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Datasheet for the decision of 10 March 2023

Case Number: T 1128/19 - 3.3.04

Application Number: 16167900.6

Publication Number: 3106468

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Language of the proceedings: EN

Title of invention:
Cross-Species-Specific PSMAXCD3 Bispecific Single Chain Antibody

Applicant:
Amgen Research (Munich) GmbH

Headword:
Bispecific Single Chain Antibody/AMGEN

Relevant legal provisions:
EPC Art. 84, 97(2), 125
RPBA Art. 12(4)

Keyword:
Divisional application - double patenting (yes)
Claims - clarity - auxiliary request 4 (no)

Decisions cited:
G 0004/19

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Beschwerdekammern

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Case Number: T 1128/19 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 10 March 2023

Appellant: (Applicant)	Amgen Research (Munich) GmbH Staffelseestrasse 2 81477 München (DE)
Representative:	Schiweck Weinzierl Koch Patentanwälte Partnerschaft mbB Ganghoferstraße 68 B 80339 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 4 December 2018 refusing European patent application No. 16167900.6 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	A. Chakravarty
	L. Bühler

Summary of Facts and Submissions

I. The applicant (appellant) filed an appeal against the decision of the examining division to refuse European patent application No. 16 167 900.6 (the application). The application is a divisional application of earlier application EP 09 783 664.7, published as EP 2 356 153, which was subsequently granted (the parent patent).

II. In the decision under appeal, the examining division considered a main and four auxiliary requests. It held that the main and auxiliary requests 1 to 3 were not allowable under Article 97(2) EPC together with Article 125 EPC, since they were in contravention of the principle of prohibition of double patenting and that auxiliary request 4 was not allowable because claim 1 lacked clarity (Article 84 EPC).

III. With the statement of grounds of appeal, the appellant maintained the main request and auxiliary requests 1 to 4 considered by the examining division and filed sets of claims of MRa and AR2a.

IV. Claims 1 to 4 of the parent patent as granted read:

"1. A bispecific single chain antibody molecule comprising a first binding domain
which specifically binds to an epitope of human and Callithrix jacchus, Saguinus oedipus or Saimiri sciureus CD3ε (epsilon) chain,
wherein said epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, or 8,
and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu,

and a second binding domain binding to prostate-specific membrane antigen (PSMA).

2. The bispecific single chain antibody molecule according to claim 1, 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.

3. The bispecific single chain antibody molecule according to claim 1 or 2, wherein the first binding domain 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.

4. The bispecific single chain antibody molecule according to any one of claims 1 to 3, wherein the second binding domain is capable of binding to human PSMA and/or a non-human primate PSMA".

Claim 5 part (aa) reads:

"5. The bispecific single chain antibody molecule according to claim 4, wherein the bispecific single chain antibody molecule comprises a group of the following sequences as CDR H1, CDR H2, CDR H3, CDR L1, CDR L2 and CDR L3 in the second binding domain selected from:
..
aa) CDR H1-3 of SEQ ID NO: 806 - 808 and CDR L1-3 of SEQ ID NO: 811 - 813;"

Claim 7 reads:

"7. The bispecific single chain antibody molecule according to claim 6, wherein the bispecific single chain antibody molecule comprises a sequence selected from:
(a) an amino acid sequence as depicted in any of SEQ ID NOs: 399, 413, 427, 441, 455, 469, 483, 497, 511, 525, 539, 553, 567, 581, 595, 609, 623, 637, 651, 665, 679, 693, 707, 721, 734, 799, 817, 863, 849, 835, 785, 899, 935, 1017, 1031, 917, 1003, 953, 971 or 989;
(b) an amino acid sequence encoded by a nucleic acid sequence as depicted in any of SEQ ID NOs: 400, 414, 428, 442, 456, 470, 484, 498, 512, 526, 540, 554, 568, 582, 596, 610, 624, 638, 652, 666, 680, 694, 708, 736 735, 800, 818, 864, 850, 836, 786, 882, 900, 936, 1018, 1032, 918, 1004, 954, 972, 990, 804, 822, 868, 886, 904, 940, 922, 958 or 976; and
(c) an amino acid sequence at least 90 % identical, more preferred at least 95 % identical, most preferred at least 96 % identical to the amino acid sequence of (a) or (b)".

V. Claim 1 of the main request reads:

"A bispecific single chain antibody molecule comprising a first binding domain which is an antigen-interaction site, which specifically binds to an epitope of human and Callithrix jacchus, Saguinus oedipus or Saimiri sciureus CD3ε (epsilon) chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, or 8, and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu, and a second binding domain binding to prostate specific membrane antigen (PSMA),

wherein the second binding domain is capable of binding to human PSMA and/or a non-human primate PSMA,

wherein the bispecific single chain antibody molecule comprises a group of the following sequences as CDR H1, CDR H2, CDR H3, CDR L1, CDR L2 and CDR L3 in the second binding domain selected from: aa) CDR H1-3 of SEQ ID NO: 806-808 and CDR L1-3 of SEQ ID NO: 811-813".

Claim 1 of auxiliary requests 1 is identical to claim 1 of the main request.

Claim 1 of auxiliary request 2 reads:

"1. A bispecific single chain antibody molecule comprising a first binding domain which is an antigen-interaction site, which specifically binds to an epitope of human and Callithrix jacchus, Saguinus oedipus or Saimiri sciureus CD3ε (epsilon) chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, or 8, and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu, and a second binding domain binding to prostate-specific membrane antigen (PSMA), 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;

wherein the first binding domain comprises a VH region comprising CDR-H 1, CDRH2 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; and

wherein the second binding domain is capable of binding to human PSMA and/or a non-human primate PSMA,

wherein the bispecific single chain antibody molecule comprises a group of the following sequences as CDR H1, CDR H2, CDR H3, CDR L 1, CDR L2 and CDR L3 in the second binding domain selected from:
aa) CDR H1-3 of SEQ ID NO: 806-808 and CDR L1-3 of SEQ ID NO: 811 -813".

Claim 1 of auxiliary request 3 reads:

"1. A bispecific single chain antibody molecule comprising a first binding domain which is an antigen-interaction site, which specifically binds to an epitope of human and Callithrix jacchus, Saguinus oedipus or Saimiri sciureus CD3ε (epsilon) chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, or 8, and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu, and a second binding domain binding to prostate-specific membrane antigen (PSMA), wherein the bispecific single chain antibody molecule comprises a sequence selected from:

(a) an amino acid sequence as depicted in any of SEQ ID NOs: 817;
(b) an amino acid sequence encoded by a nucleic acid sequence as depicted in any of SEQ ID NOs: 818; and
(c) an amino acid sequence at least 90 % identical, more preferred at least 95 % identical, most preferred at least 96 % identical to the amino acid sequence of (a) or (b)".

Claim 1 of auxiliary request 4 differs from claim 1 of the main request in that in includes the additional

feature "for use in the preclinical eva[l]uation of safety, activity and/or pharmacokinetic profile of these binding domains in primates and for use as drugs in humans.

MRa differs from the claim 1 of the main request in that in claim 3, the dependency is limited to claim 1 only.

Claim 1 of AR2a differs from claim 1 of auxiliary request 2 in that the VL-CDRs and VH-CDRs are present as "or" alternatives.

VI. The arguments of the appellant relating to the main request and auxiliary requests 1 to 3 fell into two categories. The first was that the EPC contained no legal basis, either explicitly nor implicitly by way of reference to national law (Article 125 EPC) for a prohibition of double patenting. In its submissions the appellant proposed questions to be referred to the Enlarged Board of Appeal on this issue.

The second was that the subject-matter of claim 1 of the main request and granted claim 1 of the parent were not identical because claim 1 of the main request was a narrower selection from the subject-matter of granted claim 1 of the parent patent.

Specifically, claim 1 of the main request defined the first binding domain to be an "antigen-interaction site" which was a prototypic wording used to define an antibody. Hence, the first binding domain of claim 1 of the main request was an antibody, whereas the first binding domain of granted claim 1 was not yet defined as an antibody. Accordingly, the scope of claim 1 of

the main request was narrower than that of claims of the parent patent.

In relation to auxiliary request 4, the appellant contended that claim 1 of auxiliary request 4 encompassed only *in vivo* uses. As supported by the FDA's homepage on drug development, preclinical research as mentioned in the claim included both *in vivo* and *in vitro* research. However, the preclinical evaluation of safety, activity and/or pharmacokinetic profile of the binding domains in primates (emphasis added by the board) mentioned in the claim referred only to *in vivo* methods, due the inclusion of the phrase "in primates".

VII. The board issued a communication pursuant to Article 15(1) RPBA setting out its preliminary opinion on the appeal. In this communication it informed the appellant of its preliminary opinion that the examining division's decision to refuse the main and auxiliary requests 1 to 3 for reasons of double patenting under Articles 97(2) and 125 EPC was correct in view of the Enlarged Board of Appeal's decision G 4/19 and that it agreed with the examining division that claim 1 of auxiliary request 4 lacked clarity. It also informed the appellant that it was inclined not to admit the claim requests MRa and AR2a, under the provisions of Article 12(4) RPBA 2007.

VIII. The appellant replied to the board's communication by letter including the single sentence "*We herewith withdraw our request for oral proceedings and request for a refund of the official appeal fee*". The board subsequently cancelled the oral proceedings.

IX. The appellant's requests as understood by the board are as follows:

- that the decision under appeal should be set aside and the case be remitted to the examining division with the order to grant a patent on the basis of the set of claims of the main request;
- alternatively, that the decision under appeal be set aside and the case be remitted to the examining division with the order to grant a patent on the basis of the set claims of one of auxiliary requests 1 to 4 or auxiliary requests MRa and AR2a. Alternatively, the questions proposed in the statement of grounds of appeal be referred to the Enlarged Board of Appeal (EBA). If none of these requests were allowable, the decision under appeal should be set aside and the case be remitted to the first instance for further prosecution;
- that the appeal fee be refunded.

Reasons for the Decision

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

Double patenting

Main request and auxiliary requests 1 to 3 - claim 1

2. In the decision under appeal, the examining division held that the main request and auxiliary requests 1 to 3 were not allowable under Article 97(2) EPC

together with Article 125 EPC, since they were in contravention of the principle of prohibition of double patenting with respect to the patent, EP 2 356 153, granted on the parent application, EP 09 783 664.7.

3. In its appeal, the appellant challenged the legal basis in the EPC for the principle of prohibition of double patenting, either explicitly or implicitly by way of reference to national law (Article 125 EPC) for a prohibition of double patenting. In view of this the appellant proposed questions to be referred to the Enlarged Board of Appeal in this issue. However, since the filing of the appeal, the Enlarged Board of Appeal (EPA) issued decision G 4/19, which renders the questions proposed by the appellant moot. In this decision, the EBA held that -

"*1. A European patent application can be refused under Articles 97(2) and 125 EPC if it claims the same subject-matter as a European patent which has been granted to the same applicant and does not form part of the state of the art pursuant to Article 54(2) and (3) EPC.*
2. The application can be refused on that legal basis, irrespective of whether it a) was filed on the same date as, or
b) is an earlier application or a divisional application (Article 76(1) EPC) in respect of, or
c) claims the same priority (Article 88 EPC) as the European patent application leading to the European patent already granted".

4. As noted in Section I. above, European patent EP 2 356 153 is the parent of the application under appeal. Amgen Research (Munich) GmbH is the proprietor of both the granted parent and of the (divisional)

application under appeal. Thus, the parent patent was granted to the same applicant as the applicant of the application under appeal.

5. To decide if the application under appeal was correctly refused because it contravenes the principle of prohibition of double patenting, it must further be determined whether "*it claims the same subject-matter as a European patent which has been granted to the same applicant*".

6. As noted in the decision under appeal (see point 15.1), claim 1 of the main request is a combination of claims 1 and 4 and a single embodiment (aa) from claim 5 of the granted patent. The wording of claim 1 of the application under appeal differs from that of the above mentioned claims of the patent in that it specifies that the first binding domain "is an antigen-interaction site".

7. As also noted in the decision under appeal, the subject-matter of claim 1 of the main request is an explicit alternative defined in the claims of the parent patent, being a combination the claim 1 and 4 and embodiment (aa) of claim 5 as granted.

8. The appellant was of the view that claim 1 of the main request relates to an antibody whereas claim 1 of the granted parent is not defined to be an antibody. In other words, the subject-matter of claim 1 was alleged to be a narrower selection from the subject-matter of claim 1 of the parent patent.

9. This argument is not convincing because the claim is for "a bispecific single chain antibody molecule". There is no technical reason to differentiate between

an antibody and an antibody molecule, since it goes without saying that an antibody is a molecule.

10. The main request and auxiliary requests 1 are not allowable in view of the prohibition of double patenting because they claim the same subject-matter as claimed in the parent patent.

Auxiliary request 2 - claim 1

11. As noted in the decision under appeal, claim 1 of auxiliary request 2 differs from claim 1 of the main request in that the subject-matter (and wording) of granted dependent claims 2 and 3 have been incorporated into claim 1. This subject-matter was therefore also an explicit embodiment of the granted claims.

12. Auxiliary requests 2 is not allowable in view of the prohibition of double patenting because it too claims the same subject-matter as claimed in the parent patent.

Auxiliary request 3 - claim 1

13. Claim 1 of auxiliary request 3 differs from claim 1 of the parent patent in that embodiments from dependent claim 7 have been incorporated. In addition, as was the case for claim 1 of the main request, the wording "which is an antigen-interaction site" has been added. As was the case for claim 1 of the higher ranking claim requests, it claims the same subject-matter as claimed in the parent patent.

14. Auxiliary request 3 is therefore not allowable because it violates the principle of prohibition of double patenting.

Auxiliary request 4 - claim 1

Clarity (Article 84 EPC)

15. The examining division held that the claim lacked clarity because the feature "for preclinical evaluation of safety, activity and or pharmacokinetic profile of these binding domains in primates and for use as drugs in humans" encompassed both *in vitro* and *in vivo* uses meaning that the category of the claim was not clear. Moreover, they considered that this wording also creates an ambiguity and hence a lack of clarity regarding the meaning of the term "for" in the claim.

16. The appellant contends that claim 1 of auxiliary request 4 encompasses only *in vivo* uses. As supported by the FDA's homepage on drug development, the preclinical research as mentioned in the claim included both *in vivo* and *in vitro* research. However, the preclinical evaluation of safety, activity and/or pharmacokinetic profile of the binding domains in primates (emphasis added by the board) mentioned in the claim referred only to *in vivo* methods, due the inclusion of the phrase "in primates".

17. The board is not convinced by this argument. The phrase "for use in the preclinical evaluation of safety, activity and/or pharmacokinetic profile of these binding domains in primates" is ambiguous - it can be interpreted as meaning that the claimed antibody molecule is for use in *in vitro* methods aimed at preclinical evaluation of safety, activity and/or pharmacokinetic profile of the binding domains where the ultimate patient is a primate. Alternatively, it can be understood as relating to *in vivo* methods done in primates.

18. In view of the above considerations, the board concludes that the examining division was right to hold that claim 1 lacks clarity.

Admission of auxiliary requests MRa and AR2a (Article 12(4) RPBA 2007)

19. These claim requests were filed with the statement of grounds of appeal. According to the appellant, they contain amendments done with the aim of addressing potential issues under Article 123(2) EPC.

20. The examining division did not deal with Article 123(2) EPC in the decision under appeal nor had it raised objections under it in the communication annexed to the summons to oral proceedings. Thus, the amendments made do not represent a response to new issues arising from the decision under appeal. The appellant has also not supplied any reasons why these auxiliary requests were filed only in the appeal proceedings. In view of this, the board concludes that the auxiliary requests could and should have been filed in the proceedings before the examining division. They are therefore not admitted into the proceedings under Article 12(4) RPBA 2007.

21. As no allowable claim request is on file, the appeal must be dismissed.

Reimbursement of appeal fees (Rule 103(4)(c) EPC)

22. Since the request for oral proceedings was withdrawn within one month of notification of the communication issued by the Board of Appeal in preparation for the oral proceedings and no oral proceedings took place, the appeal fee is to be reimbursed at 25%.

Order

For these reasons it is decided that:

The appeal is dismissed.

The appeal fee is to be reimbursed at 25%.

The Registrar: The Chairwoman:

I. Aperribay M. Pregetter

Decision electronically authenticated