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Datasheet for the decision of 24 March 2022

Case Number: T 0921/17 - 3.3.04

Application Number: 06730769.4

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Language of the proceedings: EN

Title of invention:
Antibody substituting for function of blood coagulation factor VIII

Patent Proprietor:
Chugai Seiyaku Kabushiki Kaisha

Opponents:
Novo Nordisk A/S
Baxalta Innovations GmbH

Headword:
Bispecific antibody/CHUGAI

Relevant legal provisions:
EPC Art. 100(a), 54(3), 100(b), 100(c), 111(1)
RPBA 2020 Art. 11, 13(2)

Keyword:

Amendments - added subject-matter - main request (no)
Late-filed evidence - admitted (no)
Novelty - main request (yes)
Late-filed argument - admitted (no)
Sufficiency of disclosure - main request - claim 3 (yes)

Decisions cited:

Catchword:

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European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 0921/17 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 24 March 2022

Appellant: (Patent Proprietor)	Chugai Seiyaku Kabushiki Kaisha 5-1, Ukima 5-chome, Kita-ku Tokyo, 115-8543 (JP)
Representative:	Vossius & Partner Patentanwälte Rechtsanwälte mbB Siebertstraße 3 81675 München (DE)
Respondent I: (Opponent 1)	Novo Nordisk A/S Novo Allé DK-2880 Bagsvaerd (DK)
Representative:	J A Kemp LLP 80 Turnmill Street London EC1M 5QU (GB)
Respondent II: (Opponent 2)	Baxalta Innovations GmbH Industriestraße 67 1220 Vienna (AT)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 8 February 2017 revoking European patent No. 1876236 pursuant to Article 101(2) and Article 101(3)(b) EPC**

Composition of the Board:

Chair	B. Claes
Members:	B. Rutz
	M. Blasi

Summary of Facts and Submissions

I. The appeal by the patent proprietor (appellant) lies from the decision of the opposition division to revoke European patent No. 1 876 236 ("the patent") entitled "*Antibody substituting for function of blood coagulation factor VIII*", based on international application PCT/JP2006/306821 (published as WO 2006/109592). The translation of the application as filed that was submitted on entry into the European regional phase ("the application") was subsequently published as EP 1 876 236.

II. Claims 1 to 3 and 5 of the application read as follows:

"1. A multispecific antibody that can functionally substitute for coagulation factor VIII, which comprises:

a first domain recognizing coagulation factor IX and/or activated coagulation factor IX; and
a second domain recognizing coagulation factor X,

wherein

the first domain comprises a first polypeptide comprising the whole or part of the H chain of an antibody against coagulation factor IX and/or activated coagulation factor IX;
the second domain comprises a second polypeptide comprising the whole or part of the H chain of an antibody against coagulation factor X; and
the first and second domains further comprise a third polypeptide comprising a shared sequence of the whole or part of the L chain of an antibody.

2. The multispecific antibody of claim 1, wherein the third polypeptide comprises the whole or part of the L chain of an antibody against coagulation factor IX, activated coagulation factor IX, or coagulation factor X.

3. The multispecific antibody of claim 1, wherein the third polypeptide comprises an antigen-binding site comprising CDR1, 2, and 3 individually selected from CDR1, 2, and 3 of each L chain of two or more antibodies, or an antigen-binding site functionally equivalent thereto.

5. A multispecific antibody that can functionally substitute for coagulation factor VIII, which recognizes coagulation factor IX and/or activated coagulation factor IX, and coagulation factor X, wherein the substitutive function of coagulation factor VIII is to reduce coagulation time by 50 seconds or more as compared to the coagulation time observed in the absence of an antibody in an activated partial thromboplastin time (APTT) test that involves warming a mixed solution of 50 µL of antibody solution, 50 µL of F. VIII-deficient plasma (Biomerieux), and 50 µL of APTT reagent (Dade Behring) at 37°C for 3 minutes, adding 50 µL of 20 mM $CaCl_2$ into the mixed solution, and then measuring the coagulation time."

Claims 1 and 3 of the patent as granted read as follows:

"1. A bispecific antibody that can functionally substitute for coagulation factor VIII and that has the activity to enhance factor X activation, which comprises:

a first domain recognizing coagulation factor IX and/or activated coagulation factor IX; and
a second domain recognizing coagulation factor X,
wherein
the first domain comprises a first polypeptide comprising the H chain of an antibody against coagulation factor IX and/or activated coagulation factor IX;
the second domain comprises a second polypeptide comprising the H chain of an antibody against coagulation factor X;
and the first and second domains both comprise a third polypeptide comprising a commonly shared L chain of an antibody against coagulation factor IX, activated coagulation factor IX, or coagulation factor X,
wherein the third polypeptide comprises an antigen-binding site comprising CDR1, 2, and 3 individually selected from CDR1, 2, and 3 of each L chain of two or more antibodies.

3. The bispecific antibody of claim 1 that recognizes coagulation factor IX and/or activated coagulation factor IX, and coagulation factor X, wherein the substitutive function of coagulation factor VIII is to reduce coagulation time by 50 seconds or more as compared to the coagulation time observed in the absence of an antibody in an activated partial thromboplastin time (APTT) test that involves warming a mixed solution of 50 µL of antibody solution, 50 µL of F. VIII-deficient plasma (Biomerieux), and 50 µL of APTT reagent (Dade Behring) at 37°C for 3 minutes, adding 50 µL of 20 mM $CaCl_2$ into the mixed solution, and then measuring the coagulation time."

Claim 1 of auxiliary request 1 reads as follows:

"1. A bispecific antibody that can functionally substitute for coagulation factor VIII and that has the activity to enhance factor X activation, which comprises:
a first domain recognizing coagulation factor IX and/or activated coagulation factor IX;
and
a second domain recognizing coagulation factor X,
wherein
the first domain comprises a first polypeptide comprising the H chain of an antibody against coagulation factor IX and/or activated coagulation factor IX;
the second domain comprises a second polypeptide comprising the H chain of an antibody against coagulation factor X;
and the first and second domains both comprise a third polypeptide comprising a commonly shared L chain of an antibody against coagulation factor IX, activated coagulation factor IX, or coagulation factor X,
wherein the third polypeptide comprises an antigen-binding site comprising CDR1, 2, and 3 individually selected from CDR1, 2, and 3 of each L chain of two or more antibodies;
wherein the substitutive function of coagulation factor VIII is to reduce coagulation time by 50 seconds or more as compared to the coagulation time observed in the absence of an antibody in an activated partial thromboplastin time (APTT) test that involves warming a mixed solution of 50 µL of antibody solution, 50 µL of F. VIII-deficient plasma (Biomerieux), and 50 µL of APTT reagent (Dade Behring) at 37°C for 3 minutes, adding 50 µL of 20 mM CaCl2 into the mixed solution, and then measuring the coagulation time."

III. The following documents are cited in the present decision:

D2 WO 2005/035756
D3 EP 1 688 488 A1
D6 WO 2004/065611
D7 EP 1 605 058 A1

IV. The opposition proceedings, initiated by two opponents, were based on the grounds of Article 100(a) EPC, in relation to novelty (Article 54 EPC) and inventive step (Article 56 EPC), and of Article 100(b) and (c) EPC.

The opposition division decided, *inter alia,* that the subject-matter of claim 1 of the main request (patent as granted) did not extend beyond the content of the application as filed (Article 100(c) EPC), but that it did lack novelty over the disclosure of document D2/D3 (Article 100(a) and Article 54(3) EPC). Document D3 represents the European patent application published in accordance with Article 158(3) EPC based on the English translation of the international patent application D2 in Japanese.

The opposition division further decided in respect of auxiliary request 1 that claim 1 (which corresponds to claim 3 of the patent) did comply with Article 123(2) EPC but that the patent failed to sufficiently disclose the invention in that claim (Article 83 EPC).

V. With the statement of grounds of appeal, the appellant *inter alia* maintained the main request, i.e. that the oppositions be rejected, and re-filed the sets of claims of auxiliary requests 1 to 5 considered in the

decision under appeal. Opponent 2 (respondent II) replied to the appeal.

VI. The board summoned the parties to oral proceedings, as requested, and informed them of its preliminary opinion in a communication under Article 15(1) RPBA 2020.

VII. At the end of the oral proceedings, which were not attended by opponent 1 (respondent I) as had been previously communicated to the board, the Chair announced the board's decision.

VIII. The appellant's submissions are summarised as follows.

Main request (patent as granted)
Amendments (Article 100(c) EPC)
Claim 1

Claims 1 to 3 of the application disclosed the claimed subject-matter. Further disclosures could be found throughout the description, e.g.:
page 2, lines 15 to 17, disclosed "*bispecific antibodies that bind specifically to both F.IX/F. IXa and F. X, and functionally substitute for F. VIIIa*";
page 11, line 19, disclosed "*antibody that can specifically bind*";
page 11, last paragraph, disclosed "*multispecific antibodies of the present invention (preferably bispecific antibodies)*";
page 15, last paragraph, disclosed "*bispecific antibodies that recognize both the enzyme F. IXa and substrate F. X*";
the examples disclosed several bispecific antibodies;
page 13, paragraph 4, disclosed "*antibodies ... comprise commonly shared L chains*";

page 16, lines 7 to 9, disclosed "*L chain of an antibody against coagulation factor IX (F. IX), activated coagulation factor IX (F. IXa), or coagulation factor X (F. X)*";
page 16, lines 10 to 13, disclosed "*In addition, a 'third polypeptide' of the present invention preferably comprises an antigen-binding site comprising CDR1, 2, and 3 each independently selected from CDR1, 2, and 3 of each of the L chains of two or more antibodies*".

The fact that the final passage mentioned above started with the wording "*In addition*" meant that the latter two features were disclosed in combination.

Claim 3

The appellant agreed with the decision of the opposition division. No further arguments were provided.

Novelty (Article 100(a) EPC and Article 54(3) EPC)
Claim 1

Document D3 disclosed, as one specific embodiment, bispecific antibodies which bound to both the blood coagulation factor IX/factor IXa and blood coagulation factor X, and functionally substituted for blood coagulation factor VIII/factor VIIIa (see paragraph [0034](a) and claim 4).

This document, however, disclosed a large number of technical options for the antibody format (see e.g. paragraphs [0011] to [0031]). The concept of common L chains in paragraph [0020] was only one option among many and was not indicated as being preferred. The use of a commonly shared L chain in the context of a

bispecific anti-factor IX(a)/anti-factor X antibody was thus not directly and unambiguously disclosed.

Sufficiency of disclosure (Article 100(b) EPC)
Claim 3

The question of boundaries (i.e. the scope) of the claim was a matter under Article 84 EPC and not Article 83 EPC (see e.g. Case Law of the Boards of Appeal, 9th edition, 2019, II.C.8.2, referring to decision T 943/00). Article 84 EPC was not a ground for opposition and the feature relating to the reduction in coagulation time based on the APTT assay was part of the granted claims (in particular granted dependent claim 3).

Even if the question of whether a particular antibody was an embodiment of the subject-matter of the claim, and in particular the specific reduction in coagulation time according to the APTT test, was a matter under Article 83 EPC, the skilled person was readily able to determine an antibody's potential to reduce the coagulation time according to claim 3 of the main request based on the information provided in the patent (see e.g. Figure 9) and common general knowledge (see e.g. document D26).

The claim did not recite a specific antibody concentration because there was not a single concentration at which antibodies should be compared. Identifying a useful concentration of the antibody to be tested was a routine concentration optimisation.

An objection with regard to the availability of the reagents used in the APTT assay was raised by respondent II for the first time during the oral

proceedings. This represented an amendment of respondent II's appeal case and therefore should not be admitted into the proceedings under Article 13(2) RPBA 2020.

The skilled person could determine, without undue burden, whether a specific antibody was within the "boundaries of the claim" and, hence, the patent disclosed the claimed invention in a manner sufficiently clear and complete for it to be carried out by the skilled person.

IX. Respondent II's submissions are summarised as follows.

Main request (patent as granted)
Amendments (Article 100(c) EPC)
Claim 1

Claim 1 of the patent as granted differed from the combination of features in claims 1 to 3 of the application in that
- the feature "*multispecific*" had been replaced by "*bispecific*";
- "*the whole or part of the H chain*" had become *"the H chain*";
- the feature "*a shared sequence of the whole or part of the L chain of an antibody*" had been narrowed to become "*a commonly shared L chain of an antibody against coagulation factor IX, activated coagulation factor IX, or coagulation factor X*"; and
- the phrase "*wherein the third polypeptide comprises an antigen-binding site comprising CDR1, 2, and 3 individually selected from CDR1, 2, and 3 of each L chain of two or more antibodies*" from claim 3 of the application had been narrowed by the removal of "*or an antigen binding site functionally equivalent thereto*".

A selection from at least five lists was thus required to arrive at the claimed subject-matter.

The omission of the words "*part of*" with regard to the L chain resulted in added subject-matter because the whole L chain of an antibody could not at the same time comprise CDRs selected from a second antibody as required by the second definition of the L chain in claim 1.

Claim 3

Claim 3, which recited a specific assay as well as a specific reduction in coagulation time, contained added subject-matter because the disclosure in claim 5 of the application which referred to the APTT assay was directed to multispecific (and not bispecific) antibodies and did not contain any of the features with regard to the first domain having the H chain, the second domain having the H chain, the common (whole) L-chain or the substituted CDRs as recited in granted claim 1.

The passage on page 18, lines 8 to 16, of the application, which immediately preceded a passage referring to the APTT assay, also failed to mention these features and was restricted to a selected set of antibodies in Figures 12 and 13. Combining the disclosure about the APTT assay on page 18 with the structural features of the antibody disclosed in other parts of the application amounted to an intermediate generalisation resulting in added subject-matter.

Novelty (Article 100(a) EPC and Article 54(3) EPC)
Claim 1

Document D3 disclosed in paragraph [0020] a method to generate bispecific antibodies with a common light chain. WO 2004/065611 (document D6), which was referenced therein, provided the skilled person with a method to generate those antibodies (see document D7, the translation of document D6, paragraph [0010]). When applying this method to the preferred target combination of document D3, i.e. factor IX(a) and factor X (see paragraph [0034](a), the examples and claims 1 to 4), the skilled person would inevitably have obtained an antibody falling within the scope of claim 1.

Sufficiency of disclosure (Article 100(b) EPC)
Claim 3

The assay described in the claim required that "*50 µL of antibody solution*" was used to determine the coagulation time and that this time had to be reduced by 50 seconds or more. However, the assay failed to mention the concentration of the antibody in the reaction mixture. Since the coagulation time depended on the concentration of the antibody in the assay (see e.g. Figures 14 and 15 of the patent), the skilled person could not reliably reproduce the claimed subject-matter.

The patent showed that the assay in the claim could have significant deviations in measurements, which would inevitably lead to contradictory results. In particular, the values for the negative control (i.e. without antibody) differed substantially between experiments (see e.g. Example 7 and Figures 7 and 8).

Under identical conditions, the coagulation time measured in the absence of an antibody varied between about 102 seconds (white bar, Figure 7) and about 83 seconds (white bar, Figure 8). The same assay was used in Example 21 and the coagulation time without antibody was about 123 seconds (see Figure 25). The range of the baseline coagulation time was thus from about 83 seconds (Figure 8) to about 123 seconds (Figure 25).

The APTT assay mentioned in the claim depended on the nature and composition of the phospholipids in the APTT reagent. It was furthermore questionable whether the APTT reagents mentioned in the claim were still available and whether the company "Dade Behring", which provided those reagents, still existed.

The unreliability of the assay represented an undue burden to the skilled person. The patent therefore did not sufficiently disclose the claimed invention.

X. The appellant requested that the decision under appeal be set aside and that the oppositions be rejected (i.e. that the patent be maintained as granted (main request)) or, alternatively, that the patent be maintained in amended form on the basis of one of the sets of claims of auxiliary requests 1 to 5.

Respondent II requested that the appeal be dismissed and that the case be remitted to the opposition division for a decision to be made on sufficiency of disclosure and inventive step, should these questions arise.

Respondent I has not made submissions and has not formulated any requests in the appeal proceedings.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 99 EPC and is admissible.

Party absent at the oral proceedings

2. Respondent I was duly summoned but did not attend the oral proceedings. The board decided to continue the proceedings in accordance with Rule 115(2) EPC and Article 15(3) RPBA 2020 in this party's absence.

Main request (patent as granted)
Added subject-matter (Article 100(c) EPC)
Claim 1

3. Claim 1 as granted differs from the combination of claims 1 to 3 of the application as follows (additions are underlined, while deletions are struck through):

"1. A ~~multispecific~~ bispecific antibody that can functionally substitute for coagulation factor VIII and that has the activity to enhance factor X activation, which comprises:
a first domain recognizing coagulation factor IX and/or activated coagulation factor IX; and
a second domain recognizing coagulation factor X,
wherein the first domain comprises a first polypeptide comprising ~~the whole or part of~~ the H chain of an antibody against coagulation factor IX and/or activated coagulation factor IX;
the second domain comprises a second polypeptide comprising ~~the whole or part of~~ the H chain of an antibody against coagulation factor X;

and the first and second domains ~~further~~ both comprise a third polypeptide comprising a commonly shared ~~sequence of the whole or part of the~~ L chain of an antibody against coagulation factor IX, activated coagulation factor IX, or coagulation factor X, wherein the third polypeptide comprises an antigen-binding site comprising CDR1, 2, and 3 individually selected from CDR1, 2, and 3 of each L chain of two or more antibodies~~, or an antigen binding site functionally equivalent thereto~~."

4. The board agrees with the decision under appeal "*that the description* [as filed] *shows that 'bispecific' is the preferred embodiment of 'multispecific'*". In this respect, page 2, lines 15 to 17, of the application discloses "*bispecific antibodies that bind specifically to both F. IX/F. IXa and F. X, and functionally substitute for F. VIIIa, more specifically, have cofactor functions to enhance F. X activation by F. IXa*" (see also page 11, last paragraph). The respective amendments in the first clause of claim 1 therefore do not add subject-matter.

5. The board also agrees with the decision under appeal that "*the omission of these two features 'whole' or 'part' which both together cover all existing possibilities - it is either the whole chain or part of the chain - there are no other possibilities, cannot represent an introduction of subject-matter*". By replacing "*the whole or part of the H chain*" by "*the H chain*", the second alternative of the definition of the H chain ("*part of*") has effectively been deleted. This amendment does not result in added subject-matter. The same applies to the deletion of "*whole or part of*" with respect to the L chain.

6. The board agrees with the appellant that the two definitions for the "*third polypeptide*" in the claim are disclosed in claims 2 and 3 as filed. Although claim 3 refers back only to claim 1 and not to claim 2, the application discloses the combination of the subject-matter of all three claims. In this regard, page 16, lines 7 to 13, of the application (lines 7 to 13), as cited by the appellant, is relevant:
"*A 'third polypeptide' of the present invention is preferably a polypeptide that comprises a whole or partial sequence of the L chain of an antibody against coagulation factor IX (F. IX), activated coagulation factor IX (F. IXa), or coagulation factor X (F. X). In addition, a 'third polypeptide' of the present invention preferably comprises an antigen-binding site comprising CDR1, 2, and 3 each independently selected from CDR1, 2, and 3 of each of the L chains of two or more antibodies or antigen-binding site functionally equivalent thereto*".
As was further submitted by the appellant, by using "*in addition*" the passage makes a connection between the two definitions. The combination in claim 1 as granted of the definitions from claims 2 and 3 as filed thus does not result in added subject-matter either.

7. Respondent II argued that "*a 'whole L chain of an antibody' cannot at the same time comprise CDRs selected from a second antibody. However, the words 'part of' (the L chain) have been omitted in granted claim 1, resulting in added subject-matter*". The board does not agree, because the passage on page 16 (see above) discloses that "*in addition*" to the third polypeptide comprising a whole or partial sequence of the L chain, it can also comprise CDR1, 2 and 3 of two or more antibodies. This disclosure implies that "*the L chain of an antibody against coagulation factor IX,*

activated coagulation factor IX or coagulation factor X" can still comprise CDRs from other antibodies. In other words, from the application as a whole (see e.g. page 16 and the examples) the skilled person understands that the L chain of an antibody is not limited to the exact sequence of the L chain of the parent antibody, but can include CDRs from other antibodies.

8. Respondent II further argued that the claimed subject-matter amounted to a combination of selections from at least five lists each having two options, i.e. "*bispecific*" vs. "*multispecific*", "*the H chain*" vs. "*part of the H chain*", "*a commonly shared L chain*" vs. "*part of the L chain*", "*CDR1, 2 or 3*" vs. "*functional equivalent thereof*". The board considers the selection of each of the alternatives and the combination thereof to be disclosed in the application for the reasons given in points 3. to 7. above. Moreover, the application discloses the preferred embodiments for each of the alternatives in the examples, which relate to bispecific antibodies with whole H and L chains and L chains with CDR1, 2 or 3 from two antibodies. The combination of these preferred options of several two-fold selections therefore does not result in added subject-matter.

9. Claim 1 therefore does not contain added subject-matter within the meaning of Article 100(c) EPC.

Claim 3

10. Respondent II objected to claim 3 (see section II.) on the ground of added subject-matter because claim 5 of the application, which referred to the APTT assay, did

not relate to bispecific antibodies having the specific features of claim 1 of the patent as granted.

11. Like the respondent, the board agrees with the decision under appeal (see section IV.) which, in the context of auxiliary request 1, in which the features of claim 3 of the patent as granted are incorporated into claim 1, found that the subject-matter of claim 1 of the patent as granted "*can be combined with the additional feature relating to the APTT without adding subject-matter because it is directly apparent to the skilled reader that the effect of the antibody on the APTT is a functional feature by which any bispecific antibody of the application can be characterized*". The opposition division in this respect also referred to the examples, in which "*the test is used ... to determine the effect of the different bispecific antibodies, with or without common L-chains and with or without CDR shuffling*". On page 18, lines 20 to 28, the application discloses APTT as a general assay to be used for testing multispecific antibodies of the invention. Based on the disclosure of the application as a whole, the skilled person was aware that bispecific antibodies are a preferred embodiment and thus included in the group of multispecific antibodies. The skilled person would therefore have considered the APTT assay disclosed in claim 5 of the application to be applicable also to the specific antibodies defined in claim 1 of the patent as granted.

12. Claim 3 therefore does not contain added subject-matter within the meaning of Article 100(c) EPC.

Admittance of novelty objection against claim 1 based on documents D2/D3 in combination with documents D6/D7 (Article 13(2) RPBA 2020)

13. A revised version of the Rules of Procedure of the Boards of Appeal (RPBA 2020) entered into force on 1 January 2020. The transitional provisions are set out in Article 25 RPBA 2020, according to which, as a general rule, the revised version applies to any appeal pending on that date, such as the present appeal.

14. In the present case, the summonses to oral proceedings were notified after the date of entry into force and the requirements under Article 25(3) RPBA 2020 are therefore not met. Article 13(2) RPBA 2020 thus applies.

15. During the oral proceedings, respondent II cited passages of document D7 (e.g. paragraph [0010]), which is the English translation of document D6 (WO 2004/065611) cited in paragraph [0020] of document D3. These passages, as submitted by respondent II, were provided as evidence that the skilled person carrying out the teaching of paragraph [0020] in document D3 would inevitably arrive at a bispecific antibody against factor IX(a) and factor X falling under the definition of claim 1.

16. Respondent II further argued that document D7 had been filed in the opposition proceedings and had therefore been in the proceedings all along. It was the appellant's own document and thus the argument could not be a surprise. The passage in document D3 (paragraph [0020]) referring to document D6 had also been referred to in the reply to the statement of grounds of appeal (see pages 7 and 8) and in a letter

in reply to the board's communication (see page 4, second full paragraph).

17. Document D7 has not been cited in writing during the appeal proceedings. The decision under appeal does not mention document D7 either. The reply to the statement of grounds of appeal only mentions paragraph [0020] of document D3; it does not refer to documents D6 and D7. Only in a letter received after the issuance of the board's communication under Article 15(1) RPBA 2020 and after the summons to oral proceedings did respondent II for the first time cite document D6, by stating that "*paragraph [0020] of D3 itself refers to document WO 2004/065611 as proposing a method which addressed the difficulties that had previously existed*", but it did not provide any detail as to what document WO 2004/065611 disclosed. Moreover, the allegation that the teaching in document D7 would "*inevitably*" lead to a bispecific antibody as claimed was not submitted prior to the oral proceedings. The board thus considers the reference to document D7 and the related submissions to be an amendment to respondent II's appeal case, made after the notification of a summons to oral proceedings, and therefore Article 13(2) RPBA 2020 applies.

18. According to Article 13(2) RPBA 2020, such an amendment is, "*in principle, not be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned*". Respondent II did not bring forward any arguments which the board could consider to represent exceptional circumstances. The board has therefore decided not to admit respondent II's argument and its supporting evidence in document D7 into the appeal proceedings.

Novelty (Article 100(a) and Article 54(3) EPC)
Claim 1

19. The claimed bispecific antibody has a first domain recognising coagulation factor IX and/or activated coagulation factor IX; and a second domain recognising coagulation factor X. It was undisputed by the parties that documents D2/D3 represented state of the art under Article 54(3) EPC and disclosed a bispecific antibody having the same targets (see e.g. document D3, paragraph [0032] in combination with paragraph [0034](a)). Although other target combinations are disclosed in document D3 (see paragraph [0034](b) to (g)), a bispecific antibody recognising factor IX/IXa and factor X which functionally substitutes for factor VIII or factor VIIIa is the preferred embodiment, as is evident from claims 1 to 4 and the examples.

20. The claimed antibody is further defined in that the first and second domains both comprise a third polypeptide comprising "*a commonly shared L chain of an antibody against coagulation factor IX, activated coagulation factor IX, or coagulation factor X*", and comprising "*an antigen-binding site comprising CDR1, 2, and 3 individually selected from CDR1, 2, and 3 of each L chain of two or more antibodies*".

21. It was a matter of debate between the parties whether the features "*of an antibody against coagulation factor IX, activated coagulation factor IX, or coagulation factor X*" and "*antigen-binding site comprising CDR1, 2, and 3 individually selected from CDR1, 2, and 3 of each L chain of two or more antibodies*" imposed limitations on the structure of the "*commonly shared L chain*" of the antibody claimed. In view of the conclusion on

novelty reached below, the board considers it unnecessary to answer this question.

22. The only reference to a commonly shared L chain in document D3 is in paragraph [0020]. This reference, however, is in the context of a list of possible methods to overcome the problem of incorrect pairing of H and L chains in a bispecific antibody outlined in paragraphs [0017] and [0018], such as: knobs-into-holes (paragraph [0019)]), common L chains (paragraph [0020]), successive expression of right-arm and left-arm L chain and H chain (paragraph [0020]), cross-linking (paragraph [0021]), leucine zippers (paragraph [0022]) and single chain antibodies (paragraph [0025]). The passage referring to a common L chain in paragraph [0020] reads: "*However, the possibility of two randomly selected types of antibodies containing the same L chain is low; thus, it is difficult to put the aforementioned idea into practice. In this respect, a method has been proposed for selection of a common L chain adapting arbitrary different H chains to show high binding ability (WO 2004/065611)*". Document D3 thus discloses that amongst the different methods for generating bispecific antibodies, the method involving "*the same L chain*" was difficult to put into practice. The solution proposed in this respect with reference to WO 2004/065611 is not described in detail, but it is outlined that "*a common L chain adapting arbitrary different H chains to show high binding ability*" could be selected. Document D3 does not disclose the structure or origin of the common L chain or how it is adapted and selected.

23. The board concludes that document D3 left the skilled person in doubt as to how to put into practice a method involving a common L chain to obtain a functional

bispecific antibody which could "*substitute for coagulation factor VIII and that has the activity to enhance factor X activation*".

24. Respondent II argued that by carrying out the teaching of document D3, the skilled person would "*inevitably*" arrive at a bispecific antibody as defined in claim 1. However, as outlined above, the disclosure of document D3 lacks essential elements about the structure and source of the common L chain and how to adapt and select it in order to arrive at a functional bispecific antibody recognising both targets. Moreover, from the disclosure of document D3 alone the skilled person did not know whether a bispecific antibody with a common L chain would have the additional functional features required by the claim, i.e. to "*substitute for coagulation factor VIII*" and to have "*the activity to enhance factor X activation*". The skilled person would thus not be able to directly and unambiguously derive from the disclosure in document D3 the use of a common L chain in a bispecific antibody against factor IX/IXa and factor X.

25. The subject-matter of claim 1 is novel within the meaning of Article 54(1),(3) EPC in combination with Article 100(a) EPC.

Admittance of new submissions with regard to sufficiency of disclosure of the invention of claim 3

26. During the oral proceedings, respondent II made submissions with regard to the sufficiency of disclosure of the patent in relation to the invention of claim 3, which had not been brought forward in writing. These submissions related to the reliability and consistency of the APTT assay based on "*common*

general knowledge" and to the availability of the APTT reagents, in particular the question of whether the company named "Dade Behring" still existed. The board considers the respective submissions to be an amendment to respondent II's appeal case after the notification of a summons to oral proceedings, and therefore Article 13(2) RPBA 2020 applies (see point 18. above).

27. Respondent II did not put forward any exceptional circumstances. Moreover, the board did not consider such exceptional circumstances to be present in the case at hand. The board has therefore decided not to admit the submissions made at the oral proceedings into the appeal proceedings. Consequently, the board has not taken those submissions into account in its considerations as regards sufficiency of disclosure.

Sufficiency of disclosure (Article 100(b) EPC) - claim 3

28. Claim 3 defines the effect of the antibody on coagulation time by referring to an activated partial thromboplastin time (APTT) test. This test involves the mixing of the antibody with standard human plasma and APTT reagent. The reaction is started by the addition of $CaCl_2$ (see Example 21, paragraph [0185], of the patent).

29. In the decision under appeal, the opposition division found that "[s]*ince the coagulation time depends on the concentration of the antibody, the skilled person does not know whether she/he is working within the boundaries of the claim or not*" and that "[t]*herefore neither the patent nor the general knowledge gives the skilled person guidance regarding the antibody concentration to be used in order to achieve a reduction of coagulation time of at least 50 seconds*

and the bispecific antibodies as claimed are considered to be insufficiently disclosed". The board does not agree because the question of the boundaries of the claim is a question under Article 84 EPC, which is not a ground for opposition. Only in specific cases where the boundaries are so unclear that the person skilled in the art is unable to carry out the invention without undue burden have some boards considered this issue also under Article 83 EPC (see Case Law of the Boards of Appeal, 9th edition, 2019, II.C.8.2).

30. As is apparent from the patent, the optimal antibody concentration for the APTT assay has to be chosen for each antibody individually (see e.g. Figure 14 for the dependence of coagulation time on the antibody concentration). Moreover, since the claim stipulates "to reduce coagulation time by 50 seconds or more as compared to the coagulation time observed in the absence of an antibody", it is the difference in coagulation time which is to be determined and not an absolute value. The argument by respondent II that the assay failed to mention the concentration of the antibody in the reaction mixture which was linked to the coagulation time does not address why the skilled person with the teaching of the patent at hand and in view of common general knowledge on the filing date was not in a position to determine an optimal concentration for a given antibody and to compare the coagulation time at that concentration against a negative control.

31. Respondent II also argued that the APTT test disclosed in the patent was not reliable because the coagulation values for the negative control varied between 83 and 123 seconds. The board does not see this as an issue which would have posed an undue burden on the skilled person. A variation in the value of the negative

control due to slightly different reaction conditions would equally affect the value in the presence of the antibody and thus be cancelled out when calculating the difference. The board therefore cannot see how this would prevent the skilled person from carrying out the invention.

32. The invention of claim 3 is sufficiently disclosed in the patent within the meaning of Article 100(b) EPC.

Remittal to the opposition division (Article 111(1) EPC and Article 11 RPBA 2020)

33. The issue of inventive step was not dealt with in the decision under appeal. The only document considered in the decision with respect to the issue of novelty is document D2/D3, which is state of the art under Article 54(3) EPC and thus not available under Article 56 EPC. Furthermore, the issue of sufficiency of disclosure was not dealt with in a complete manner because only claim 1 of auxiliary request 1, which corresponds to claim 3 of the main request, was addressed in that respect in the decision under appeal. The board does not agree with respondent II that it had already addressed the relevant issues in its communication. The board moreover considers that the references to the date of filing of the application forming the basis of the patent or the patent term, respectively, do not outweigh the considerations relating to the absence of a decision by the opposition division on the remaining issues. In exercising its discretion under Article 111(1) EPC, the board finds that special reasons present themselves for remitting the case to the opposition division for further prosecution, which is consistent with the primary

object of the appeal proceedings being to review the decision under appeal in a judicial manner.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division for further prosecution.

The Registrar: The Chair:

I. Aperribay B. Claes

Decision electronically authenticated