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Datasheet for the decision of 21 September 2023

Case Number: T 1435/20 - 3.3.04

Application Number: 16172335.8

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Language of the proceedings: EN

Title of invention:
Treatment of paroxysmal nocturnal hemoglobinuria patients by an inhibitor of complement

Applicant:
Alexion Pharmaceuticals, Inc.

Headword:
Paroxysmal nocturnal hemoglobinuria / ALEXION PHARMACEUTICALS

Relevant legal provisions:
EPC Art. 76(1), 83, 84, 123(2)
EPC R. 139
RPBA 2020 Art. 12(4), 12(6), 13(2)

Keyword:

Admittance (no) - Auxiliary requests 1, 2A, 6, 7A and 9 to 17
Added subject-matter (yes) - Main request and auxiliary requests 3 and 5
Clarity (no) - Auxiliary requests 2 and 7
Sufficiency of disclosure (no) - Auxiliary requests 4 and 8

Decisions cited:

G 0003/89, G 0011/91, G 0007/93, G 0002/21

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Case Number: T 1435/20 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 21 September 2023

Appellant: (Applicant)	Alexion Pharmaceuticals, Inc. 100 College Street New Haven, CT 06510 (US)
Representative:	J A Kemp LLP 80 Turnmill Street London EC1M 5QU (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 28 January 2020 refusing European patent application No. 16172335.8 pursuant to Article 97(2) EPC**

Composition of the Board:

Chair	M. Pregetter
Members:	B. Claes
	L. Bühler
	B. Rutz
	A. Bacchin

Summary of Facts and Submissions

I. The appeal of the applicant (appellant) lies from the decision of the examining division refusing European patent application No. 16 172 355.8 entitled "*Treatment of paroxysmal nocturnal hemoglobinuria patients by an inhibitor of complement*". The application is a divisional application of European patent application No. 11 001 632.6, which itself is a divisional application of European patent application No. 07 753 249.7 filed under the PCT as an international patent application ("application as filed") and published as WO 2007/106585.

II. The examining division decided that claim 1 of the main request and of auxiliary requests 1, 2, 4 and 6 did not meet the requirements of Articles 76(1) and 123(2) EPC. Claim 1 of auxiliary requests 3 and 5 did not to relate to added subject-matter, but the claimed subject-matter lacked inventive step. The sets of claims of auxiliary requests 4A and 6A were not admitted into the proceedings.

III. With the statement of grounds of appeal, the appellant submitted sets of claims of a main request and an auxiliary request 1, a second auxiliary request, an auxiliary request 2A, third to seventh auxiliary requests, an auxiliary request 7A, an eighth auxiliary request and auxiliary requests 9 to 17. The sets of claims of the main request and of the second auxiliary request, of auxiliary request 2A, of the third to fifth auxiliary requests, of the seventh auxiliary request, of auxiliary request 7A and of the eighth auxiliary request were identical to the requests dealt with by the examining division, albeit renumbered. Auxiliary

requests 1, 6 and 9 to 17 were new to the proceedings. The appellant submitted arguments as to why the decision of the examining division was wrong in respect of the requests dealt with and why the new requests were allowable.

IV. The appellant was summoned to oral proceedings, and subsequently the board issued a communication under Article 15(1) RPBA setting out its preliminary opinion on matters that seemed to be of particular significance for the decision.

V. During the oral proceedings, the appellant filed new sets of claims of the main request, of the fifth auxiliary request, and of auxiliary requests 9 and 14. At the end of the oral proceedings, the Chair announced the board's decision.

VI. The wording of claim 1 of each request dealt with by the board and relevant to the decision is reproduced at the beginning of the corresponding parts of the reasons for the decision below. The appellant's relevant arguments relating to these requests are also summarised in these parts.

VII. In assessing the requirements of Article 123(2) EPC, the board makes reference to the text of the international patent application (see section I.). The passages referred to are identical to the corresponding passages in the parent application and the application under consideration.

VIII. The following documents are referred to in this decision:

D16: Press release by Alexion Pharmaceuticals dated 16 March 2007

D31: Declaration by Dr Leonard Bell

IX. The appellant requested that the decision under appeal be set aside and a patent be granted on the basis of the set of claims of the main request filed during the oral proceedings, or alternatively on the basis of the set of claims of one of auxiliary request 1, the second auxiliary request, auxiliary request 2A, the third to seventh auxiliary requests, auxiliary request 7A, the eighth auxiliary request and auxiliary requests 9 to 17, all filed with the statement of grounds of appeal except for the fifth auxiliary request and auxiliary requests 9 and 14, which were filed during the oral proceedings.

Reasons for the Decision

Main request and fifth auxiliary request

Admittance

1. Both requests were filed during the oral proceedings and were admitted into the proceedings by the board (Article 13(2) RPBA). However, in view of the fact that the requests were held not allowable (see later), it is not necessary for the board to provide reasons for admitting them.

Claim 1 - amendments - correction (Rule 139 EPC) and added subject-matter (Articles 76(1) and 123(2) EPC)

2. Claim 1 of the main request differs from claim 1 of the main request dealt with by the examining division solely in the replacement of 214 by 236 in the context of the range of residues of SEQ ID NO: 4, and reads as follows:

"*1. A pharmaceutical composition comprising an antibody that binds C5 in a 300mg single unit dosage form comprising 30 ml of a 10 mg/ml sterile, preservative free solution, wherein* ***the antibody comprises*** *a heavy chain consisting of SEQ ID NO: 2 and* ***a light chain consisting of residues 23 to 236 of SEQ ID NO: 4****, for use in treating a patient suffering from paroxysmal nocturnal hemoglobinuria (PNH).*" (emphasis added by the board)

3. What is claimed is a pharmaceutical composition in a further-medical-use format wherein the C5-binding antibody comprises "a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of residues 23 to 236 of SEQ ID NO: 4". It is undisputed that the only references to SEQ ID NO: 4 in the disclosure of the application as filed are found on page 5, lines 30 to 33 ("*In certain embodiments, the antibody that binds C5 or an active antibody fragment thereof comprises a heavy chain and a light chain, wherein the heavy chain consists of SEQ ID NO: 2 and the light chain consists of SEQ ID NO: 4*") and on page 44, where the amino acid sequence of "SEQ ID NO: 2 — Eculizumab Heavy chain" as well as the 236 amino acid long sequence of "SEQ ID NO: 4 - Eculizumab Light chain" are reproduced. It is equally undisputed that the application as filed does

not explicitly disclose the length limitation "residues 23 to 236" for SEQ ID NO: 4.

4. The appellant however submitted that the length limitation "residues 23 to 236" for SEQ ID NO: 4 in the claim to define the antibody that binds C5 in the claimed pharmaceutical composition corrected an obvious error which met the requirements of Rule 139 EPC and Article 123(2) EPC.

5. In opinion G 3/89 (OJ EPO 1993, 117) and decision G 11/91 (OJ EPO 1993, 125), the Enlarged Board of Appeal held that corrections under Rule 88, second sentence, EPC 1973 (now Rule 139, second sentence, EPC) were special cases of an amendment within the meaning of Article 123 EPC and fell under the prohibition of extension laid down therein. In accordance with the established case law of the boards of appeal, in the case of a proposed amendment under Article 123(2) EPC or of a correction under Rule 139 EPC, the factual disclosure of the patent application as filed has to be established to a rigorous standard, namely the standard of certainty "beyond reasonable doubt" (see Case Law of the Boards of Appeal, 10th edition, 2020 ["CLBA"], II.E.5).

6. Based on the Enlarged Board's rulings in the opinion and the decision, for a correction in the description, claims or drawings to be allowable under Rule 139, second sentence, EPC, the boards apply a two-step approach (see also CLBA, II.E.4.2) in which both of the following must be established:

(i) it is obvious that the application as filed contains such an obvious error that a skilled person is in no doubt that this information is not correct and

cannot be meant to read as such. Accordingly, it must be obvious that an error is present and has to be objectively recognisable by the skilled person using common general knowledge; and

(ii) the skilled person using common general knowledge would directly and unequivocally ascertain the precise proposed correction. The correction of the error should be obvious in the sense that it is immediately evident that nothing else would have been intended than what is offered as the correction.

7. Concerning the first aspect of the two-step approach, the appellant submitted, and the board can agree, that it was common general knowledge that antibodies are secreted proteins produced from precursor light and heavy chain polypeptides in cells, which precursors each comprise a signal peptide and a mature polypeptide. The signal peptides are cleaved off in the endoplasmic reticulum (ER) of the expressing cell and the mature polypeptide then folds to form the mature protein. The board also agrees that, commonly, recombinant chimeric and humanised antibodies such as the antibody referred to in the claim are produced in transfected mammalian cells from DNA vectors (see also explicit disclosure in the description of the application as filed on page 19, lines 6 to 7 that monoclonal antibodies may be produced in transfected cells, such as CHO cells and NSO cells).

8. The appellant concluded that the skilled person thus knew "*with certainty*" that a given engineered therapeutic antibody comprising a heavy chain and a light chain is produced in cells and therefore that a "*signal peptide was never present*" in the therapeutic antibody, and continued that, based on common general

knowledge, the skilled person would immediately recognise the signal peptide in SEQ ID NO: 4 in view of the starting methionine residue followed by a stretch of 21 mainly hydrophobic amino acids and the fact that the peptide sequence of 236 residues was longer than the average light chain of a mature antibody, which ranged from 211 to 217. The skilled person would therefore immediately recognise that defining the antibody as comprising a light chain variable region consisting of SEQ ID NO: 4 constituted an error.

9. The board is not convinced by the appellant's arguments that criterion i) of the two-step approach in point 6. is met, i.e. that the statement of "a light chain variable region consisting of SEQ ID NO: 4" in the application as filed on page 5 and "SEQ ID NO: 4 - Eculizumab Light chain" on page 44 (see point 3.) constituted such an obvious error that a skilled person was in no doubt that this information was not correct (see point 6.).

10. First, the board has seen no arguments as to why the skilled person, when confronted with the statement "a light chain variable region consisting of SEQ ID NO: 4" as such in the disclosure of the application, would *prima facie* be alerted and consequently prompted to consider and analyse the corresponding sequence depicted on page 44 with a view to determining the presence of particular functional parts/compounds in the unannotated amino acid sequence, in this case an ER signal sequence.

11. Second, even when inspecting the sequence of SEQ ID NO: 4 depicted on page 44 and noting a starting methionine residue followed by a stretch of mainly hydrophobic amino acids (which stretch is in fact 25

amino acids long and also includes the amino acids at positions 23, 24 and 25) and the slightly above-average light chain length for a mature antibody, the skilled person would not, as the appellant has alleged, immediately recognise that the depicted sequence of SEQ ID NO: 4 constituted an error because it included a signal peptide, but instead could, at best, be caused to doubt that the depicted sequence was the sequence it purported to represent. This state of doubt, however, does not equate to the requirement, in the case in hand, for the skilled person to have *no* doubt that the depicted sequence is an error and cannot be intended to be read as such.

12. In view of the above considerations, the board concludes that the appellant's case on criterion i) of the two-step approach in point 6. must fail. Accordingly, for this reason alone, the two-step approach cannot lead to the conclusion that the amendment of the feature "a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4" to "a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of residues 23 to 236 of SEQ ID NO: 4" constitutes an allowable correction under Rule 139 EPC.

13. In view of the above negative conclusion on step i), the board does not deem it necessary to deal with the appellant's further arguments relating to criterion ii) of the two-step approach, which without exception emphasise in more technical detail that the skilled person would investigate and consequently identify the exact length of a leader peptide in the depicted amino acid sequence for SEQ ID NO: 4 on page 44 of the application as filed.

14. The request for correction is thus rejected and the claim fails to meet the requirements of Articles 76(1) and 123(2) EPC.

15. Claim 1 of the fifth auxiliary request corresponds to claim 1 of auxiliary request 2 dealt with by the examining division (214 replaced by 236) and is identical to claim 1 of the current main request (see point 2.), with the additional feature "wherein the pharmaceutical composition is to be administered by intravenous infusion" at the end of the claim.

16. The board's conclusions in points 9. to 14. above on the requirements of Articles 76(1) and 123(2) EPC and Rule 139 EPC concerning claim 1 of the main request apply *mutatis mutandis* to claim 1 of the fifth auxiliary request.

Auxiliary request 1 and sixth auxiliary request - admittance

17. Claim 1 of auxiliary request 1 reads:

"*1. A pharmaceutical composition comprising an antibody that binds C5 in a 300mg single unit dosage form comprising 30 ml of a 10 mg/ml sterile, preservative free solution, wherein* ***the antibody is eculizumab and comprises a heavy chain consisting of SEQ ID NO: 2,*** *for use in treating a patient suffering from paroxysmal nocturnal hemoglobinuria (PNH).*" (emphasis added by the board)

18. This request was first filed in the appeal proceedings with the statement of grounds of appeal and its admittance is governed by Article 12(4) RPBA, which provides the board with the discretion to admit such a request in view of, *inter alia*, the suitability of the

amendment for overcoming issues which led to the decision under appeal.

19. As compared with claim 1 of the main request (see point 2.), the claim now specifies that the C5-binding antibody is "eculizumab and comprises a heavy chain consisting of SEQ ID NO: 2" and lacks a reference to SEQ ID NO: 4. The appellant referred to the disclosure on page 5, lines 28 to 29 ("*In certain embodiments, the pharmaceutical composition comprises eculizumab*.") and on page 44 (see point 3. above) as the basis for the amendments. The board is not persuaded, however, that these passages provide an adequate basis for defining the C5-binding antibody by reference to "eculizumab" and SEQ ID NO: 2 without an explicit reference to SEQ ID NO: 4. Indeed, the skilled person would not directly and unambiguously derive from the disclosure on page 5, lines 31 to 33 and on page 44 (see point 3. above), using common general knowledge, a generalised "eculizumab" antibody defined solely by having a heavy chain consisting of SEQ ID NO: 2 without at the same time comprising a light chain consisting of SEQ ID NO: 4.

20. Thus, in view of the above considerations, the amendment amounts to an undisclosed intermediate generalisation of the disclosure of the application as filed, contrary to the requirements of Article 123(2) EPC. Accordingly, the amendment is not suitable for overcoming the added subject-matter issues which the examining division raised with regard to claim 1 of the main request. The board therefore did not admit the request into the proceedings (Article 12(4) RPBA).

21. Claim 1 of the sixth auxiliary request is identical to claim 1 of auxiliary request 1 (see point 17.), with the additional feature "wherein the pharmaceutical composition is to be administered by intravenous infusion" at the end of the claim.

22. The board's conclusions in points 18. to 20. above on the requirements of Article 123(2) EPC concerning claim 1 of auxiliary request 1 apply *mutatis mutandis* to claim 1 of auxiliary request 6. The board therefore equally did not admit this request into the proceedings (Article 12(4) RPBA).

Second and seventh auxiliary requests - clarity

23. Claim 1 of the second auxiliary request is identical to claim 1 of auxiliary request 4 dealt with by the examining division, and reads:

"*1. A pharmaceutical composition comprising an antibody that binds C5 in a 300mg single unit dosage form comprising 30 ml of a 10 mg/ml sterile, preservative free solution, wherein* ***the antibody is obtainable by transfecting cells with*** *a heavy chain consisting of SEQ ID NO: 2 and* ***a light chain consisting of SEQ ID NO: 4,*** *for use in treating a patient suffering from paroxysmal nocturnal hemoglobinuria (PNH).*" (emphasis added by the board)

24. This claim provides that the antibody referred to in the claim is "obtainable by transfecting cells with" a heavy chain (here a protein consisting of SEQ ID NO: 2) and a light chain (here a protein consisting of SEQ ID NO: 4). However, from a technical point of view cells are routinely not transfected with proteins but

rather are transfected with DNA (from which proteins may then in turn be expressed).

25. The appellant agreed that cells would be transfected with DNA encoding the recited amino acid sequences, but argued that the skilled person would give the claim a technically sensible meaning and understand that the claim is in fact intended to refer to an antibody that is "obtainable by transfecting cells with" a DNA encoding SEQ ID NO: 2 and a DNA encoding SEQ ID NO: 4, and the feature therefore did not introduce any ambiguity.

26. Agreeing with the appellant in this argument would however contravene the general principle established in the case law on clarity of claims that the meaning of the essential features of a claim should be clear to the skilled person from the wording of the claim alone (see CLBA, II.A.3.1).

27. The board thus concurs with the examining division that the definition of the antibody in the claim lacks clarity (Article 84 EPC).

28. Claim 1 of the seventh auxiliary request (identical to claim 1 of auxiliary request 6 dealt with by the examining division) is identical to claim 1 of the current second auxiliary request (see point 23.), with the additional feature "wherein the pharmaceutical composition is to be administered by intravenous infusion" at the end of the claim.

29. This claim thus comprises the same definition of the antibody as claim 1 of the second auxiliary request, and consequently and *mutatis mutandis* this claim too is

contrary to the technical understanding of the skilled person and thus lacks clarity (Article 84 EPC).

Auxiliary requests 2A and 7A – admittance

30. Claim 1 of auxiliary request 2A is identical to claim 1 of auxiliary request 4A dealt with by the examining division, and reads:

"*1. A pharmaceutical composition comprising an antibody that binds C5 in a 300mg single unit dosage form comprising 30 ml of a 10 mg/ml sterile, preservative free solution, wherein* ***the antibody is obtainable by producing in transfected cells*** *a heavy chain consisting of SEQ ID NO: 2 and* ***a light chain consisting of SEQ ID NO: 4,*** *for use in treating a patient suffering from paroxysmal nocturnal hemoglobinuria (PNH).*" (emphasis added by the board)

31. The auxiliary request (see also point II. above) was filed at the end of the oral proceedings before the opposition division and was not admitted into the proceedings. The appellant re-submitted the request with the statement of grounds of appeal. At the oral proceedings before the board, the appellant objected that the examining division had not exercised its discretion in a reasonable manner, because the appellant had reason to believe that the auxiliary request had been considered by the examining division and was thus on file.

32. Article 12(6) RPBA codifies that the board shall not admit requests which were not admitted in the proceedings leading to the decision under appeal, unless the decision not to admit them suffered from an error in the use of discretion or unless the

circumstances of the appeal case justify their admittance.

33. As to the first aspect of Article 12(6) RPBA, the board only assesses whether the examining division has correctly exercised its discretion to (not) admit the request(s) into the proceedings. This review must be limited since, when reviewing such a decision, it is not the function of the board to review all the facts and circumstances of the case as if it were in the place of the department of first instance and to decide whether it would have exercised discretion in the same way as that department. The board in principle overrules the decision in the exercise of its discretion only if the department of first instance has either failed to exercise its discretion in accordance with the correct principles or has exercised its discretion in an arbitrary or unreasonable way and has thus exceeded the proper limits of its discretion (CLBA, V.A.3.4.1.b: see in particular decision G 7/93 in OJ EPO 1994, 775, reasons 2.6). If this is not the case, the request concerned remains excluded from the proceedings unless admittance is justified under the second aspect of Article 12(6) RPBA (see point 38. below).

34. In the decision under appeal, the examining division justified not admitting the request into the proceedings by referring to the following considerations:
i) the request was late-filed during the oral proceedings (approx. 5 p.m.);
ii) the request was not submitted in reaction to a change in the examining division’s opinion;
iii) in discussions with the applicant earlier in the oral proceedings in the context of auxiliary request 4

it had already been emphasised by the examining division that the wording of claim 1 of auxiliary request 4A would not overcome the deficiencies that the examining division saw for that request under Articles 76(1), 84 and 123(2) EPC; and
iv) since the amended and claimed subject-matter did not attempt to overcome the objections as to lack of inventive step relating to the claimed subject-matter of auxiliary requests 3 and 5, it was thus clearly not allowable.

35. In the context of point iii) above, the appellant referred to the minutes of the oral proceedings (dated 27 January 2020, "minutes" hereafter) and the annexes to those minutes (which are on file in the electronic dossier in the related case T 1515/20 only: see entry of 7 February 2020 in that dossier) to explain that during the discussion of auxiliary request 4 filed as **annex B** during the oral proceedings (minutes, point 17, relevant feature "wherein the antibody is obtainable by transfecting cells with a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4", see also point 23. above) the interpretation of claim 1 was discussed based on proposals of both the examining division and the applicant. One of these proposals was submitted by the applicant in handwritten form as **annex E**, labelled as fifth auxiliary request (minutes, points 21 to 23, relevant feature "the antibody comprises a heavy chain and a light chain and is obtainable by producing in transfected cells a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4") and later provided in typed form (minutes, point 27). After the examining division then noted that the typed version of auxiliary request 4 filed as **annex G** (relevant feature "the antibody is obtainable by producing in transfected

cells a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4") differed from the version filed as **annex B** ("wherein the antibody is obtainable by transfecting cells with a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4"), the applicant stated that in its understanding the version of auxiliary request 4 in the form of **annex G** had been discussed and was thus on file, but then filed a typed version of auxiliary request 4 corresponding to annex B as annex J as the final version of auxiliary request 4 (minutes, points 28 to 29). Auxiliary request 2A, in which claim 1 is identical to claim 1 of auxiliary request 4A (**annex L**) as filed at the oral proceedings in opposition (relevant feature "wherein the antibody is obtainable by producing in transfected cells a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4"), was identical to annex G and should therefore be admitted into the proceedings.

36. The board cannot concur with the appellant that, because a certain version of claim 1 (annex G), albeit on a theoretical level, had been discussed with the examining division, a subsequently filed request containing that claim (here auxiliary request 4A, now 2A) should have been admitted into the proceedings by the examining division. Indeed, according to point iii) in point 34. above, the examining division in the (theoretical) discussions with the applicant earlier during the oral proceedings in the context of auxiliary request 4 had emphasised, as it also did for the other proposals discussed (including annex E, see point 23 of the minutes: "*None of these proposals were preliminarily considered by the ED to overcome the objection under Article 84 EPC and none of them was formally presented at this point as a further*

request"), that the wording of claim 1 of auxiliary request 4A would not overcome the deficiencies that the examining division saw for that request under Articles 76(1), 84 and 123(2) EPC, and was thus not clearly allowable (see appealed decision, section H)). Admitting the request under such circumstances would in the board's opinion certainly not have furthered procedural economy.

37. Thus, also having regard to the appellant's submissions in this context, the board is satisfied that the examining division has exercised its discretion to not admit this request into the proceedings in accordance with the correct principles and has not exercised its discretion in an unreasonable way.

38. As to the second aspect of Article 12(6) RPBA, the board has not seen reasons on the part of the appellant for holding that particular circumstances of the appeal could justify the board admitting the auxiliary request into the proceedings either.

39. In view of the above considerations, the board decided not to admit and consider auxiliary request 2A in the appeal proceedings.

40. Claim 1 of auxiliary request 7A is identical to claim 1 of auxiliary request 6A dealt with by the examining division and is identical to claim 1 of the current auxiliary request 2A (see point 30.), with the additional feature "wherein the pharmaceutical composition is to be administered by intravenous infusion" at the end of the claim.

41. The examining division did not admit this request into the proceedings for the same reasons as for auxiliary

request 2A (see point 34.). Accordingly, the board also decided *mutatis mutandis* not to admit and consider auxiliary request 7A in the appeal proceedings.

Third auxiliary request - added subject-matter

42. Claim 1 of the third auxiliary request is identical to claim 1 of auxiliary request 1 dealt with in the decision under appeal, and reads:

"*1. A pharmaceutical composition comprising an antibody that binds C5 in a 300mg single unit dosage form comprising 30 ml of a 10 mg/ml sterile, preservative free solution, wherein* ***the antibody comprises*** *the heavy chain amino acid sequence shown in SEQ ID NO: 2 and* ***the light chain amino acid sequence shown in SEQ ID NO: 4,*** *for use in treating a patient suffering from paroxysmal nocturnal hemoglobinuria (PNH).*" (emphasis added by the board)

43. The claim now defines the antibody as comprising "the heavy chain amino acid sequence shown in SEQ ID NO: 2 and the light chain amino acid sequence shown in SEQ ID NO: 4". The appellant did not contest that the "shown in" wording had not been used in the application as filed. Nevertheless, as submitted by the appellant, because the application as filed on page 5, lines 28 to 29 disclosed that: "*In certain embodiments, the pharmaceutical composition comprises eculizumab.*" and the heavy and light chain amino acid sequences of eculizumab were shown in SEQ ID NO: 2 and SEQ ID NO: 4 on page 44, respectively, and the skilled person knew that SEQ ID NO: 4 was not the mature sequence but contained a signal peptide, the application was a direct and unambiguous basis for an antibody that comprised the heavy chain amino acid sequence shown in

SEQ ID NO: 2 and the light chain amino acid sequence shown in SEQ ID NO: 4.

44. In the section on the main request and auxiliary request 5 (see points 2. to 16.), the board decided that the amendment of the feature "a light chain consisting of SEQ ID NO: 4" to "a light chain consisting of residues 23 to 236 of SEQ ID NO: 4", i.e. excluding a precise 22 amino acid long signal peptide from the N-terminus of the amino acid sequence depicted in SEQ ID NO: 4 on page 44, did not comply with the requirements of Articles 76(1) and 123(2) EPC, and introduced added subject-matter. This conclusion also applies to claim 1 of this auxiliary request as construed by the appellant above, as the skilled person is not considered to immediately recognise that the amino acid sequence depicted in SEQ ID NO: 4 includes both a particular signal peptide sequence and the mature light chain sequence, and directly and unambiguously derive a (mature) light chain sequence shown in SEQ ID NO: 4 from the application as filed.

45. Accordingly, claim 1 of this auxiliary request does not comply with the requirements of Articles 76(1) and 123(2) EPC.

Fourth and eighth auxiliary requests - sufficiency of disclosure

46. Claim 1 of the fourth auxiliary request is identical to claim 1 of auxiliary request 3 dealt with by the examining division, and reads:

"*1. A pharmaceutical composition comprising an antibody that binds C5 in a 300mg single unit dosage form comprising 30 ml of a 10 mg/ml sterile, preservative*

free solution, wherein ***the antibody comprises a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4****, for use in treating a patient suffering from paroxysmal nocturnal hemoglobinuria (PNH).*" (emphasis added by the board)

47. Claim 1 is formulated in a further-medical-use format in which the binding of the recited antibody to C5 is the mechanistic explanation for the therapeutic effect, i.e. the suitability thereof in the medical use. In its decision G 2/21, the Enlarged Board of Appeal recently held that the proof of a claimed therapeutic effect has to be provided in the application as filed (see in particular reasons 74 and 77). Thus the evidence for the binding of the antibody claimed to C5 had to be in the application as filed.

48. The parts of the application as filed which purportedly provide experimental data in support of the further-medical-use format of the claim, the so-called "TRIUMPH trial" on pages 27 to 40, were conducted with an antibody designated "eculizumab". Throughout the appeal, the appellant has maintained that this "eculizumab" antibody used in the TRIUMPH trial was *not* the antibody as it is now defined in the claim, i.e. comprising "a light chain *consisting* of SEQ ID NO: 4" (including, as argued by the appellant, an N-terminal 22 amino acid long ER signal peptide, see points 3. and 4. above).

49. Accordingly, in order to assess whether the application sufficiently discloses the technical effect claimed, i.e. C5 binding of the antibody for treating a patient suffering from paroxysmal nocturnal hemoglobinuria (PNH), it needs to be established what exactly the

sequence of the eculizumab antibody of the TRIUMPH trial was.

50. The sole indication in the application as filed of the origin and identity of "eculizumab" used in the TRIUMPH trial is on page 28, lines 7 to 9 of the application as filed, where it is disclosed that "*Patients were randomly assigned on a one-on-one basis to receive either placebo or eculizumab (Soliris™, Alexion Pharmaceuticals, Inc.) within 10 days of the qualifying transfusion*."

51. A substantial part of the appellant's case in appeal (e.g. inventive step) has been based on arguments to the effect that the structure of the antibody designated "eculizumab" was not derivable from any of the disclosures in the state of the art and that all scientists working with eculizumab prior to the filing date were in fact bound by confidentiality with regard to the structure of eculizumab. However, and without having to go into any detail on these arguments, which were based on various items of documentary evidence and declarations, by the same token accepting the appellant's argument means that without the identification of the structure of eculizumab in the form of Soliris™ obtainable from Alexion Pharmaceuticals, Inc. in the application as filed, the structural particularities of the antibody designated eculizumab used in the TRIUMPH trial and reported on in the application were equally not available to the skilled person at the filing date. In fact, this conclusion of non-availability based on confidentiality seems, indeed, to find corroboration in the appellant's press release, one day after the filing date of the application, announcing that the company had received marketing approval from the U.S. Food and Drug

Administration (FDA) for Soliris™ (eculizumab), the first therapy approved for PNH (see document D16, first paragraph and the declaration in document D31, point 2).

52. As a consequence of these considerations based on the appellant's arguments, it must be concluded that the structure of the antibody used in the TRIUMPH trial was not known to the skilled person (at all) when the application was filed. It however follows from this fact that the disclosed results of this TRIUMPH trial cannot be verified to apply equally to the C5-binding antibody now referred to in the claim which comprises a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4. The TRIUMPH trial can therefore not serve as evidence for the C5-binding activity of this antibody and the resulting therapeutic effect as required by the claim.

53. Accordingly, and in the absence of any indications that the unusual antibody defined in the claim has the required therapeutic effect, the patent application fails to sufficiently disclose the claimed invention of auxiliary request 4 (Article 83 EPC).

54. Claim 1 of the eighth auxiliary request is identical to claim 1 of auxiliary request 5 dealt with by the examining division and is identical to claim 1 of the current auxiliary request 4 (see point 46.), with the additional feature "wherein the pharmaceutical composition is to be administered by intravenous infusion" at the end of the claim.

55. This claim thus comprises the same definition of the antibody as claim 1 of auxiliary request 4, and consequently and *mutatis mutandis* the application as

filed also fails to sufficiently disclose this claimed invention, contrary to the requirements of Article 83 EPC.

Auxiliary requests 9 to 17

56. Claim 1 of these auxiliary requests corresponds to claim 1 of the main request, auxiliary request 1, auxiliary request 2A, the third to sixth auxiliary requests, auxiliary request 7A and the eighth auxiliary request, respectively, with the additional feature that the claimed composition has a pH of 7. The appellant has not submitted dedicated arguments that this amendment would overcome the deficiencies of the higher-ranking auxiliary requests. The board accordingly has seen no reason to admit and consider these requests in the proceedings (Article 12(4) RPBA for auxiliary requests 10 to 13 and 15 to 17 filed with the statement of grounds of appeal and Article 13(2) RPBA for auxiliary requests 9 and 14 filed during the oral proceedings).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chair:

I. Aperribay M. Pregetter

Decision electronically authenticated