatiramer acetate;
measuring the amount of pyro-glutamate (pyro-Glu) in the purified glatiramer acetate, and
selecting the purified glatiramer acetate for use in the preparation of a pharmaceutical composition if the amount of pyro-Glu in the purified glatiramer acetate is 2000-7000 ppm."

"7. A method for preparing a pharmaceutical composition comprising glatiramer acetate, comprising:
polymerizing N-carboxy anhydrides of L-alanine, benzyl-protected L-glutamic acid, trifluoroacetic acid (TFA) protected L-lysine and L-tyrosine to generate a protected copolymer;
treating the protected copolymer to partially depolymerize the protected copolymer and deprotect benzyl protected groups and deprotecting TFA-protected lysines to generate glatiramer acetate;
purifying the glatiramer acetate;
measuring the amount of pyro-glutamate (pyro-Glu) during or after the polymerizing step;
measuring the amount of pyro-glutamate (pyro-Glu) in the purified glatiramer acetate;
selecting the purified glatiramer acetate for use in the preparation of a pharmaceutical composition if the amount of pyro-Glu in the purified glatiramer acetate is 2000-7000 ppm; and
preparing a pharmaceutical composition comprising at least a portion of the selected purified glatiramer acetate."

"8. A method for preparing a pharmaceutical composition comprising glatiramer acetate, comprising:
polymerizing N-carboxy anhydrides of L-alanine, benzyl-protected L-glutamic acid, trifluoroacetic acid (TFA) protected L-lysine and L-tyrosine to generate a protected copolymer;
treating the protected copolymer to partially depolymerize the protected copolymer and deprotect benzyl protected groups and deprotecting TFA-protected lysines to generate glatiramer acetate;
purifying the glatiramer acetate,
measuring the amount of pyro-glutamate (pyro-Glu) during or after the partial depolymerization step;
measuring the amount of pyro-glutamate (pyro-Glu) in the purified glatiramer acetate;
selecting the purified glatiramer acetate for use in the preparation of a pharmaceutical composition if the amount of pyro-Glu in the purified glatiramer acetate is 2000-7000 ppm; and
preparing a pharmaceutical composition comprising at least a portion of the selected purified glatiramer acetate."

XV. The documents cited during the proceedings before the opposition division and the board of appeal include the following:

D1 WO 2006/029393
D6 Boerner R. & Clouse K., 2005, BioProcess International, pp. 50-56
D13 WO 95/31990
D25 "Citizen Petition" by Teva Neuroscience, 26 September 2008
D28 FDA's reply to the Eighth Petition of Teva, 16 April 2015

D32 Expert opinion Prof. Liskamp, 7 September 2016, 18 pages
D33 Houben-Weyl "Synthesis of Peptides and Peptidomimetics", 20 November 2002, pp. 454-460
D34 Copaxone® public assessment report
D35 WO 2006/029393
D36 Copaxone® product information leaflet
D37 Second expert opinion Prof. Liskamp, 13 July 2017, 13 pages
D38 Extract of FDA's Code of Federal Regulations 21, 1 April 2017
D39 "Introduction to NMR", experimental report, five pages
D40-O2 Teva, SEC Filings, 10 July 2018, two pages
D40-O3 FDA's Compliance Program Guidance Manual, 30 pages
D41 Opinion by Dr Lansing, 29 July 2021, eight pages
D42 Third expert opinion by Prof. Liskamp, 1 November 2021, nine pages
D43 IUPAC-IUB Joint Commission on Biochemical Nomenclature; Eur. J. Biochem. 138, 9-37, 1984

XVI. Appellant I's submissions, in so far as relevant to the present decision, may be summarised as follows:

Admission of documents

Document D39 was filed at the earliest opportunity on appeal, in compliance with Article 12(2) RPBA. Although it had been available to the patent proprietor earlier, filing it had not been deemed necessary until opponent 2 submitted D32 at the Rule 116 EPC deadline. At that point in time, it would have no longer been possible for the patent proprietor to submit a further document in the written proceedings. D39 had nevertheless been available to the opponents since 2017, having been

filed in a related case, so it had not come as a surprise. Moreover, it was simply an analysis that helped to explain the chemistry underpinning the invention, in order to show that it did not correspond to classic chemistry as alleged in D32.

D41 was helpful for understanding the chemistry behind the process of glatiramer acetate (GA) manufacture and the opponents had had the opportunity to react to it.

Main request: Rule 80 EPC

The amendment to claim 7 as granted (claim 5 of the main request) was in response to an objection under Article 100(c) EPC, so it complied with Rule 80 EPC.

Main request: Article 56 EPC, claims 1 and 2

The opposition division's findings concerning the inventive step of claims 1 and 2 resulted from a misinterpretation of the claim, contrary to established case law, under which claims should be read in a technically sensible way, taking into account the whole disclosure of the patent, with a mind willing to understand, and ruling out those interpretations that were illogical or did not make technical sense. It was apparent from the patent (paragraphs [0005], [0006], [0009], [0016], [0028] and [0035]) that the stated range of pyro-glutamate (pyro-Glu) should be read in relation to GA alone otherwise the claim would not make sense. Therefore, the technical effect was achieved across the whole scope of claims 1 and 2.

Auxiliary request 1: Rule 80 EPC, Article 84 EPC, Article 123(2) and (3) EPC

The amendment to claims 1 and 2, significantly reducing the scope of the claims, was occasioned by a ground for opposition, as required by Rule 80 EPC.

Claims 1 and 2 could only be interpreted as referring to a batch "consisting of" GA. The term "batch" had a clear meaning, particularly in the context of chemical production, as evident from the FDA's definition in D38. It would thus be immediately clear for the skilled person that a batch of GA indicated a specific quantity of the substance GA produced during a single manufacturing cycle. Article 84 EPC was thus fulfilled.

As to Article 123(2) EPC, there was a verbatim basis for "batch of glatiramer acetate" in paragraph [0016]. This passage could be combined with e.g. paragraphs [0005], [0020] and [0026] of the application as filed, which disclosed the specifically claimed methods.

Article 123(3) EPC was also fulfilled because the subject-matter covered by the amended claims was already part of the claims as granted. Contrary to the opponent's arguments, the expression "composition comprising an amino acid polymer" did not require an amino acid copolymer plus at least one other component to be present. As per established case law, the meaning of "composition comprising" encompassed both "consisting of or containing", and the term "comprising" could be replaced by "consisting of" without adding matter.

Auxiliary request 1: Article 56 EPC

The problem solved by the patent was established in D25, which explained that there was a need to facilitate consistent and controlled manufacture of GA

for pharmaceutical use and to demonstrate that the GA had the same characteristics as the product on the market. Despite being slightly post-published, D25 served as contemporaneous evidence for the issue. Document D13 was the closest prior art and the difference was determining the amount of pyro-Glu and using that parameter to help provide batch-to-batch consistency and show identity. The problem was solved, as shown in Table 2 of the patent and confirmed in document D28. There was nothing in the art suggesting this solution to the problem since it was the patent that had established that pyro-Glu was formed and why it was a signature (see paragraph [0034]; Table 1, paragraph [0050]). The solution was not obvious from D13 – or from D1 if taken as the closest prior art – as neither disclosed pyro-Glu at all. In fact, although GA had long been in production, pyro-Glu had never been mentioned in the related literature and would not be expected to form under GA manufacture conditions. The skilled person would not turn to D6 since it only mentioned antibodies and was therefore irrelevant for a synthetic non-biological complex drug such as GA. Moreover, D6 was directed not to identifying structural signatures but to impurities and variants which should be minimised (page 53, bottom of left-hand column).

XVII. Appellant II's arguments, in so far as relevant to the present decision, may be summarised as follows:

Admission of documents

Document D39 could have been submitted much earlier in the proceedings as it was already in the patent proprietor's possession. The patent proprietor could have submitted it any time either before or during oral proceedings, or the proprietor could have requested

postponement of oral proceedings. D32 only reported on classic chemistry and was not complex, so it would have been possible to react to it. Since D39 was not part of the appealed decision, it should not be discussed.

The justification for the late-filing of document D41 should not be accepted.

Main request: Article 56 EPC, claims 1 and 2

It was the wording of the claims that was relevant, not what was meant by them. It was apparent that there had to be a difference between measuring in a batch of a composition comprising GA (as in claims 1 and 2) versus measuring in the purified GA as in claims 6 to 8. In view of the claims' wording, the problem could not be considered solved over the whole scope of the claims.

Auxiliary request 1: Rule 80 EPC, Article 84 EPC, Article 123(2) and (3) EPC

The amendment could not be seen as a *bona fide* attempt to overcome the inventive-step objection. Moreover, deleting a claim element led to new issues in relation to patentability. Therefore, the request should not have been admitted into the proceedings pursuant to Rule 80 EPC.

There was no unequivocal generally accepted meaning for "batch of substance" in the relevant art, it being apparent from the description (paragraph [0019]) that the term had no specific meaning. The amendment thus rendered the claims unclear.

The term "preparation" in paragraph [0016] referred not to a batch but to a pharmaceutical preparation, as

apparent from paragraph [0014]; by definition, a preparation comprised an active substance and at least an excipient. Moreover, this passage was not in the context of selecting a batch. Further passages (such as page 8, line 8 and page 12, lines 17 to 18) did not provide a basis either because they neither related directly and unambiguously to a batch nor referred to selecting a batch with the claimed pyro-Glu range. Hence, the claims contravened Article 123(2) EPC.

Contrary to the opposition division's conclusions, it could not be accepted, nor was it supported by the application, that a batch of a composition comprising GA encompassed (i) a batch with GA by itself, (ii) a batch with GA and some impurities and (iii) a batch with GA and intentionally added ingredients. Hence, amending claims to allegedly options (i) and (ii) represented an unallowable extension of scope (Article 123(3) EPC).

Auxiliary request 1: Article 56 EPC, claims 1 and 2

The manufacture of GA was well known in the art, e.g. D1 and D13. D1, which was a more recent publication specifically relating to GA and referred back to D13 (page 2, last paragraph), was the closest prior art. D1 was concerned with determining residual impurities (page 21, lines 19 et seq.) and disclosed an improvement in the manufacturing process by predetermining the percentage of brominated tyrosine (page 19, lines 14 et seq.). Claim 55 (and 58 relating to GA) was almost identical to claims 6 to 8 of auxiliary request 1, the only difference being that brominated tyrosine was measured rather than pyro-Glu. The technical effect was that pyro-Glu was used to ensure consistency in the production of GA. The

technical problem was to provide an alternative test for consistency, and the problem was solved by the claimed subject-matter as evidenced by the data in Table 2 of the patent. Contrary to appellant I's arguments, the skilled person would expect pyro-Glu to be present in GA (D33). D6 also disclosed the same purpose as the patent, namely "defining your product profile and maintaining control over it" (title; page 51, top of the left-hand column of the abstract). From D33 the skilled person knew about pyro-Glu formation in proteins that occurred in nature, and since these had the same sequences as synthetic polypeptides the skilled person would expect the same effects to be present in the synthetic polypeptides too. In view of this knowledge and in line with the strategy of D6, the skilled person would merely have to measure and find an amount of pyro-Glu within the claimed range.

XVIII. Appellant III's arguments, submitted in writing and in so far as relevant to the present decision, may be summarised as follows:

Main request: Rule 80 EPC

Claim 7 failed to comply with Rule 80 EPC; an independent claim had been converted into a dependent claim.

Main request: Article 56 EPC, claims 1 and 2

The opposition division had correctly decided that claims 1 and 2 did not involve an inventive step. Appellant I's arguments that the claim had been misinterpreted were without merit; "comprising" had a well-known meaning.

Auxiliary request 1: Rule 80 EPC, Article 84 EPC, Article 123(2) and (3) EPC

For the same reasons as with the main request, auxiliary request 1 did not comply with Rule 80 EPC.

The amendment rendered the claims unclear. Because the established wording "consisting of" had not been used, it was unclear whether the claim was indeed intended to exclude all materials other than GA or to be directed to something in between that position and a completely open claim, such as that provided by the "comprising" wording. Even if it were accepted that further intentionally added constituents were excluded but some impurities or by-products might be present, the question arose as to what impurities might be present.

Paragraph [0016], indicated as a basis for the amendment, related to the pre-selected relationship between pyro-Glu in a batch of glatiramer and a reference value, which implied that batches were made by equivalent methods and could then be released for commerce, even if they contained impurities. The claims thus contravened Article 123(2) EPC.

Article 123(3) EPC was not fulfilled. "Composition" added something over a compound per se, i.e. required that "two or more substances" were present together. This requirement was no longer present in the amended claims, meaning that the scope was broader.

Auxiliary request 1: Article 56 EPC

The claimed range had no technical effect in terms of pharmacological profile of the glatiramer. Moreover, in the case of claims 1 and 2, since a GA composition also

allowed for the presence of impurities and by-products, the ppm pyro-Glu attributable to GA would be confused with the pyro-Glu attributable to impurities and by-products. Accordingly, the technical problem could only be formulated as merely providing a method for measuring an alternative product variant. The solution would be obvious because pyro-Glu was expected to be present in any copolymer containing terminal glutamic acid residues. As was apparent from the patent (paragraph [0034], particularly lines 39 to 42 and 45 to 46), there were too many variables involved and simply copying the amount of pyro-Glu in the GA composition would not make it possible to assess the quality or even the manufacturing steps; this was evidenced by the deviating sample A in Table 2. Since the claim referred to a composition comprising GA, meaning that other batches of GA not having the claimed pyro-Glu range might be included, the pyro-Glu amount was meaningless for the final product. Additionally, the concentration of pyro-Glu was not even consistent between individual samples of Copaxone®, as evident from the broad range obtained of 2 500 to 6 500 ppm (paragraphs [0052] to [0054] and Table 2 of the patent). There was no single test which could be used to conclude that GA had been consistently produced in relation to Copaxone®, due to the inherently highly variable and non-consistent nature of GA. Lastly, the amount of pyro-Glu measured was completely dependent on the analysis method. If the skilled person were to use a different (as yet unknown and undisclosed) analysis method, they would inevitably arrive at a completely different pyro-Glu value or range. Hence, third parties would be unable to determine whether they were working in the scope of the claim.

XIX. Appellant I (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the claims of the main request filed as auxiliary request 1 with the statement of grounds of appeal or, alternatively, that the opponents' appeals be dismissed, implying the maintenance of the patent on the basis of auxiliary request 1 filed as auxiliary request 2 with the statement of grounds of appeal. Appellant I moreover requested that documents D38, D39 and D41 be admitted into the proceedings.

Appellant II (opponent 2) requested that the decision under appeal be set aside and that European patent No. 2277050 be revoked. It also requested that documents D35 to D37, D40-O2, D42 and D43 be admitted into the proceedings and that documents D39 and D41 not be admitted into the proceedings.

Appellant III (opponent 3) had requested in writing that the decision under appeal be set aside and that European patent No. 2277050 be revoked.

Reasons for the Decision

1. The appeals are admissible.

2. Oral proceedings took place in the absence of appellant III, which had been duly summoned but decided not to attend, as stated in letter dated 21 September 2021. In accordance with Rule 115(2) EPC, the board decided to continue the proceedings in its absence.

Moreover, pursuant to Article 15(3) RPBA the board was not obliged to delay any step in the proceedings,

including its decision, by reason only of the absence at the oral proceedings of any party duly summoned. Accordingly, the absent party was treated as relying only on their written case.

3. Admission of documents

3.1 A number of documents were filed during the appeal proceedings: documents D35 to D37 (filed by appellant II with the grounds of appeal), D38 and D39 (filed by appellant I with the reply to the opponents' statements of grounds of appeal), D40-O2 (filed as D40 by appellant II with the letter dated 12 July 2018), D40-O3 (filed as D40 by appellant III with the letter dated 8 August 2018), D41 (filed by appellant I with the letter dated 30 July 2021), and D42 and D43 (filed by appellant II with the letter dated 1 November 2021). Appellant II requested that documents D39 and D41 not be admitted into the proceedings.

Documents D35 to D39

3.2 Pursuant to Article 12(4) RPBA 2007 (which is applicable in this case), everything presented by the parties with the statement of grounds of appeal or reply is to be taken into account but the board has the power to hold inadmissible facts, evidence or requests which could have been presented or were not admitted in the first-instance proceedings.

3.3 There were no objections against the admission of documents D35 to D38, and the board saw no reasons to hold them inadmissible either. The board thus decided not to exclude these documents from the proceedings (Article 12(4) RPBA 2007).

3.4 As to document D39, the following is noted.

3.4.1 According to appellant I, D39 was filed as a reaction to document D32, which was itself only filed on the Rule 116 EPC deadline. Yet appellant I would have had the opportunity to file D39 within the time period between the Rule 116 EPC deadline and the date of oral proceedings or at the oral proceedings before the opposition division. It is true that it would have been late-filed, but appellant I could have then argued that it could not have been filed any earlier since it had been filed as a reaction to D32. Moreover, by appellant I's own admission (letter of reply to opponents' grounds of appeal, page 3, fourth paragraph), appellant I had been in possession of this document since 2016. The board thus accepts appellant II's arguments that appellant I could and should have submitted D39 in the first-instance proceedings. Moreover, the board fails to see how this document, which is essentially aimed at demonstrating experimentally what is already disclosed in the patent, may be of relevance for the discussion of inventive step.

3.4.2 The board thus decided to hold document D39 inadmissible (Article 12(4) RPBA 2007).

Documents D40-O2, D40-O3 and D41 to D43

3.5 Documents D40-O2 and D40-O3 were filed after the replies to the grounds of appeal. Although they were filed in 2018, i.e. long before the entry into force of the RPBA 2020, the requirements of Article 13(1) RPBA 2020 still apply (Article 25(2) RPBA 2020). As per Article 13(1) RPBA 2020, any amendment to a party's appeal case after it has filed its grounds of appeal or reply is subject to the party's justification for its

amendment and may be admitted only at the board's discretion. The board exercises its discretion in view of, *inter alia*, the current state of the proceedings, the suitability of the amendment to resolve the issues which were admissibly raised by the other party in appeal proceedings or raised by the board, and whether the amendment is detrimental for procedural economy.

3.6 D40-O2, submitted in the context of inventive step, is a two-page document from Teva explaining that they would like to avoid competition for their product Copaxone®. D40-O3, submitted in the context of Article 123(3) EPC, is a compliance programme guidance manual from the FDA. As regards D40-O2, appellant II merely stated that it represented "a reactive document supporting our reaction to a newly raised laps-of-time [sic.] argument of the patentee" (letter of 12 July 2018, last page, section 48). Apart from this reference, there is only one other reference to D40-O2 in appellant II's submissions: in section 39 of the letter of 12 July 2018. The board, however, fails to see how this disclosure may be relevant for the inventive-step discussion. As to D40-O3, appellant III did not provide any justification for filing it, let alone for filing it late. The only reference to D40-O3 in appellant III's submissions is on page 2, first and second paragraphs, of the letter dated 8 August 2018, in which the passage on page 4, third paragraph of D40-O3 is cited as providing a definition of active pharmaceutical ingredient (API). The board does not consider that this definition adds anything to the file or is of any relevance for the assessment of Article 123(3) EPC. The board thus considers that admitting D40-O2 and D40-O3 would run counter to procedural economy. Accordingly, these documents were not admitted

into the proceedings, pursuant to Article 13(1) RPBA 2020.

3.7 Documents D41 to D43 were all filed in 2021 after notification of the summons to oral proceedings. The requirements of Article 13(2) RPBA 2020 apply, under which any amendment to a party's case made after notification for oral proceedings shall, in principle, not be taken into account, unless there are exceptional circumstances which have been justified with cogent reasons by the party concerned.

3.8 The board fails to see any exceptional circumstances that would justify submitting these documents, nor have the parties provided any such justification. Document D41 was allegedly submitted in response to D40-O2 while documents D42 and D43 were submitted as a reaction to D41. Since D40-O2 was not admitted into the proceedings, there is no reason to admit D41 and, consequently, no reason to admit D42 and D43 either.

3.9 Accordingly, the board decided not to admit any of documents D41 to D43 into the proceedings (Article 13(2) RPBA 2020).

4. Main request

4.1 Rule 80 EPC

4.1.1 Appellant III argued that claim 7 did not comply with the requirements of Rule 80 EPC because "an independent claim ha[d] been converted into a dependent claim".

4.1.2 Claim 7 of the main request is an independent claim, so the board assumes that appellant III instead meant to refer to claim 5, which corresponds to claim 7 as

granted. Contrary to appellant III's arguments, it is apparent that claim 7 as granted had been drafted in the format of a dependent claim but with an incorrect dependency, which led to a claim interpretation that had no basis in the application as filed. In the main request, this dependency has been amended to overcome the objection under Article 100(c) EPC against claim 7 as granted. Hence, the amendment in question has been occasioned by a ground for opposition and fulfils Rule 80 EPC.

4.2 Articles 84 and 123(2) and (3) EPC

4.2.1 The opposition division concluded that the set of claims before it complied with the above EPC requirements, and the opponents did not raise objections under any of them on appeal. Hence, the opposition division's conclusions in this respect are still valid.

4.3 Article 56 EPC

4.3.1 The patent at issue is generally directed to GA production methods. As taught in paragraph [0001] of the patent, GA (also known as copolymer-1 and marketed as the active ingredient in Copaxone® by Teva Pharmaceutical Industries Ltd., Israel) is used to treat the relapsing-remitting form of multiple sclerosis (RRMS). According to the Copaxone® product label, GA consists of the acetate salts of synthetic polypeptides, containing four naturally occurring amino acids, L-glutamic acid, L-alanine, L-tyrosine and L-lysine, with a reported average molar fraction of 0.141, 0.427, 0.095 and 0.338, respectively. Chemically, GA is designated L-glutamic acid polymer with L-alanine, L-lysine and L-tyrosine, acetate

(salt). Since slight manufacture variations are expected to potentially lead to product variability, the patent aims to provide methods for ensuring product consistency. This is achieved by measuring the amount of pyro-Glu in each GA batch and selecting those batches with a pyro-Glu amount in a predetermined range (which broadly corresponds to the range measured in the commercial product Copaxone®). According to the patent (paragraph [0005]): "The invention is based (...) on the identification and characterization of L-pyroGlutamic Acid (pyro-Glu) as a structural signature of glatiramer acetate (GA). Analysis of this signature component of GA is useful to assess product and process quality in the manufacture of GA."

4.3.2 Document D1, which discloses the production of an amino acid copolymer (GA; see claims 55 and 58), can be considered the closest prior art. The distinguishing feature between the claimed subject-matter and D1 is that pyro-Glu is measured and this measurement forms the basis for selecting the GA batch that has been produced, the aim being to select a batch comprising 2 000 to 7 000 ppm pyro-Glu.

4.3.3 As to the technical effect of this distinguishing feature, it has not been disputed that the claimed range for the amount of pyro-Glu is a structural signature which makes it possible to ensure consistency when producing a GA preparation. However, claims 1 and 2 refer to a "batch of a composition comprising glatiramer acetate" and require that the amount of pyro-Glu in said batch is 2 000 to 7 000 ppm. Since this wording means that the batch is not necessarily composed solely of GA and that GA need not be the composition's main component, the board considers the stated range to be meaningless because it can be a

structural signature for GA compositions only, not for compositions with GA and something else, e.g. another amino acid copolymer. Hence, there is no technical effect linked to this difference over the whole scope of claims 1 and 2, and the technical problem is thus to be formulated as simply providing a process for selecting batches of compositions comprising GA on the basis of a measurement of one parameter.

4.3.4 The claimed solution solves the above problem but it is obvious because the skilled person would just measure pyro-Glu or any other equally likely parameter in order to select batches of compositions comprising GA. As it was common general knowledge that pyro-Glu was produced from glutamate residues that were known to be one of the four amino acids in the GA compositions, the skilled person would certainly have expected some amount of pyro-Glu to be measured in batches of compositions comprising GA. Since the stated range is not associated with any technical effect, it was just one among various equally likely alternative ranges.

4.3.5 Appellant I disagreed that document D1 was the closest prior art, instead asserting that the closest prior art document was D13, and essentially argued that if the claim was read with a mind willing to understand and in the light of the description it was apparent that the stated amount of pyro-Glu related solely to GA.

4.3.6 The board agrees that both D1 and D13 can be considered the closest prior art. However, it accepts appellant II's argument that D1 is a more suitable starting point for the inventive-step discussion as it is a much more recent publication than D13 and even refers back to D13. In any case, inventive step can only be acknowledged if the claims are not obvious starting

from any suitable prior-art document, i.e. also from D1.

4.3.7 The board also agrees that the claims are to be read with a mind willing to understand and in a technically sensible way. However, it is established case law that the description cannot be relied on to read into the claims implicit restrictive features which are not suggested by the explicit wording of the claims, in particular when the wording gives the skilled reader clear, credible technical teaching. Claims 1 and 2 refer to a batch of a composition comprising GA; a technically sensible interpretation of this expression is as given above: a composition which comprises GA but not necessarily as the sole or main component. The fact that claims 6 to 8 explicitly refer to measuring in the purified GA further supports the idea that claims 1 and 2 are to be interpreted differently. Moreover, this interpretation does not contradict the description, which also refers to a composition comprising GA or an amino acid copolymer in general (e.g. paragraph [0006] of the patent).

4.3.8 The board thus concludes that claims 1 and 2 of the main request lack inventive step (Article 56 EPC).

5. Auxiliary request 1

5.1 Rule 80 EPC

5.1.1 Rule 80 EPC stipulates that amendments can be made to the patent, provided that said amendments are occasioned by a ground for opposition under Article 100 EPC. Appellant II argued that the claims of auxiliary request 1 did not comply with Rule 80 EPC and should therefore not be admitted into the proceedings.

5.1.2 In auxiliary request 1, claims 1 and 2 have been amended by replacing the expression "a batch of a composition comprising glatiramer acetate" with the expression "a batch of glatiramer acetate", in an attempt to overcome the inventive-step objection raised against these claims. The board thus considers that the amendments have been occasioned by a ground for opposition and constitute a *bona fide* attempt to overcome that objection.

5.1.3 As to appellant II's arguments that the amendments give rise to new issues and are not suitable to overcome the inventive-step objection, the following is noted. Whether or not new issues arise in view of an amendment is irrelevant for Rule 80 EPC, which only requires the amendments to be occasioned by grounds for opposition. Moreover, Rule 80 EPC does not require the amendment to successfully overcome the objection, which of course can only be determined after examining the claimed subject-matter.

5.1.4 The board thus concludes that auxiliary request 1 complies with Rule 80 EPC.

5.2 Article 84 EPC

5.2.1 Appellants II and III asserted that the amendment made to claims 1 and 2, replacing "a batch of a composition comprising glatiramer acetate" with "a batch of glatiramer acetate" rendered the claims unclear because it was not apparent what was covered by this term.

5.2.2 Appellant I argued that the term "batch" had a clear definition in the art, given in D38. Hence, in the context of the patent, batch meant a specific quantity

of the substance GA produced during a single manufacturing cycle. The board concurs with appellant I and the opposition division that this definition means a composition that is essentially composed of GA, possibly with impurities or by-products resulting from the manufacture, but not comprising any further intentionally added constituents. Since these impurities or by-products will be ones that naturally result from the manufacturing process, the skilled person would readily be able to identify them, contrary to appellant III's arguments that it would be unclear what impurities or by-products might be present.

5.2.3 Accordingly, this interpretation does not exclude the possibility that polypeptides comprising pyro-Glu may be present in the GA batch. Contrary to appellant II's arguments, GA does not consist solely of acetate salts of synthetic polypeptides containing four natural polypeptides (L-glutamic acid, L-alanine, L-tyrosine and L-lysine) in given average molar fractions as reported in paragraph [0001] of the application as filed. Rather, these four amino acids in the reported average molar fractions are the starting material for producing GA and, in the course of GA production, will give rise to other types of amino acids, such as pyro-glutamic acid residues.

5.2.4 Moreover, the board does not accept appellant II's arguments that a batch of GA is to be interpreted as being equivalent to the clinically approved Copaxone®, which of course comprises excipients (D34). As is very much apparent from several passages in the description and in the claims directed to pharmaceutical compositions, a batch of GA is the drug substance produced from four natural amino acids by the methods described in the patent and in the prior art (D1, D13).

The aim of the patent is to provide batches of GA that can be considered equivalent to the GA compositions used in the commercially available product and which can therefore be used to manufacture pharmaceutical compositions by adding pharmaceutical excipients and possibly other ingredients afterwards.

5.2.5 The board therefore concludes that the subject-matter of claims 1 and 2 of auxiliary request 1 complies with Article 84 EPC.

5.3 Article 123(2) EPC

5.3.1 Paragraph [0025] of the application as filed teaches that the pyro-Glu amount in GA can be used as a signature component of GA "that can be evaluated to assess the GA manufacturing process and product quality". The last sentence of paragraph [0026] then teaches that "Pyro-Glu is present in GA in a range of 2000-7000 ppm and can be assessed to identify or evaluate GA and its method of manufacture, and/or to evaluate the quality or suitability of a GA product for pharmaceutical use". Although this passage refers not to a "batch of" GA but only to GA, it is nevertheless clear that it relates to evaluating pyro-Glu in batches of GA, i.e. in specific amounts of product prepared within a single manufacturing cycle (D38). This is also apparent from the description as a whole, which repeatedly refers to batches, and in particular when read in combination with paragraph [0016], which explicitly refers to a batch of GA in the context of checking that the value for the amount of pyro-Glu has a pre-selected relationship with the reference value. The board thus considers that the application as filed provides a basis for claims 1 and 2 of auxiliary request 1.

5.3.2 The board disagrees with appellant II's arguments that the term "preparation" in paragraph [0020] of the application as filed corresponds not to a batch but to a pharmaceutical preparation as mentioned in paragraph [0014]. Paragraph [0014] refers to a pharmaceutical preparation as an alternative to a batch, further teaching that "the concentration of pyro-Glu in the batch is within a predetermined range, e.g. 2000-7000 ppm" (emphasis added). In between these two paragraphs, paragraphs [0016] and [0018] also teach measuring pyro-Glu in the batch.

5.3.3 The board thus concludes that auxiliary request 1 fulfils Article 123(2) EPC.

5.4 Article 123(3) EPC

5.4.1 The board agrees with appellant I and considers that the expression "a composition comprising glatiramer acetate" is to be construed as being directed to a composition that necessarily contains GA and may, but need not, contain something else. Hence, claims 1 and 2 as granted, referring to "a composition comprising glatiramer acetate", also encompassed the embodiment of a composition consisting of GA. Accordingly, the scope of claims 1 and 2 of auxiliary request 1 has been restricted but not shifted in relation to the scope of claims 1 and 2 as granted. The board disagrees with appellant III's arguments that the term "composition" necessarily means that more than one compound has to be present.

5.4.2 The board thus concludes that Article 123(3) EPC is fulfilled.

5.5 Article 56 EPC

5.5.1 Document D1 is the closest prior art and, as concluded above in relation to the main request, the distinguishing feature is that pyro-Glu is measured and this measurement forms the basis for selecting the batch of GA, the aim being to select a batch comprising 2 000 to 7 000 ppm pyro-Glu.

5.5.2 Since the claimed range for the amount of pyro-Glu is a structural signature which makes it possible to ensure consistency when producing a GA preparation, the technical effect of the distinguishing feature is being able to define a parameter that can be used to select batches which are consistent with, i.e. have the same characteristics as, the commercially approved product. The technical problem is thus formulated as providing a process that makes it possible to select batches of GA which have the necessary quality and suitability for pharmaceutical use. The board is satisfied that the claimed solution solves this problem.

5.5.3 According to paragraph [0028] of the patent, the physiochemical characteristics of the commercially available GA product Copaxone®, other than molecular weight and amino acid composition, were not specified on the approved label for the product or in other available literature. As reflected in D25 (a document which can be taken as contemporaneous evidence but is not prior art since it was published slightly after the filing date of the patent), there was a need to identify further parameters that could be used to conclude that a GA preparation had the same characteristics as the product on the market, so that it could be considered suitable for pharmaceutical use.

5.5.4 None of the available prior-art documents disclosing GA manufacture, such as D1 and D13, discloses the presence of pyro-Glu in the preparations, let alone that it could be used as a structural signature for the GA composition. In fact, at no point do any of these documents refer to the need to measure any parameters in order to assess product consistency.

5.5.5 Appellants II and III argued that it was common general knowledge that pyro-Glu was produced from glutamic acid residues and, since glutamic acid was known to be one of the four amino acids in the GA compositions, the skilled person would certainly have expected some amount of pyro-Glu to be measured in batches of compositions comprising GA. However, there was no indication in the prior art that the amount of pyro-Glu could be indicative of the consistency of the GA preparations.

5.5.6 The patent was the first document to disclose that evaluating the pyro-Glu content of a sample of GA made it possible to identify non-conforming compositions, which would not be detected by merely looking at molar mass and amino acid composition (paragraph [0028] and Table 2 of the patent). Moreover, the inventors disclosed that the mechanism underpinning this observation was directly linked to the manufacturing method, meaning that differences in the manufacturing method could lead to different pyro-Glu amounts. As stated in the patent in paragraph [0029]: "The production of GA entails both polymerization of amino acids and partial depolymerization of the resulting peptides. It has now been found that depolymerization is highly specific and non-stochastic and occurs to a disproportionately high extent to the N-terminal side of glutamate residues. Indirectly, this results in

pyro-Glu GA as a signature structural characteristic of GA, surprisingly occurring primarily as a consequence of depolymerization. Pyro-Glu is present in GA in a range of 2000-7000 ppm and can be assessed to identify or evaluate GA and its method of manufacture, and/or to evaluate the quality or suitability of a GA product for pharmaceutical use."

5.5.7 The board thus considers that a skilled person looking for a process to allow them to select batches of GA with the necessary quality and suitability for pharmaceutical use would not arrive at the claimed solution in an obvious way.

5.5.8 According to appellant II, document D1 already disclosed an improvement to the GA manufacturing process by predetermining the percentage of brominated tyrosine (D1, page 19, lines 14 et seq.), meaning that the distinguishing feature between the claimed subject-matter and D1 was that pyro-Glu was measured rather than brominated tyrosine. The technical problem was thus to be formulated as providing an alternative test for consistency in GA production. Since pyro-Glu was expected to be present in GA preparations (D33) and D6 specifically mentioned pyro-Glu in the context of "defining your product profile and maintaining control over it", all the skilled person would have to do to arrive at an amount within the claimed range was to follow the teachings of D6 and measure the amount of pyro-Glu in the marketed GA product.

5.5.9 The board disagrees with appellant II's formulation of the technical problem as that of providing an alternative test for consistency in GA production. Contrary to appellant II's arguments, D1 is not concerned with testing for consistency in GA

production. Rather, it identifies brominated tyrosine as an undesirable component of the preparation to be kept below a given maximum amount. Moreover, the board disagrees that D6 would prompt the skilled person to measure the amount of pyro-Glu as an indicator of consistency in the production of the desired product. D6 lists pyro-Glu among a long list of possible contaminants or by-products that should be looked for and controlled, and is specifically related to antibodies, not to synthetic polypeptides. As explained above, the production of pyro-Glu during GA manufacture is very specifically linked to the manufacturing method used, and this could not have been derived from D6.

5.5.10 The board also disagrees with appellant III's formulation of the technical problem as being that of providing a method for measuring an alternative product variant. It is true that the claimed range does not have any technical effect in terms of pharmacological profile of the glatiramer, but it does have a technical effect, namely that, as explained above, it makes it possible to select batches which are consistent with, i.e. have the same characteristics as, the commercially approved product. It is also true that a GA composition may contain impurities and by-products, but the board disagrees that this would render the measured pyro-Glu amount meaningless. The aim of measuring the pyro-Glu amount is to determine that a given characteristic which has been identified as a structural signature is present despite different manufacturing processes that are liable to lead to different impurities and/or by-products, thus making it possible to conclude that the product is consistent with the marketed product. Moreover, the fact that the final composition may comprise further components, including further batches of GA, is irrelevant for the claimed subject-matter,

which merely requires that batches having the claimed range of pyro-Glu are selected; their use and whether or not they are used in combination with other components are outside the scope of the claim.

5.5.11 A further argument made by appellant III was that the concentration of pyro-Glu was not even consistent between individual samples of Copaxone®, as evident by the broad range obtained of 2 500 to 6 500 ppm (paragraphs [0052] to [0054] and Table 2 of the patent), meaning that pyro-Glu could not be used as a measure of consistency between different batches. The board notes that the inventors identified the claimed range as being characteristic of the marketed composition and that there is no evidence to dispute that a batch with a pyro-Glu amount within this range (and otherwise also having the characteristic molecular weight) would have the same characteristics as marketed GA. The FDA has accepted this parameter as being indicative of a product with the same quality as the GA compositions already on the market (D28, page 28, section 3). Additionally, in view of the inherently highly variable nature of GA, a broader range may be accepted while still ensuring that the product has a given consistency.

5.5.12 Appellant III further argued that the amount of pyro-Glu measured was dependent on the analysis method, with completely different results being obtained by different methods, and that, since the claim did not indicate what analysis method was to be used, the skilled person would be unable to determine whether or not they were working within the scope of the claim.

5.5.13 For the board, this argument is more so an objection of a lack of clarity against a feature that had been

present in the claims as granted and was therefore not open to clarity objections in the opposition proceedings. In so far as this argument can be read in the context of inventive step as indicating that the parameter is meaningless for lack of any indication of the analysis method used, the board notes that different analysis methods are not expected to give significantly different results; the usual degree of variation between analysis methods is not such as to render the obtained results incomparable. The patent itself teaches that "[w]hatever method is used to measure pyro-Glu in the batch or sample, and whatever units are used to express the measured pyro-Glu in the batch or sample, the concentration of pyro-Glu in the selected batch is between 2000 and 7000 ppm" (paragraph [0016]). Moreover, appellant III did not provide any evidence to contest this statement and back up its assertion that significantly different results would be obtained.

5.5.14 The board thus concludes that the claims of auxiliary request 1 fulfil the requirements of Article 56 EPC.

5.6 Conclusion

5.6.1 No further objections against auxiliary request 1 were put forward on appeal. The board therefore considers that the opposition division's decision maintaining the patent as amended on the basis of the claims of what was then auxiliary request 2 (now auxiliary request 1) remains valid.

Order

For these reasons it is decided that:

The appeals are dismissed.

The Registrar: The Chairwoman:

M. Schalow M. Pregetter

Decision electronically authenticated