Unified Patent Court
Einheitliches Patentgericht
Juridiction unifiée du brevet

Appeal n°:
UPC_CoA_405/2024
APL_40553/2024

FINAL ORDER

of the Court of Appeal of the Unified Patent Court
concerning an application for provisional measures
issued on 20 December 2024

HEADNOTE

1. A linguistic error, a spelling mistake or any other inaccuracy in a patent claim can only be corrected by way of interpretation of the patent claim if the existence of an error and the precise way to correct it are sufficiently certain to the average skilled person on the basis of the patent claim, taking into account the description and the drawings and using common general knowledge.

2. The patent claim must be interpreted from the perspective of the person skilled in the art. The applicant's assertions during the grant proceedings, and in particular the TBA's endorsement thereof, can be seen as an indication of the view of the person skilled in the art at the filing date.

APPELLANT (APPLICANT IN THE PROCEEDINGS BEFORE THE COURT OF FIRST INSTANCE)

Alexion Pharmaceuticals, Inc.
121 Seaport Blvd, 02210 Boston (MA), United States

hereinafter: Alexion,

represented by attorneys-at-law Wolrad Prinz zu Waldeck und Pyrmont, Dr. Christopher Stothers and Elena Hennecke (Freshfield Bruckhaus Deringer) and patent attorneys Gregor König and Claudia Hertzsch (Szynka Tilmann von Renesse)

RESPONDENTS (DEFENDANTS IN THE PROCEEDINGS BEFORE THE COURT OF FIRST INSTANCE)

1. Amgen Technology (Ireland) Unlimited Company
Pottery Road, A96 F2A8, Dun Laoghaire, Dublin, Ireland

2. Amgen N.V.
Telecomlaan 5-7, 1831 Machelen, Belgium

3. Amgen GmbH
Riesstraße 24, 80992 Munich, Germany

4. Amgen GmbH
Franz-Josefs-Kai 47, 1010 Vienna, Austria

5. Amgen AB
Gustav IIIs Blvd 54, 16974 Solna, Sweden

6. Amgen S.A.S.
18-20 Quai du Point du Jour, 92100 Boulogne-Billancourt, France

7. Amgen s.r.l.
Via Enrico Tazzoli 6, 20154 Milan, Italy

8. Amgen Biofarmacêutica Lda.
Avenida José Malhoa, 19, 1070- 157 Lisboa, Portugal

9. Amgen Zdravila D.O.O.
Šmartinska cesta 140, 1000 Ljubljana, Slovenia

hereinafter: Amgen,

represented by attorneys-at-law Prof. Dr. Tilman Müller-Stoy, Dr. Tobias Wuttke and Dr. Dominik Woll and patent attorneys Dr. Axel Berger and Dr. Markus Ackermann (Bardehle Pagenberg) and attorney-at-law Tim Harris (Osborne Clark)

PATENT AT ISSUE
EP 3167888

PANEL AND DECIDING JUDGES
Panel 1a:
Klaus Grabinski, president of the Court of Appeal
Peter Blok, legally qualified judge and judge-rapporteur
Emmanuel Gougé, legally qualified judge
Eric Enderlin, technically qualified judge
Anna Hedberg, technically qualified judge

LANGUAGE OF THE PROCEEDINGS

English

IMPUGNED ORDER OF THE COURT OF FIRST INSTANCE

- □ Orders of the Court of First Instance of the Unified Patent Court, Local Division Hamburg dated 26 June 2024 (without grounds) and 17 July 2024 (with grounds).
- □ Numbers attributed by the Court of First Instance:
  UPC_CFI_124/2024
  ACT_13886/2024
  ORD_38032/2024

DATE OF THE ORAL HEARING:

4 November 2024

FACTS AND REQUESTS OF THE PARTIES

Alexion

1. Alexion is the parent company of the Alexion group, a global pharmaceutical company. Alexion and its affiliated companies market a range of pharmaceuticals for the treatment of rare diseases. These include Soliris®, a biopharmaceutical drug which is authorised for treatment of the following rare diseases:
   - paroxysmal nocturnal hemoglobinuria (hereinafter: PNH),
   - atypical hemolytic uremic syndrome (hereinafter: aHUS),
   - refractory generalized myasthenia gravis (hereinafter: gMC), and
   - neuromyelitis optica spectrum disorders (hereinafter: NMOSD).

   The active ingredient in Soliris® is a recombinant humanized monoclonal antibody, which was given the International Non-proprietary Name (INN) “eculizumab” in 2002.

2. Eculizumab was covered by a patent family held by Alexion for a class of antibodies, including US 6 355 245 (exhibit FBD 14, hereinafter: Evans) and EP 0 758 904 with the priority date of 2 May 1994, and by a supplementary protection certificate. The supplementary protection certificate expired in April 2020.

3. In 1999, Alexion entered eculizumab in the Chemical Abstract Service (hereinafter: CAS) database Registry, which discloses information on chemical substances. Alexion entered the wrong sequence in the CAS database. The sequence was corrected in 2009.

4. Alexion is the proprietor of European Patent 3 167 888 B1 for “treatment of paroxysmal nocturnal hemoglobinuria by an inhibitor of complement” (hereinafter: the patent at issue).

The patent at issue

5. The patent at issue is a divisional application of the European patent application 2 359 834 A1 (hereinafter: EP 834), which is a divisional application of the European patent application 2 001 490 A1 (hereinafter: EP 490) which was filed as the international patent application WO 2007/106585. The patent application underlying the patent at issue was published on 17 May 2017. WO 2007/106585 was filed on 15 March 2007. It claims the priority of US 783070 P which was filed on 15 March 2006. The grant of the patent was published on 1 May 2024. Unitary effect was granted by the decision of the European Patent Office (hereinafter: EPO) of 13 May 2024. On 2 May 2024, Samsung Bioepis NL B.V. (hereinafter: Samsung) filed an opposition against the grant of the patent at issue.

6. The patent at issue claims an antibody which is described as suitable for use as an inhibitor of a component of the immune system called "Complement component 5" (hereinafter: C5). According to the description, the claimed antibody binds to C5 and thereby prevents the cleavage of C5 into its fragments C5a and C5b, which is the beginning of an immune response. The claimed antibody is described as suitable for use in the treatment of, for example, PNH, a life-threatening blood disease whereby the patient's own immune system destroys erythrocytes (red blood cells). The red blood cells of these patients lack the protective proteins which are required to prevent an attack by C5.

7. Advantageous C5-binding monoclonal antibodies were known on the priority date of the patent at issue. For example, Evans, cited in paragraph [0064] of the patent at issue, discloses such antibodies. The description of the patent at issue names the preferred whole antibody which Evans discloses "eculizumab" (par. [0064]).

8. The relevant claims of the patent at issue read as follows:

    1. An antibody that binds C5 comprising a heavy chain consisting of SEQ ID NO:2 and a light chain consisting of SEQ ID NO:4.

    2. A pharmaceutical composition comprising the antibody of claim 1.

9. Par. [0134] of the description of the patent at issue shows the amino acid sequences SEQ ID NO:2 and SEQ ID NO:4. Under the heading "SEQ ID NO: 4 – Eculizumab Light chain" it presents the following sequence of 236 amino acids:

MDMRVPAQLLGLLLLWLRGARCDIQMTQSPSSLSASVGDRVTITCGASENIYGAL
NWYQQKPGKAPKLLIYGATNLADGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQ
NVLNTPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKV
QWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQG
LSSPVTKSFNRGEC

10. The SEQ ID NO: 4 sequence shown in par. [0134] of the patent at issue is not identical to the sequence of the light chain disclosed in the corrected CAS database entry for eculizumab in 2009. SEQ ID NO: 4 has 22 extra amino acids at the beginning of the sequence (the N-terminus).

11. In the examination proceedings of the patent at issue, the Technical Board of Appeal (hereinafter: TBA) rejected Alexion's main request (TBA 21 September 2023, T 1515/20). In this request, the feature SEQ ID NO:4 of claim 1 was replaced by the sequence extending from amino acids 23 to 236 of SEQ ID NO:4. According to the TBA, such a claim did not constitute an allowable correction under Rule 139 of the Implementing Regulations to the Convention on the Grant of European Patents (hereinafter: EPC Rules) and introduced added matter within the meaning of Art. 76(1) and 123(2) of the Convention on the Grant of European Patents (European Patent Convention, hereinafter: EPC). The TBA ordered the Examining Division to grant the patent on the basis of auxiliary request 5, which is the patent at issue in its current form. In the interpretation of the TBA, feature SEQ ID NO:4 includes the 22 extra amino acids. The TBA examined the claimed subject matter on the basis of this interpretation and concluded it is novel, involves an inventive step and is sufficiently disclosed.

Amgen

12. Amgen is a part of the pharmaceutical group Amgen. Since July 2023, Amgen has placed BEKEMV® (hereinafter: the contested product), a biosimilar product of Soliris® containing the monoclonal antibody eculizumab, on the market of several Contracting Member States of the UPC. BEKEMV ® is currently approved for the European market in the embodiment "300 mg Concentrate for solution for infusion" for PNH.

Related proceedings

13. In Germany, a subsidiary of Alexion conducted preliminary injunction proceedings against Amgen based on market exclusivity rights for the indications aHUS, gMC and NMOSD under Regulation (EC) 141/2000 on orphan medicinal products. The preliminary injunction granted by the Munich Regional Court, was overturned by the Munich Higher Regional Court.

The first instance proceedings

14. Alexion lodged an application for provisional measures against Amgen with the Hamburg Local Division of the Court of First Instance, requesting that the Court order that Amgen, in summary:
    I. cease and desist from infringing claim 2 of the patent at issue;
    II. pay a penalty of € 250,000 for each individual breach of the order under I.;
    III. surrender the infringing products; and
    IV. pay the costs of the proceedings.

15. Amgen requested that the Court, in summary, 1) dismiss the application, 2) order that Alexion bear all legal costs and expenses incurred by Amgen and 3) order that the order is immediately enforceable.

16. By an order without grounds dated 26 June 2024 (hereinafter: the impugned order), the Court of First Instance dismissed Alexion's application, ordered Alexion to pay the costs of the proceedings and set the value of the dispute at € 100,000,000. The grounds of the order were delivered on 17 July 2024. The reasoning of the Court of First Instance can be summarized as follows:
    - The Court is convinced with a sufficient degree of certainty that the patent at issue is infringed by the offer and distribution of the contested product. On summary examination, the contested product makes direct and literal use of the technical teaching of claim 2 of the patent at issue;
    - Claim 2 protects a pharmaceutical composition comprising an antibody with a light chain of SEQ ID No. 4 without the first 22 amino acids;
    - The skilled person would have recognized that the sequence ID NO: 4 of the light chain is not correctly reproduced. The skilled person interpreting patent claim 2 using their general knowledge would have seen that the amino acid sequence at the N-terminus of the SEQ ID NO: 4 shows typical features of a signal peptide. A comparison with the sequence of eculizumab in the CAS database and/or alternatively a search with SignalP would have led the skilled person to the exact length of the signal peptide;
    - This view is supported by technical and functional considerations. On the one hand, the skilled person would have difficulties in producing a corresponding antibody with the signal peptide. If, on the other hand, he were able to produce such an unusual antibody, he would have recognised that it has no binding capacity for C5;
    - This understanding is consistent with the description of the patent at issue. The specification of the patent at issue refers to eculizumab more than 100 times, also making clear that eculizumab is a highly preferred embodiment of the patent at issue;
    - The parts of the grant history of the patent at issue cited by the parties do not shed any new light on this interpretation and are not inconsistent with the Court's interpretation;

- The validity of the patent at issue is not certain to the extent required for the ordering of provisional measures;
- When assessing the likelihood of validity, the Court not only needs to consider the likelihood of invalidity based on its own assessment, but also needs to take into account the likelihood of an invalidity decision on the patent at issue by the EPO. In general, the Court's own assessment and the EPO's decision on the validity of the patent should not differ, as both legal bodies apply the same legal standard. There might be a difference, when the Court interprets a patent claim differently than the EPO, so that the validity arguments are inevitably different;
- Irrespective of the question of whether the Court considers the patent at issue to be valid in light of Amgen's arguments concerning the validity of the patent at issue, it is the opinion of the Court that it is reasonably likely that the EPO will revoke the patent due to lack of sufficient disclosure under Art. 83 EPC;
- The TBA was of the opinion that, based on a literal understanding of claim 2, the patent at issue protects an antibody with the light chain SEQ ID NO: 4. Attempts by Alexion to obtain protection for an antibody consisting of a light chain with SEQ ID NO: 4 without the 22 N-terminus amino acids were expressly rejected. That means that the TBA only approved the "unusual" antibody with a light chain including the 22 N-terminus amino acids. For this antibody, the TBA accepted the assertion of Alexion that "the position of the three respective CDR sequences in SEQ ID NO: 4, which are instrumental for the specific binding properties required by the claim, is sufficiently distanced from the N-terminal signal peptide to dissuade the skilled person from having doubts that this longer light chain would also bind to C5 as required by claim 1". On this assumption, the TBA concluded that the claimed antibody is sufficiently disclosed in the patent at issue.
- However, this assumption can no longer be upheld in the present litigation as Alexion itself is of the opinion that an antibody with the complete SEQ ID NO: 4, i.e. in the presence of the signal peptide, is not functional. On that basis, the technical teaching according to the patent might not be sufficiently disclosed and would likely be revoked by the opposition division. Accordingly, based on the TBA's claim construction and the applicant's own submissions and evidence in these proceedings, there is a substantial probability that granted claim 2 will be regarded as non-patentable by the EPO;
- All attempts by Alexion to correct SEQ ID NO: 4 or to convince the EPO that SEQ ID NO: 4 has to be interpreted without the signal peptide sequence were dismissed. The TBA has also considered several claim requests in family members of the patent in suit, which related to eculizumab as such, but decided that such claims are insufficiently disclosed. Taking all these elements into account, the Court is not at all convinced that the Opposition Division of the EPO will share the opinion of the Court on the question of claim construction and may decide that the patent is invalid;
- The application for provisional measures must therefore be dismissed: an infringement of the patent at issue can be established by the Court; however, it cannot be established to the necessary degree of certainty that the patent at issue is valid.

17. Alexion lodged an appeal against the impugned order. In its amended statement of appeal and statement of grounds of appeal, Alexion submitted the following requests:

Main request

I. The impugned order is revoked;
II. The application for provisional measures is remitted to the panel of the Court of First Instance to which it was previously assigned;
III. Amgen is ordered to pay the costs of the appeal;

Alternative request

I. the impugned order is revoked;
II. Amgen is ordered to cease and desist from infringing claim 2 of the patent at issue;
III. Amgen is ordered to pay a penalty of € 250,000 for each individual breach of the order under II.;
IV. Amgen is ordered to surrender the infringing products;
V. Amgen is ordered to pay the costs of the proceedings.

18. In addition, Alexion requested expedition of the appeal pursuant to Rule 9.3(b) of the Rules of Procedure of the Unified Patent Court (hereinafter: RoP). By order of 30 July 2024, the Court of Appeal rejected this request.

19. The grounds of the appeal can be summarized as follows:
- The Court of First Instance erred when making its decision dependent on a potentially deviating decision that the Opposition Division of the EPO may give in the future, and in basing its assessment on the prediction that the EPO will not follow the claim construction of the Court of First Instance;
- The Court of First Instance also erred in assuming that the Opposition Division might consider the patent at issue to be insufficiently disclosed in future proceedings. The Opposition Division will adopt the same claim construction as the Court of First Instance;
- If the Court of Appeal agrees with Alexion that the Court of First Instance should not have refused the application for provisional measures on conjecture regarding a future decision of the EPO, it should refer the case back to the Court of First Instance. The Court of First Instance has already fully heard detailed arguments on all aspects of validity. In addition, proceeding this way will ensure that Alexion is protected as soon as possible against the continuing infringements.

20. Amgen responded to the appeal, requesting that the Court of Appeal reject the appeal and order Alexion to pay the costs of the appeal proceedings. The reasons can be summarized as follows:
- The main request that Alexion submitted in its amended statement of appeal is inadmissible, because i) it isolates a specific legal question out of the overall legal assessment by the Court

of First Instance, and ii) is a partial withdrawal of the appeal which Alexion initially brought without any limitation;
- Alexion's request to refer the case back to the Court of First Instance for decision is unfounded;
- The Court of First Instance correctly found that the validity of the patent at issue is insufficiently certain;
- The Court of First Instance was entitled to consider the likely decision of the Opposition Division;
- The Court of First Instance correctly inferred the Opposition Division's likely decision on validity;
- The Court of First Instance was correct to find that the EPO would reach the same conclusion on claim construction despite the evidence submitted by Alexion;
- The Court of First Instance was correct to find that the EPO will maintain its position on claim construction;
- The Court of First Instance's claim construction is legally flawed. The clear wording of the claim covers an antibody with the first 22 amino acids of SEQ ID NO:4. The skilled person would not have disregarded precisely amino acids 1-22 of SEQ ID NO:4. The Court of First Instance has prioritized the intended success of the invention over a proper assessment of the skilled person's interpretation of the claims. The Court of First Instance should have taken into account the prosecution history when deciding on claim construction;
- Based on a correct claim construction the Court of First Instance would have found that the patent at issue is not infringed;
- The Court of First Instance failed to recognize that the validity of the patent at issue is not sufficiently certain, irrespective which claim construction the Court of Appeal adopts. The subject-matter of the patent at issue is not enabled, is not novel and does not involve inventive step;
- In addition, the Court of First Instance would have had to dismiss the application in view of interests of Amgen that outweigh the interests of Alexion.

GROUNDS FOR THE ORDER

Subject matter of the appeal

21. Pursuant to R. 222.1 RoP, the subject matter of the appeal is constituted by the requests, facts, evidence and arguments submitted by the parties under R. 221, 225, 226, 236 and 238 RoP, thus including the facts, evidence and arguments submitted by the respondent in the Statement of response.

22. During the oral hearing, Alexion withdrew its main request. The Court of Appeal will therefore only decide on Alexion's alternative request.

23. As the Court of Appeal will consider below, Alexion's alternative request, for revocation of the impugned order and for the grant of provisional measures, must be dismissed on the basis of the facts, evidence and arguments concerning the interpretation and insufficient disclosure of claims 1 and 2 of the patent at issue which Amgen submitted in the Statement of response. The Court of Appeal may therefore leave open whether Alexion's complaints against the impugned order are well-founded.

Claim interpretation

24. The person skilled in the art is a person having a degree in molecular biology and several years of experience in the field of antibody engineering.

25. In this case, the common general knowledge of the person skilled in the art should be considered at the filing date of the patent at issue (15 March 2007), as it is not disputed that the priority claim is not valid.

26. From the perspective of the person skilled in the art, claim 2 protects a pharmaceutical composition comprising an antibody that comprises two structural elements (a heavy chain consisting of SEQ ID NO:2 and a light chain consisting of SEQ ID NO:4) and that, by virtue of these elements, has the ability to bind C5.

27. This understanding is supported by the patent specification, which must always be taken into account when interpreting a patent claim. Par. [0020] mentions that "in certain embodiments, the antibody that binds C5 or an active antibody fragment thereof comprises a heavy and a light chain, wherein the heavy chain consists of SEQ ID NO: 2 and the light chain consists of SEQ ID NO: 4".

28. There is no indication in the patent specification that a part of the light chain can or should be excluded from the SEQ ID NO:4 as defined in par. [0134].

29. These findings are not put into question by the Court of First Instance. Nevertheless, the Court of First Instance interprets claim 2 as excluding the first 22 amino acids of SEQ ID NO:4. Its understanding of claim 2 is based on the assumption that at the relevant date of the patent at issue, the average skilled person would have recognized that the sequence SEQ ID NO:4 is not correctly reproduced, as such person would have realised that the start sequence at the N-terminus has typical features of a signal peptide (impugned order, section II.2.b)). In addition, the average skilled person would have been able to determine the precise length of the signal peptide sequence, as SEQ ID NO:4 is identified in par. [0134] of the patent specification as "Eculizumab light chain". When trying to resolve their initial suspicion that SEQ ID.:NO 4 is erroneous, the average skilled person would have verified the sequence in the CAS database entry for Eculizumab, irrespective of the fact that the sequence of the light chain SEQ ID NO:4 in CAS and the patent differs by one further amino acid. This point of view is supported by the

opinions of Prof. [redacted] (exhibit FBD8), who also refers to Lehninger's textbook on the Principles of Biochemistry (exhibit FBD38a), and Prof. [redacted] (exhibit FBD37).

30. In contrast to these findings of the Court of First Instance, the TBA in its decision of 21 September 2023 rejected Alexion's request to grant the patent with claim 1 excluding the first 22 amino acids of SEQ ID NO:4 (see T 1515/20, par. 2: "… a light chain consisting of residues 23 to 236 of SEQ ID NO: 4"). It based its decision on settled case law of the EPO Boards of Appeal according to which in the case of a proposed amendment under Art. 123(2) EPC or a correction under Rule 139 EPC, it must be established that

    a. It is obvious that the application as filed contains an error which is so obvious that the average skilled person has 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 average skilled person using common general knowledge; and
    b. The average 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 (T 1515/20, par. 6).

31. According to the TBA, it was common knowledge that antibodies are secreted proteins produced from precursor light chain 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 of the expressing cell and the mature polypeptide then folds to form the mature protein (T 1515/20, par. 7).

32. However, the TBA was not of the opinion that the statement in the application of "a light chain variable region consisting of SEQ ID NO: 4" and "SEQ ID NO: 4 – Eculizumab Light Chain" constituted such an obvious error that a person skilled in the art would have no doubt that this information is incorrect.

33. The Court of First Instance did not ignore these findings of the TBA. The Court of First Instance, however, stated that the interpretation of a patent claim is not dependent on a no doubt requirement. Rather, the average skilled person, taking the purpose of every patent claim into account, to provide the person skilled in the art with a technical teaching which, if carried out, leads to the intended success of the invention, would recognize that the claimed antibody with the included signal peptide in the light chain SEQ ID NO: 4 is not able to bind to C5. The contrary was asserted by the applicant during the granting procedure without providing any evidence. However, in the present proceedings it is undisputed between the parties that the light chain SEQ ID NO: 4 is not able to bind to C5. The average skilled person would therefore try to interpret the claim in such a way that it leads to the intended success of the invention, in

the case at hand the ability to bind C5 and function as a drug. This includes recognising typical features of a signal peptide sequence at the N-Terminus of SEQ ID NO: 4.

34. These considerations of the Court of First Instance are legally flawed.

35. The patent claim is the decisive basis for determining the protective scope of the European patent and the description and the drawings must always be used as explanatory aids for the interpretation of the patent claim (Court of Appeal 26 February 2024, UPC_CoA_335/2023 App_576355/2023, *NanoString/10x*, p. 26). A linguistic error, a spelling mistake or any other inaccuracy in a patent claim can only be corrected by way of interpretation of the patent claim if the existence of an error and the precise way to correct it are sufficiently certain to the average skilled person on the basis of the patent claim, taking into account the description and the drawings and using common general knowledge.

36. This standard combines adequate protection for the patent proprietor, as it allows the proprietor to correct a linguistic error, a spelling mistake or any other inaccuracy in a patent claim by way of interpretation of the patent claim, with a reasonable degree of legal certainty for third parties, as a correction is only possible if the error and the correction are sufficiently certain to the average skilled person. It is a rather strict standard since an error as such implies some legal uncertainty for third parties.

37. In the present case, the existence of an error and the way to correct it are not sufficiently certain to the average skilled person.

38. The Court of Appeal concurs with the TBA that there are no arguments as to why the average skilled person, in the context of claim interpretation, would be prima facie alerted and consequently prompted to consider and analyse the corresponding sequence in order to determine the presence of particular functional parts/compounds in the unannotated amino acid sequence (T 1515/20, par. 10). Alexion failed to submit such arguments. Alexion refers to the statements of its experts Dr. [redacted] (exhibits FBD 17A, FBD 17B and FBD 17C), Prof. [redacted] (exhibit FBD 37), Prof. [redacted] (exhibit FBD 38) and Prof. [redacted] (exhibit FBD 39) and the expert statement of Prof. [redacted] which Samsung filed in parallel proceedings (submitted in these proceedings by Alexion as exhibit FBD 40), but these statements also do not provide any reasons why the average skilled person would analyse the sequence. The experts were not asked to provide such reasons. Instead, they were presented with statements informing them of the presence of a signal peptide of 22 amino acids in SEQ ID NO: 4 and/or were asked questions that presuppose that the average skilled person would analyse the sequence, such as the question “whether the skilled person could recognize that the sequence of amino acids 1-22 in the light chain SEQ ID NO:4 […] is a so-called signal sequence” (declaration of Prof. [redacted] FBD 37, par. 3).

39. The Court of Appeal also concurs with the TBA in its finding that, even when inspecting the sequence of SEQ ID NO: 4, the average skilled person would not immediately have recognised that the depicted sequence of SEQ ID NO: 4 constituted an error. Instead, the average skilled person could, at most, be caused to doubt that the sequence depicted is the sequence it purports to represent (T 1515/20, par. 11). Alexion's submissions fail to call these findings into question. Alexion argues, on the basis of the expert statements of Dr. [redacted] Prof. [redacted] Prof. [redacted] and Prof. [redacted] (exhibits FBD 17A-C and 37-39), that the average skilled person analysing the light chain SEQ ID NO:4 would have recognised features typical of a signal peptide. However, even if this were the case, the average skilled person would not know whether these amino acids in SEQ ID NO: 4 were an error rather than an unusual part of an antibody.

40. Alexion argues that the average skilled person would consider the inclusion of a signal peptide in the sequence of SEQ ID NO: 4 to be an error, because such person would have known that signal peptides are cleaved off during the production of antibodies by the ordinary cell-based methods. Alexion referred in this context to the expert opinions of Dr. [redacted] (exhibit FBD 17A-C) and Prof. [redacted] (exhibit FBD 38) and to the findings of the TBA in the granting proceedings (T 1515/20, par. 7). On the other hand, Amgen argued, on the basis of the expert statement of Prof. [redacted] (exhibit FBD 40), that the skilled person would be aware of a number of alternative production methods, including the use of E. coli cells as described in Chen (exhibit 2 to FBD 40), which do not result in the cleavage of signal peptides. These alternative approaches may be non-routine for antibody production and may require a significant research effort, as Prof. [redacted] acknowledges. However, patent claim 2 is not limited to pharmaceutical compositions comprising antibodies produced by routine methods. Par. [0074] of the description even expressly states that the production of the antibody by any particular method is *not* required. Furthermore, assuming that the average skilled person would recognise that the first amino acids of sequence of SEQ ID NO: 4 resemble those of a signal peptide, the average skilled person may be aware that unusual production methods are required. Knowledge of the ineffectiveness of routine production methods is therefore not sufficient.

41. Equally insufficient is Alexion's argument, based on the statements of Prof. [redacted] (exhibit FBD 38) and Prof. [redacted] (exhibit FBD 40), that the average skilled person would know that an antibody comprising a light chain consisting of SEQ ID NO:4, including the first 22 amino acids, would "highly likely" not bind C5 due to the presence of hydrophobic amino acids. This submission itself implies that the skilled person would not rule out that the antibody could bind C5 and that he would therefore leave open the possibility that there is no error in SEQ ID NO:4.

42. Moreover, in the proceedings before the TBA, Alexion submitted that the position of the three respective CDR sequences in SEQ ID NO:4 is sufficiently distant from the N-terminal signal peptide to dissuade the skilled person from doubting that this longer light chain would also

bind to C5 as required by the patent claims. This argument was accepted by the TBA, which accordingly concluded that the claimed antibody was sufficiently disclosed in the patent (T 1515/20, par. 35 and 36). This confirms that it is not sufficiently certain for the average skilled person that the longer light chain was an error.

43. The Court of First Instance took the view that Alexion's aforementioned assertions in the proceedings before the TBA must not be considered as Alexion abandoned them and, now in the proceedings before the Court, takes the view that an antibody with the complete SEQ ID NO: 4, including the first 22 amino acids, is not functional. However, this view ignores the fact that the patent claim must be interpreted from the perspective of the person skilled in the art. Alexion's assertion during the grant proceedings, and in particular the TBA's endorsement thereof, can be seen as an indication of the view of the person skilled in the art at the filing date.

44. The fact that the description of the patent at issue makes numerous references to eculizumab, confirms rather than alters this assessment. Alexion argues that the average skilled person would assume that the claimed antibody is the antibody called eculizumab, which according to the description has been used successfully in clinical trials and therefore must be producible in a reliable and economically meaningful manner. However, the description discusses eculizumab in the background art section (par. [0003]) and expressly presents it as an antibody that was known in the prior art (par. [0064]). This is consistent with the average skilled person's common general knowledge that eculizumab was known for years, had gone through clinical trials and was even entered in the CAS database. This is a strong indication to the average skilled person that the patent at issue claims an antibody other than the eculizumab antibodies of the prior art, including the one used in the clinical trials. Secondly, if the average skilled person nevertheless assumed that the patent at issue claims the same antibody, consulting the CAS database for eculizumab would not help to check the accuracy of the sequence. It is common ground that on the filing date of the patent at issue, the CAS database contained an incorrect sequence for eculizumab, with more than 100 additional amino acids. The skilled person would thus find out that the patent at issue claims an antibody other than the antibody known as eculizumab.

45. In addition, it is not sufficiently certain for the average skilled person that the alleged error must be corrected by deleting exactly 22 amino acids from the sequence of SEQ ID NO: 4. Alexion argues that the average skilled person would know the length of the signal peptide. However, its own expert states that the typical length of a signal peptide varies between 13 and 36 amino acids (expert statement of Prof. [redacted] exhibit FBD 38, p. 3). Alexion failed to demonstrate that the average skilled person would know, on the basis of their common general knowledge, that in this case the length is exactly 22 amino acids. The experts argue that the average skilled person would expect a signal peptide of 22 amino acids on the basis of various criteria or their "intuitive assessment", but all assume that the skilled person would

consult a catalogue or database for confirmation. The Court of Appeal can leave open the question of whether the average skilled person, in the context of claim interpretation, can be expected to consult catalogues and databases to check how a perceived error in the claim should be corrected. Even if the average skilled person would do so, it would not be sufficiently certain that the signal peptide consists of 22 amino acids for the following reasons.

46. Alexion refers to Dr. [redacted] catalogue of known signal peptide sequences (Annex D to exhibit FBD 17A), which discloses a sequence identical to the first 22 amino acids of SEQ ID NO: 4. To find this sequence the skilled person would have to search specifically for information on kappa light chains of subgroup I. Alexion failed to demonstrate that the patent discloses that the sequence of SEQ ID NO: 4 comprises a kappa light chain of this subgroup or that this was common general knowledge. Alexion refers to publications by Thomas (Thomas et. al., 'Inhibition of complement activity by humanized anti-C5 antibody and single chain Fv', exhibit FBD 22) and Evans, but does not argue that these publications are part of the common general knowledge and does not show that these publications disclose the specific subgroup. Moreover, even within the relevant subgroup, Kabat discloses signal peptides of different lengths.

47. In addition, Alexion refers to the SignalP and NCBI BlastP databases. However, if the skilled person were to use these databases, he would at best obtain information of statistical relevance, such as a 95,9% probability that the cleavage site is between position 22 and 23 (exhibit FBD 18a). This is not a sufficient degree of certainty, as these statistics still leave open a significant possibility that the signal peptide is of a different length and that thus confirmation by experiments is required. Alexion – correctly – did not argue that the result of such experiments may be taken into account in the context of claim interpretation.

Conclusion

48. It follows that claim 2 must be interpreted as meaning that the claimed pharmaceutical composition comprises an antibody comprising a light chain consisting of SEQ ID NO: 4 including the first 22 amino acids. Based on this claim interpretation, it is more likely than not that the subject matter of claim 2 is insufficiently disclosed within the meaning of Art. 83 EPC. As noted by the Court of First Instance, Alexion itself and its expert Prof. [redacted] have stated that an antibody with the complete SEQ ID NO: 4 does not bind C5 and is not suitable for formulation as a pharmaceutical composition and used as a drug. Therefore, there is not a sufficient degree of certainty that claim 2 of the patent at issue is valid. The decision of the Court of First Instance to dismiss Alexion's application for provisional measures, and to order Alexion to pay the costs of the proceedings, was therefore correct. The Court of Appeal will reject the appeal.

49. As the unsuccessful party, Alexion must bear the costs of the appeal proceedings.

ORDER

I. The appeal is rejected;

II. Alexion is required to bear the costs of the appeal proceedings.

This order was issued on 20 December 2024.

Klaus Grabinski President of the Court of Appeal	KLAUS STEFAN MARTIN Grabinski Digitally signed by KLAUS STEFAN MARTIN Grabinski Date: 2024.12.20 08:15:28 +01'00'
Peter Blok Legally qualified judge and judge-rapporteur	Peter Hendrik Blok Digitally signed by Peter Hendrik Blok Date: 2024.12.20 09:25:58 +01'00'
Emmanuel Gougé Legally qualified judge	EMMANUEL, LUCIEN, RENÉ GOUGÉ Digitally signed by EMMANUEL, LUCIEN, RENÉ GOUGÉ Date: 2024.12.19 19:33:44 +01'00'
Eric Enderlin Technically qualified judge	Eric, André Enderlin Signature numérique de Eric, André Enderlin Date : 2024.12.19 19:20:22 +01'00'
Anna Hedberg Technically qualified judge	Anna Hedberg Digitally signed by Anna Hedberg Date: 2024.12.19 14:36:30 +01'00'