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Datasheet for the decision of 12 March 2019

Case Number: T 0628/15 - 3.3.04

Application Number: 08735000.5

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Language of the proceedings: EN

Title of invention:
Cross-species-specific bispecific binders

Patent Proprietor:
Amgen Research (Munich) GmbH

Opponents:
01: F. Hoffmann-La Roche AG
02: Janssen Biotech, Inc.

Headword:
Cross-species-specific bispecific binders/AMGEN

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

Keyword:
Main request, auxiliary request 1 - amendments - allowable (no)
Auxiliary requests AUX1b, AUX1c and 2 - admitted into proceedings (no)

Decisions cited:
G 0003/89, G 0011/91, G 0002/10

Catchword:
-

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Case Number: T 0628/15 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 12 March 2019

Appellant I/Respondent: (Patent Proprietor)	Amgen Research (Munich) GmbH Staffelseestrasse 2 81477 München (DE)
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Appellant III: (Opponent 02)	Janssen Biotech, Inc. 800/850 Ridgeview Drive Horsham PA 19044 (US)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 5 February 2015 concerning maintenance of the European Patent No. 2155788 in amended form.**

Composition of the Board:

Chair	G. Alt
Members:	B. Claes
	P. De Heij

Summary of Facts and Submissions

I. European patent No. 2 155 788 (hereinafter "the patent") was granted for European patent application No. 08 735 000.5, which is based on international patent application PCT/EP2008/002663 (hereinafter "the application") and was published as WO 2008/119566.

Claims 1, 3, 4 and 7 of the application read:

"1. A polypeptide comprising a first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3ε (epsilon) chain and a second binding domain capable of binding to EGFR, Her2/neu or IgE of a human and/or a non-chimpanzee primate, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, or 8.

3. The polypeptide according to any one of claims 1 or 2, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3ε chain comprises a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from:

(a) CDR-L1 as depicted in SEQ ID NO:27, CDR-L2 as depicted in SEQ ID NO:28 and CDR-L3 as depicted in SEQ ID NO:29;
(b) CDR-L1 as depicted in SEQ ID NO:117, CDR-L2 as depicted in SEQ ID NO: 118 and CDR-L3 as depicted in SEQ ID NO: 119; and
(c) CDR-L1 as depicted in SEQ ID NO:153, CDR-L2 as depicted in SEQ ID NO: 154 and CDR-L3 as depicted in SEQ ID NO: 155.

4. The polypeptide according to any one of claims 1 or 2, wherein the first binding domain capable of binding

to an epitope of human and non-chimpanzee primate CD3ε chain comprises a VH region comprising CDR-H 1, CDR-H2 and CDR-H3 selected from:

(a) CDR-H1 as depicted in SEQ ID NO:12, CDR-H2 as depicted in SEQ ID NO: 13 and CDR-H3 as depicted in SEQ ID NO:14;

(b) CDR-H1 as depicted in SEQ ID NO:30, CDR-H2 as depicted in SEQ ID NO:31 and CDR-H3 as depicted in SEQ ID NO:32;

(c) CDR-H1 as depicted in SEQ ID NO:48, CDR-H2 as depicted in SEQ ID NO:49 and CDR-H3 as depicted in SEQ ID NO:50;

(d) CDR-H1 as depicted in SEQ ID NO:66, CDR-H2 as depicted in SEQ ID NO:67 and CDR-H3 as depicted in SEQ ID NO:68;

(e) CDR-H1 as depicted in SEQ ID NO:84, CDR-H2 as depicted in SEQ ID NO:85 and CDR-H3 as depicted in SEQ ID NO:86;

(f) CDR-H1 as depicted in SEQ ID NO:102, CDR-H2 as depicted in SEQ ID NO: 103 and CDR-H3 as depicted in SEQ ID NO:104;

(g) CDR-H1 as depicted in SEQ ID NO:120, CDR-H2 as depicted in SEQ ID NO:121 and CDR-H3 as depicted in SEQ ID NO:122;

(h) CDR-H1 as depicted in SEQ ID NO:138, CDR-H2 as depicted in SEQ ID NO: 139 and CDR-H3 as depicted in SEQ ID NO:140;

(i) CDR-H1 as depicted in SEQ ID NO:156, CDR-H2 as depicted in SEQ ID NO: 157 and CDR-H3 as depicted in SEQ ID NO:158; and

(j) CDR-H1 as depicted in SEQ ID NO:174, CDR-H2 as depicted in SEQ ID NO:175 and CDR-H3 as depicted in SEQ ID NO:176.

7. The polypeptide according to any one of claims 1 to 6, wherein the first binding domain capable of

binding to an epitope of human and non-chimpanzee primate CD3ε chain comprises a VL region and a VH region selected from the group consisting of:

(a) a VL region as depicted in SEQ ID NO: 17 or 21 and a VH region as depicted in SEQ ID NO: 15 or 19;

(b) a VL region as depicted in SEQ ID NO:35 or 39 and a VH region as depicted in SEQ ID NO:33 or 37;

(c) a VL region as depicted in SEQ ID NO:53 or 57 and a VH region as depicted in SEQ ID NO:51 or 55;

(d) a VL region as depicted in SEQ ID NO:71 or 75 and a VH region as depicted in SEQ ID NO:69 or 73;

(e) a VL region as depicted in SEQ ID NO:89 or 93 and a VH region as depicted in SEQ ID NO:87 or 91 ;

(f) a VL region as depicted in SEQ ID NO:107 or 111 and a VH region as depicted in SEQ ID NO: 105 or 109;

(g) a VL region as depicted in SEQ ID NO: 125 or 129 and a VH region as depicted in SEQ ID NO:123 or 127;

(h) a VL region as depicted in SEQ ID NO: 143 or 147 and a VH region as depicted in SEQ ID NO:141 or 145;

(i) a VL region as depicted in SEQ ID NO: 161 or 165 and a VH region as depicted in SEQ ID NO:159 or 163; and

(j) a VL region as depicted in SEQ ID NO: 179 or 183 and a VH region as depicted in SEQ ID NO: 177 or 181."

II. Appeals were filed by the patent proprietor and by both opponents against the interlocutory decision of the opposition division finding that, on the basis of **auxiliary request 3** which was filed on 3 December 2014, the patent met the requirements of the EPC.

Claims 1 and 4 of auxiliary request 3 read:

"1. A polypeptide comprising a first binding domain which is an antibody capable of binding to an epitope of human and Callithrix jacchus, Saguinus oedipus or Saimiri sciureus CD3ε chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NO:2, 4, 6, or 8 and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu, and a second binding domain capable of binding to EGFR, Her2/neu or IgE of a human and/or a non-chimpanzee primate,

wherein the first binding domain comprises a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from:
(a) CDR-L1 as depicted in SEQ ID NO:27, CDR-L2 as depicted in SEQ ID NO:28 and CDR-L3 as depicted in SEQ ID NO:29;
(b) CDR-L1 as depicted in SEQ ID NO:117, CDR-L2 as depicted in SEQ ID NO: 118 and CDR-L3 as depicted in SEQ ID NO: 119; and
(c) CDR-L1 as depicted in SEQ ID NO:153, CDR-L2 as depicted in SEQ ID NO: 154 and CDR-L3 as depicted in SEQ ID NO: 155, and
wherein the first binding domain comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 selected from:
(a) CDR-H1 as depicted in SEQ ID NO:12, CDR-H2 as depicted in SEQ ID NO: 13 and CDR-H3 as depicted in SEQ ID NO:14;
(b) CDR-H1 as depicted in SEQ ID NO:30, CDR-H2 as depicted in SEQ ID NO:31 and CDR-H3 as depicted in SEQ ID NO:32;
(c) CDR-H1 as depicted in SEQ ID NO:48, CDR-H2 as depicted in SEQ ID NO:49 and CDR-H3 as depicted in SEQ ID NO:50;
(d) CDR-H1 as depicted in SEQ ID NO:66, CDR-H2 as

depicted in SEQ ID NO:67 and CDR-H3 as depicted in SEQ ID NO:68;

(e) CDR-H1 as depicted in SEQ ID NO:84, CDR-H2 as depicted in SEQ ID NO:85 and CDR-H3 as depicted in SEQ ID NO:86;

(f) CDR-H1 as depicted in SEQ ID NO:102, CDR-H2 as depicted in SEQ ID NO: 103 and CDR-H3 as depicted in SEQ ID NO:104;

(g) CDR-H1 as depicted in SEQ ID NO:120, CDR-H2 as depicted in SEQ ID NO:121 and CDR-H3 as depicted in SEQ ID NO:122;

(h) CDR-H1 as depicted in SEQ ID NO:138, CDR-H2 as depicted in SEQ ID NO: 139 and CDR-H3 as depicted in SEQ ID NO:140;

(i) CDR-H1 as depicted in SEQ ID NO:156, CDR-H2 as depicted in SEQ ID NO: 157 and CDR-H3 as depicted in SEQ ID NO:158; and

(j) CDR-H1 as depicted in SEQ ID NO:174, CDR-H2 as depicted in SEQ ID NO:175 and CDR-H3 as depicted in SEQ ID NO:176.

4. The polypeptide according to any one of claims 1 to 3, wherein the first binding domain comprises a VL region and a VH region selected from the group consisting of:

(a) a VL region as depicted in SEQ ID NO: 17 or 21 and a VH region as depicted in SEQ ID NO: 15 or 19;

(b) a VL region as depicted in SEQ ID NO:35 or 39 and a VH region as depicted in SEQ ID NO:33 or 37;

(c) a VL region as depicted in SEQ ID NO:53 or 57 and a VH region as depicted in SEQ ID NO:51 or 55;

(d) a VL region as depicted in SEQ ID NO:71 or 75 and a VH region as depicted in SEQ ID NO:69 or 73;

(e) a VL region as depicted in SEQ ID NO:89 or 93 and a VH region as depicted in SEQ ID NO:87 or 91 ;

(f) a VL region as depicted in SEQ ID NO:107 or 111 and

a VH region as depicted in SEQ ID NO: 105 or 109;
(g) a VL region as depicted in SEQ ID NO: 125 or 129 and a VH region as depicted in SEQ ID NO:123 or 127;
(h) a VL region as depicted in SEQ ID NO: 143 or 147 and a VH region as depicted in SEQ ID NO:141 or 145;
(i) a VL region as depicted in SEQ ID NO: 161 or 165 and a VH region as depicted in SEQ ID NO:159 or 163; and
(j) a VL region as depicted in SEQ ID NO: 179 or 183 and a VH region as depicted in SEQ ID NO: 177 or 181."

III. In the decision under appeal, the opposition division had held, *inter alia*, that the subject-matter of claim 1 of this request did not extend beyond the content of the application. The opposition division had furthermore held that the subject-matter of claims 1 and 2 of the main request and auxiliary request 1 lacked novelty pursuant to Article 54(3) EPC. It did not admit auxiliary request 2 into the proceedings as it considered that the amendments contained in claim 1 did not overcome the lack of novelty under Article 54(3) EPC.

IV. The patent proprietor filed, with their statement of grounds of appeal, a new main request and three auxiliary requests. The main request and auxiliary requests 1 and 2 were filed in response to the findings of lack of novelty under Article 54(3) EPC. Auxiliary request 3 was identical to the same request considered by the opposition division. In addition, one new document was submitted.

V. In their respective statements of grounds of appeal, the opponents (hereinafter "appellant II" and "appellant III" for opponents 1 and 2, respectively) submitted that the claims of auxiliary request 3 lacked compliance with the requirements of Articles 56, 83 and 123(2) EPC. Appellant III filed four new documents.

VI. In its reply to the appeals of appellants II and III (section V), with a letter dated 29 October 2015, the patent proprietor submitted auxiliary request 4 with handwritten amendments and a declaration comprising experimental data. As support for claim 1 of auxiliary request 4, the patent proprietor merely referred to the "*Sequence Table of the application as filed*".

Claim 1 of auxiliary request 4, in the typed version, submitted with the letter dated 14 January 2019, read:

"1. A polypeptide comprising a first binding domain which is an antibody capable of binding to an epitope of human and Callithrix jacchus, Saguinus oedipus or Saimiri sciureus CD3e chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NO:2, 4, 6, or 8 and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu, and a second binding domain capable of binding to EGFR, Her2/neu or IgE of a human and/or a non-chimpanzee primate,
wherein the first binding domain comprises a VL region comprising CDR-L1, CDR-L2 and CDR-L3 and wherein the first binding domain comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 selected from:
(a) CDR-L1 as depicted in SEQ ID NO:27, CDR-L2 as depicted in SEQ ID NO:28 and CDR-L3 as depicted in SEQ ID NO:29 and
CDR-H1 as depicted in SEQ ID NO:12, CDR-H2 as

depicted in SEQ ID NO:13 and CDR-H3 as depicted in SEQ ID NO:14;

(b) CDR-L1 as depicted in SEQ ID NO:27, CDR-L2 as depicted in SEQ ID NO:28 and CDR-L3 as depicted in SEQ ID NO:29 and
CDR-H1 as depicted in SEQ ID NO:30, CDR-H2 as depicted in SEQ ID NO:31 and CDR-H3 as depicted in SEQ ID NO:32;

(c) CDR-L1 as depicted in SEQ ID NO:27, CDR-L2 as depicted in SEQ ID NO:28 and CDR-L3 as depicted in SEQ ID NO:29 and
CDR-H1 as depicted in SEQ ID NO:48, CDR-H2 as depicted in SEQ ID NO:49 and CDR-H3 as depicted in SEQ ID NO:50;

(d) CDR-L1 as depicted in SEQ ID NO:27, CDR-L2 as depicted in SEQ ID NO:28 and CDR-L3 as depicted in SEQ ID NO:29 and
CDR-H1 as depicted in SEQ ID NO:66, CDR-H2 as depicted in SEQ ID NO:67 and CDR-H3 as depicted in SEQ ID NO:68;

(e) CDR-L1 as depicted in SEQ ID NO:117, CDR-L2 as depicted in SEQ ID NO:118 and CDR-L3 as depicted in SEQ ID NO:119 and CDR-H1 as depicted in
SEQ ID NO:84, CDR-H2 as depicted in SEQ ID NO:85 and CDR-H3 as depicted in SEQ ID NO:86;

(f) CDR-L1 as depicted in SEQ ID NO:27. CDR-L2 as depicted in SEQ ID NO:28 and CDR-L3 as depicted in SEQ ID NO:29 and
CDR-H1 as depicted in SEQ ID NO:102, CDR-H2 as depicted in SEQ ID NO:103 and CDR-H3 as depicted in SEQ ID NO:104;

(g) CDR-L1 as depicted in SEQ ID N0:117, CDR-L2 as depicted in SEQ ID N0:118 and CDR-L3 as depicted in SEQ ID N0:119 and
CDR-H1 as depicted in SEQ ID NO:120, CDR-H2 as depicted in SEQ ID N0:121 and CDR-H3 as depicted in

SEQ ID NO:122;

(h) CDR-L1 as depicted in SEQ ID NO:27, CDR-L2 as depicted in SEQ ID NO:28 and CDR-L3 as depicted in SEQ ID NO:29 and
CDR-H1 as depicted in SEQ ID NO: 138, CDR-H2 as depicted in SEQ ID NO: 139 and CDR-H3 as depicted in SEQ ID NO:140;

(i) CDR-L1 as depicted in SEQ ID NO: 153, CDR-L2 as depicted in SEQ ID NO:154 and CDR-L3 as depicted in SEQ ID NO:155 and
CDR-H1 as depicted in SEQ ID NO: 156, CDR-H2 as depicted in SEQ ID NO: 157 and CDR-H3 as depicted in SEQ ID NO:158;

(j) CDR-L1 as depicted in SEQ ID NO:153, CDR-L2 as depicted in SEQ ID NO:154 and CDR-L3 as depicted in SEQ ID NO:155 and
CDR-H1 as depicted in SEQ ID NO: 174, CDR-H2 as depicted in SEQ ID NO: 175 and CDR-H3 as depicted in SEQ ID NO:176."

VII. Appellant II submitted in its reply to the appeal of the patent proprietor (section IV), *inter alia*, that that none of the newly filed claim requests (here: main request and auxiliary requests 1 and 2) complied with the EPC. The letter was accompanied by two documents. Appellant III submitted that these newly filed requests should not be admitted into the proceedings and that they failed to comply with the EPC. The letter was accompanied by ten further documents.

VIII. In response to the replies of appellants II and III (section VII), the patent proprietor submitted, with a letter dated 15 March 2016, a new main request and auxiliary requests 1, 1A, 2 and 2A, replacing the formerly filed main request and auxiliary requests 1

and 2 (see section IV). Auxiliary requests 3 and 4 were maintained unamended.

IX. Both appellants II and III responded to the reply of the patent proprietor (section VI) and submitted a number of new documents.

X. In a communication pursuant to Article 15(1) RPBA, the board informed the parties of its preliminary appreciation of certain substantive and legal matters concerning the appeals. The board was, *inter alia*, of the opinion that the new requests filed with the letter of the patent proprietor dated 15 March 2016 (see section VIII), should be admitted into the proceedings. However, the board was also of the opinion that at least one claim of each of these requests infringed the requirements of Article 123(2) EPC. Furthermore, claim 1 of the main request lacked clarity (Article 84 EPC), and claim 1 of auxiliary requests 1 and 2 was held to include undisclosed disclaimers given that they excluded more from the scope of the claims than was disclosed in the document held by the opposition division to be detrimental to novelty under Article 54(3) EPC of the subject-matter of claim 1 of the main request and auxiliary request 1 before them (see section III). The board was also of the preliminary opinion that the mere reference to the "*Sequence Table of the application as filed*" (see section II) as support for claim 1 of auxiliary request 4 was vague and ambiguous and did not enable the board to conclude that the claim complied with the requirements of the EPC.

XI. In reply to the board's communication, appellant II requested the board to consider the admissibility of

the claim requests filed by the patent proprietor earlier in the appeal proceedings.

XII. The patent proprietor submitted, in response to the board's communication, nine further first auxiliary requests, all being further variations of auxiliary request 1 filed earlier (i.e. 1B, 1Ba, 1C, 1Ca, 1D, 1E, 1Ea, 1F, 1Fa), and a new auxiliary request 5. In the latter request, claim 1 was limited - as compared to claim 1 of auxiliary request 4 (see section VI) - to part (j) of the enumerated combinations of VL regions comprising CDR-L1, CDR-L2 and CDR-L3 and VH regions comprising CDR-H1, CDR-H2 and CDR-H3 comprised in the first binding domain of the claimed polypeptide. The main request as well as auxiliary requests 2 and 2A were withdrawn. Three further documents were filed, including a document referred to in the present decision as document D80.

D80: document entitled "Combinations of VH (CDR-Hs) and VH (CDR-Ls)" indicating schematically the particular CDR sequence comprised in the respective VL and VH region of the ten particular antibodies disclosed in the application.

XIII. Appellant III replied to the latest submission of the patent proprietor and questioned the late filing of the variations to auxiliary request 1.

XIV. On 7 March 2019 the patent proprietor indicated in writing that they "*wish*[ed] *to discuss the following claim requests during the upcoming oral proceedings:*

1. New main request (previous auxiliary request 3 as filed 15 June 2015)

2. New auxiliary request 1 (previous auxiliary request 4 as filed 29 October 2015)
3. New auxiliary request 2 (previous auxiliary request 5 as filed 14 January 2019)".

XV. The next day, in response to a written query from the board, the patent proprietor confirmed withdrawing all the claim requests filed earlier and different from the main request and new auxiliary requests 1 (see section VI) and 2 (see section XII) mentioned in the submission of 7 March 2019.

XVI. During the oral proceedings which were held on 12 March 2019, the patent proprietor (hereinafter "respondent") withdrew their appeal and filed two further claim requests, i.e. new auxiliary request AUX1b and new auxiliary request AUX1c. At the end of the oral proceedings, the chair announced the decision of the board.

Claim 1 of new auxiliary request AUX1b combined claims 1 and 4 of the main request (see sections II and XIV) and read:

"1. A polypeptide comprising a first binding domain which is an antibody capable of binding to an epitope of human and Callithrix jacchus, Saguinus oedipus or Saimiri sciureus CD3ε chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NO:2, 4, 6, or 8 and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu, and a second binding domain capable of binding to EGFR, Her2/neu or IgE of a human and/or a non-chimpanzee primate,
wherein the first binding domain comprises a VL region and a VH region selected from the group consisting of:

(a) a VL region as depicted in SEQ ID NO: 17 or 21 and a VH region as depicted in SEQ ID NO: 15 or 19;
(b) a VL region as depicted in SEQ ID NO:35 or 39 and a VH region as depicted in SEQ ID NO:33 or 37;
(c) a VL region as depicted in SEQ ID NO:53 or 57 and a VH region as depicted in SEQ ID NO:51 or 55;
(d) a VL region as depicted in SEQ ID NO:71 or 75 and a VH region as depicted in SEQ ID NO:69 or 73;
(e) a VL region as depicted in SEQ ID NO:89 or 93 and a VH region as depicted in SEQ ID NO:87 or 91 ;
(f) a VL region as depicted in SEQ ID NO:107 or 111 and a VH region as depicted in SEQ ID NO: 105 or 109;
(g) a VL region as depicted in SEQ ID NO: 125 or 129 and a VH region as depicted in SEQ ID NO:123 or 127;
(h) a VL region as depicted in SEQ ID NO: 143 or 147 and a VH region as depicted in SEQ ID NO:141 or 145;
(i) a VL region as depicted in SEQ ID NO: 161 or 165 and a VH region as depicted in SEQ ID NO:159 or 163; and
(j) a VL region as depicted in SEQ ID NO: 179 or 183 and a VH region as depicted in SEQ ID NO: 177 or 181."

Claim 1 of new auxiliary request AUX1c was restricted to embodiments (b), (i) and (j) of claim 1 of auxiliary request 1 (see sections VI and XIV), which were renumbered (a), (b) and (c), respectively.

XVII. The arguments of appellants II and III, in as far as they are relevant for the decision, can be summarised as follows:

Main request - claim 1 - added subject-matter (Article 123(2) EPC)

The claim was for a polypeptide having a first binding domain comprising a VL region comprising one of three specific CDR combinations and a VH region comprising one of ten specific further CDR combinations, and a second binding domain binding to at least three further secondary molecules. The claim therefore covered 90 different bi-specific polypeptides.

Claims 3 and 4 as filed each depended on claim 1 or 2, but were, however, not interdependent. They therefore did not disclose the combination of the VL and VH regions in terms of specific CDR combinations. Also the application as a whole, in particular page 29, line 25 - where it is stated that that the listed VL CDRs are "*particularly preferred*" - to page 30, last line - where it is stated that the listed VH CDRs are "*an alternative embodiment*" - did not disclose the combination as claimed, neither explicitly nor implicitly. Thus, for the skilled person, the claimed subject-matter was not directly and unambiguously derivable from the application because polypeptides with these VL and VH CDR combinations were not disclosed in the application.

The skilled person was aware of the interdependency of light chain and heavy chain CDRs for providing particular binding specificities. Although the application might disclose a number of specific antibodies and a certain redundancy as regards the interdependency of light chain and heavy chain CDRs (see document D80), this could not however be held to mean that necessarily all combinations were binding CD3 as required by the claim. Therefore, the specific anti-

CD3ε chain antibodies disclosed in the application also did not support the VL and VH CDR combinations claimed.

In fact, specific combinations of whole sequences of VL and VH, which were listed on page 31, line 11 to last line as "*more preferably*", were comprised in the first binding domain of the disclosed polypeptides.

Examples 20 to 25 and Tables 4, 5, 6 and 8 of the application merely disclosed some polypeptides having particular combinations of first binding domains binding to the CD3ε chain, referred to as whole sequences of VL and VH, and with one of the second binding domains as listed in the claim, i.e. subsets of possible combinations covered by the claim.

The claim therefore related to added subject-matter (Article 123(2) EPC).

Auxiliary request 1 - claim 1 - added subject-matter (Article 123(2) EPC)

The VL and VH regions of the specifically disclosed antibodies also contained other sequences than the CDRs which define the VL and VH regions in the claim. The wording of the claim, therefore, was an intermediate generalisation of the disclosure in the application which constituted new technical information. Hence, the constructs as now claimed found no basis in the application and thus infringed the requirements of Article 123(2) EPC.

Admission of further auxiliary requests into the appeal proceedings

New auxiliary request AUX1b

The request was only filed during the oral proceedings after the board had given its opinion that claim 1 of the main request and auxiliary request 1 related to added subject-matter; it was not filed in response to the communication of the board in which such an opinion had already been expressed. The request was thus filed very late, and it needed to be assessed whether the request was *prima facie* allowable and contributed to procedural expediency. In fact, the request was another attempt to move the goal posts to overcome concerns and objections which had been known to the respondent much earlier and did not expedite the proceedings.

The amendment had a substantial impact on the assessment of the claimed subject-matter in relation to inventive step as the VL and VH regions were now defined by reference to their whole sequences and no longer by reference to certain CDR combinations contained therein.

If the board were to admit the auxiliary request into the proceedings, then appellant II requested to be allowed to submit an updated version of earlier submitted experimental data as a new document into the proceedings.

New auxiliary request AUX1c

The arguments submitted for not admitting auxiliary request AUX1b equally applied to this request.

The selection in claim 1 of three particular alternative embodiments of claim 1 of auxiliary request 1 could not remedy the fact that this claim constituted an intermediate generalisation of the disclosure of the application and constituted new technical information. Hence, the constructs as now claimed also did not find any basis in the application.

Auxiliary request 2

The request was not filed with the respondent's reply to the appellants' grounds of appeal but was filed after the board had issued a communication. It was thus late filed as it could have been filed earlier.

Claim 1 of this request still referred to the VL and VH regions of the first binding domain as defined by the CDR combinations and did not define these by the whole VL and VH region sequence. The claim therefore did not overcome the objection that claim 1 of auxiliary request 1 related to added subject-matter.

XVIII. The arguments of the respondent, in as far as they are relevant for the decision, can be summarised as follows:

Main request - claim 1 - added subject-matter (Article 123(2) EPC)

By referring to original claim 1, claims 3 and 4 of the application disclosed an embodiment in which the binding molecules of the invention comprised the VL region CDR combinations listed in claim 3 together with the VH region CDR combinations listed in claim 4. It was common practice to combine the subject-matter of claims which referred back to the same claim.

Further specific disclosure of the subject-matter of the claim was based on the first paragraph on page 30, lines 1 to 7, which directly and logically linked the aforementioned CDRs of the VL region with the subsequent CDRs of the VH region.

The application disclosed ten specific antibodies (see e.g. Figure 3) as having specific combinations of CDRs of the VL region and CDRs of the VH region. The summary data provided in document D80, which were all obtained from the application, demonstrated ten partly redundant combinations of VL CDRs and VH CDRs (the VL CDR combination of part (a) of the claim was disclosed to combine with six VH CDR combinations of the claim, and the VL CDR combination of each of parts (b) and (c) of the claim was disclosed to combine with two other VH CDR combinations of the claim). The application therefore provided explicit indications that all combinations were envisaged by the inventors and provided no indication that particular VL and VH CDR combinations could not be combined to provide CD3ε chain binding.

Examples 20 to 25 of the application, in particular the tables referred to therein, additionally disclosed bi-specific molecules containing the second binding domains referred to in the claim.

The application hence provided explicit indicators that all the combinations of the claim were desired embodiments and that they were not surprising to the skilled person.

Auxiliary request 1 - claim 1 - added subject-matter (Article 123(2) EPC)

As the claim was now restricted to the particular combinations of CDRs of the specific VL and VH regions of the antibodies which were explicitly disclosed in the application, and as these were demonstrated in examples 20 to 25 to be combinable with the indicated second binding domain, the same arguments as for the main request applied to this claim.

Admission of further auxiliary requests into the appeal proceedings

New auxiliary request AUX1b

It came as a surprise that the board had decided that claim 1 of auxiliary request 1 related to added subject-matter.

Claim 1 was now restricted to subject-matter which was disclosed in original claim 7 of the application, i.e. to the particular combinations of the whole VL and VH regions of the ten antibodies specifically disclosed in the application, and thus found a basis in the application. Claim 1 of the request corresponded to claim 4 of the main request and had thus already been on file.

The amendments to the claim were not expected to have an impact on inventive step. The latter resided in fact in the identification and selection of the particular CD3 epitope, which had not been changed by the amendments.

New auxiliary request AUX1c

Claim 1 of this request was now restricted to three particular embodiments of claim 1 of the auxiliary request 1. These specific embodiments found particular basis in examples 20 to 25 of the application, with reference to the constructs disclosed therein.

The same arguments submitted for admitting auxiliary request AUX1b also applied to this request.

Auxiliary request 2

The request was filed in direct response to the board's communications and constituted a bona fide attempt to take the board's concerns regarding the claims of auxiliary request 1 into account. Claim 1 was now specifically limited to the disclosed antibody I2C.

XIX. The final requests of the parties were:

Appellants I and II requested that the decision under appeal be set aside and the patent be revoked.

The respondent requested that the appeals of the opponents be dismissed (main request) or, alternatively, that the decision under appeal be set aside and the patent be maintained on the basis of the claims of auxiliary request 1 (filed as auxiliary request 4 with a letter dated 29 October 2015) or, alternatively, on the basis of the claims of auxiliary requests AUX1b and AUX1c (filed during the oral proceedings), or, further alternatively, on the basis of auxiliary request 2 (filed as auxiliary request 5 with a letter dated 14 January 2019).

Reasons for the Decision

1. The appeals of the opponents are admissible.

Main request - claim 1 - added subject-matter (Article 123(2) EPC)

2. In preparation for the oral proceedings, the board had expressed in a communication (see section X) its preliminary opinion that the claim infringed the requirements of Article 123(2) EPC. After hearing the parties during the oral proceedings, the board remained of the same opinion.

3. The so-called "*gold standard*" developed in the case law of the boards of appeal is that any amendment to, *inter alia*, a claim can, irrespective of the context of the amendment, only be made within the limits of what the skilled person would derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing from the whole of the application (see the decisions of the Enlarged Board of Appeal G 3/89, OJ 1993, 117; G 11/91, OJ 1993, 125; and G 2/10, OJ 2012, 376).

4. The respondent has not submitted that the claimed subject-matter was disclosed verbatim in the application but developed three lines of argument in support of its implicit disclosure in the application as a whole.

5. In a first line of argument the respondent referred to claim 1 and claims 3 and 4 of the application (see section I) and submitted that these claims disclosed the binding molecules of the invention comprising the VL region CDR combinations of claim 3 together with,

and in combination with, the VH region CDR combinations of claim 4 because the subject-matter of claims which refer back to the same claim could be combined.

6. The board notes that claims 3 and 4 of the application as filed each independently refer to claim 1 or claim 2, respectively, and are thus not worded as being inter-dependent. Accordingly, whereas this claim constellation may disclose a first binding domain, either comprising a VL region comprising a CDR combination selected from the list in claim 3 (three CDR combinations), or comprising a VH region comprising a CDR combination selected from the list in claim 4 (ten CDR combinations), it does not, however, directly and unambiguously disclose such first binding domains combining VL and VH regions comprising CDRs from both lists in claims 3 and 4, let alone a combination of each and every of the potential 30 combinations of VL region CDR combinations and VH region CDR combinations.

7. Furthermore, the board can not agree with the respondent in this context - and has seen no evidence for holding so - that in this claim constellation a combination of the dependent claims constitutes "common" practice of claim construction. Therefore, the board concludes that the claims of the application fail to provide any basis for the subject-matter of the claim.

8. In a second line of argument the respondent referred to the disclosure of the application, in particular to page 29, line 25 to page 30, last line. These passages read as follows:

"*It is particularly preferred for the polypeptide of the invention that the first binding domain capable of*

binding to an epitope of human and non-chimpanzee primate CD3ε chain comprises a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from: (a) (...); (b) (...); and (c) (...).

The variable regions, i.e. the variable light chain ("L" of "VL") and the variable heavy chain ("H" or "VH") are understood in the art to provide the binding domain of an antibody. This variable regions harbor the complementary determining regions.
The term "complementary determining region" (CDR) is well known in the art to dictate the antigen specificity of an antibody. The term "CDR-L" or "L CDR" refers to CDRs in the VL, whereas the term "CDR-H" or "H CDR" refers to the CDRs in the VH.

In an alternatively preferred embodiment of the polypeptide of the invention the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3ε chain comprises a VH region comprising CDR-H 1, CDR-H2 and CDR H3 selected from: (a) (...); (....); and (j) (...)." (emphasis added by the board. Note: "(...)" is the respective text of the corresponding part in the claim).

9. The second paragraph of the citation (which corresponds to the first paragraph on page 30, lines 1 to 7, of the application) concerns a general definition which has no direct link with the polypeptides referred to in the preceding or following paragraph. The board is not persuaded, therefore, that this paragraph links the aforementioned CDRs of the VL region with the subsequently mentioned CDRs of the VH region, as contended by the respondent.

10. The board furthermore notes that the paragraph referring to the three specific VL region CDR combinations and the paragraph referring to the ten specific VH region CDR combinations states that these are "*particularly preferred for the polypeptide of the invention*" and "*an alternatively preferred embodiment of the polypeptide of the invention*", respectively. Therefore, similar to the situation for the dependent claims above (see point 6), these paragraphs of the description of the application do not directly and unambiguously disclose a combination of both lists, and certainly not a combination of each and every one of the potential 30 combinations of VL region CDR combinations and VH region CDR combinations. Accordingly, this disclosure can also not support the wording of the claim for the purpose of the assessment under Article 123(2) EPC.

11. In a third line of argument the respondent pointed out the ten identified single chain antibodies, disclosed and referred to in the application (see e.g. Figure 3, document D80 and the "sequence table", spanning pages 115 to 233 of the application) as having specific combinations of CDR combinations of the VL region and specific combinations of CDR combinations of the VH region. The respondent submitted that the summary data provided in document D80, which were entirely obtained from the application, demonstrated ten, partly redundant, combinations of VL CDRs and VH CDRs. The application therefore provided explicit indicators that all VL and VH CDR combinations were desired embodiments, which were not surprising to the skilled person, and there was no indication that particular VL and VH CDR combinations could not be combined to provide CD3ε chain binding. Hence, any combination of the three VL region CDR combinations with any of the

ten VH region CDR combinations was envisaged by the inventors.

12. The board agrees with the respondent that the data summary in document D80 demonstrates that the specific single chain antibodies disclosed in the application support a certain redundancy as regards the interdependency of light chain and heavy chain CDRs. However, the board agrees with the appellants that this does not necessarily constitute a direct and unambiguous disclosure of all combinations of CDR combinations of the VL region and CDR combinations of the VH region as referred to in the claim and thus cannot provide any basis for the claim. Accordingly, this line of argument of the respondent also fails.

13. In view of the above considerations the board concludes that claim 1 does not meet the requirements of Article 123(2) EPC.

Auxiliary request 1 - claim 1 - added subject-matter (Article 123(2) EPC)

14. The claim now explicitly recites ten particular combinations of VL and VH region CDR combinations which correspond to the ten specifically identified antibodies of the application.

15. The board notes, however, that the specifically disclosed antibodies comprise particular whole VL and VH regions, i.e. which also contain further particular sequences in addition to the CDRs now defined in the claim. Indeed, on page 31, line 11 to last line, the application refers to particularly combined whole VL and VH regions of the disclosed antibodies as opposed to particular VL and VH regions solely defined by the

sequences of their CDR combinations. Therefore, these disclosures cannot be accepted as appropriate basis for polypeptides, comprising a first and a second binding domain, the first one being defined merely by reference to the CDRs of their VL and VH regions.

16. Similarly, examples 20 to 25 and the tables in the application relating thereto disclose some polypeptides which, albeit comprising a first and a second binding domain, again have particular combinations of first binding domains binding to the CD3ε chain, defined by the sequence of their whole VL and VH region.

17. In view of the above considerations, the board can concur with the appellants that the wording of the claim constitutes a so-called intermediate generalisation of the disclosure of the application, which in the present case constitutes new technical information not disclosed in the application. Hence, the constructs as now claimed in claim 1 find no basis in the application and constitute added subject-matter (Article 123(2) EPC).

Admission of further auxiliary requests into the appeal proceedings

New auxiliary request AUX1b

18. The request was filed during the final stages of the oral proceedings after the board had expressed its opinion that claim 1 of auxiliary request 1 related to added subject-matter, and was ranked by the respondent before auxiliary request 2, which had been filed earlier in the proceedings.

19. Pursuant to Article 13(1) RPBA, the board shall exercise its discretion to admit such a request into the appeal proceedings in view of, *inter alia*, the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy.

20. The board notes that prior to filing the request at this late stage of the proceedings, the respondent had already afforded themselves a number of alternative but consecutive attempts to overcome concerns of the appellants and the board regarding the requirements of Article 123(2) EPC. Reference can be made, for example, to auxiliary requests 1 and 2, which were still pending when request AUX1b was filed and also to a number of requests submitted earlier by the respondent but which have since been withdrawn. The board therefore agrees with the appellants that submitting the request amounts to yet another consecutive attempt to "*move the goal posts*" to overcome concerns and objections which had been known to the respondent much earlier and that doing so would not expedite the proceedings.

21. In addition, the board considers that, as also witnessed by the expressed wish of appellant II to be allowed to submit new evidence in case of admission of this claim request, the amendment to claim 1 would appear to - at least potentially - have a substantial impact on the assessment of inventive step of the claimed subject-matter.

22. In view of the above considerations, the board, exercising its discretion pursuant to Article 13(1) RPBA, decided not to admit this request into the appeal proceedings.

New auxiliary request AUX1c

23. This request was filed even later, during the final stages of the oral proceedings, i.e. only after the board had expressed its opinion that claim 1 of auxiliary request 1b related to added subject-matter. It was ranked by the respondent after auxiliary request AUX1b, but yet again before auxiliary request 2, which had been filed earlier in the proceedings. Therefore also in the context of the assessment whether to admit this auxiliary request into the proceedings, the board notes first that the request constitutes a further consecutive attempt to "*move the goal posts*" to overcome concerns and objections which had been known to the respondent earlier.

24. In the context of claim 1 of this request, however, the board also refers to points 14 to 17 above, where the board expressed the conclusion that claim 1 of auxiliary request 1 constituted a so-called intermediate generalisation of the disclosure of the application and constituted new technical information which was not disclosed in the application.

25. The board agrees with the appellants that the restriction in claim 1 of auxiliary request AUX1c to three particular alternative embodiments of claim 1 of auxiliary request 1 cannot remedy the fact that each embodiment of this claim constitutes an intermediate generalisation of the disclosure of the application and constitutes new technical information. Hence, *prima facie*, the particular constructs to which claim 1 is now restricted also constitute technical information that does not find any basis in the application contrary to the requirements of Article 123(2) EPC.

Consequently, auxiliary request AUX1c was not of a nature that could expedite the proceedings either.

26. In view of the above considerations the board, exercising its discretion pursuant to Article 13(1) RPBA, decided not to admit this request into the appeal proceedings.

Auxiliary request 2

27. The request was filed by the respondent as auxiliary request 5 in reaction to the board's communication, setting out its appreciation of certain substantive and legal matters concerning the appeal (see section XII) and not, as could reasonably be expected, already earlier with the respondent's reply to the respective statements of grounds of appeal of the appellants. The board therefore concurs with the appellants that the request was filed late and hence constitutes an amendment to the respondent's case. Consequently, it is at the board's discretion to admit it into the proceedings and consider it (Article 13(1) RPBA).

28. The respondent justified the filing of the request at this late point of the proceedings as being a direct response to the communication of the board stating, *inter alia*, that auxiliary request 2 could meet the concerns of the board regarding added subject-matter in the claims of auxiliary request 1 (formerly filed as auxiliary request 4 with the respondent's reply to the statements of grounds of appeal of the appellants; see point VI) and constituted a bona fide attempt to overcome such concerns.

29. When filing this claim request, the respondent had omitted to indicate in writing why the claims of this

request should be considered to remedy the deficiencies identified by (the appellants and) the board in relation to auxiliary request 1 (formerly auxiliary request 4), and instead submitted that "*The new AR5 basically corresponds to the AR4 filed with our letter dated 15 March 2016, now limiting the VH and VL to the VH and VL of the antibody IC2. In sum, filing of AR5 only further limits the subject matter that has already been presented in AR4. As submitted earlier, AR4 complies with the requirements of Art.123(2) EPC, (...). Since a further limitation of subject matter does not infringe any of these provisions, also the subject matter of AR5 complies with these requirements.*"

30. The board notes first that this submission does not allow the conclusion that the request was filed by the respondent to remedy any of the concerns from the board's side in relation to added subject-matter; and second that, the submission misrepresents the inserted amendments. Indeed, as was correctly submitted by the appellants, claim 1 of this request is, although now limited to a single combination of a VL and a VH regions, i.e. derivable from antibody I2C, still referring only to the particular CDR variations of these regions and not to the VL and VH regions as a whole (see points 13 to 15 above). Accordingly, *prima facie*, the claim request cannot overcome the deficiencies noted for a higher ranking and earlier filed request.

31. In view of the above considerations, the board, exercising its discretion pursuant to Article 13(1) RPBA, decided not to admit this request into the appeal proceedings.

Conclusion

32. In view of the above findings, the board notes that no allowable claim request is pending in these appeal proceedings. Accordingly, the patent is to be revoked.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chair:

S. Lichtenvort G. Alt

Decision electronically authenticated