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Datasheet for the decision of 21 July 2015

Case Number: T 2048/10 - 3.3.08

Application Number: 01941978.7

Publication Number: 1292619

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Language of the proceedings: EN

Title of invention:
B7-RELATED NUCLEIC ACIDS AND POLYPEPTIDES AND THEIR USES FOR IMMUNOMODULATION

Patent Proprietor:
Bristol-Myers Squibb Company

Opponents:
MacroGenics, Inc.
CABINET CAMUS LEBKIRI

Headword:
B7-H3 splice variants, antagonist antibodies/BRISTOL-MYERS SQUIBB

Relevant legal provisions:
EPC Art. 123(2), 114(2), 54
RPBA Art. 13(1), 12(4), 12(2)

Keyword:
Main Request - admissibility (yes); added subject-matter (no)
Remittal to first instance for further prosecution (yes)

This datasheet is not part of the Decision.
It can be changed at any time and without notice.

Decisions cited:
T 0301/87, T 0189/01, T 1120/01, T 0027/04, T 1069/08, T 0018/09, T 1621/09

Catchword:

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Case Number: T 2048/10 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 21 July 2015

Appellant: (Opponent 1)	MacroGenics, Inc. 1500 East Gude Drive Rockville, MD 20850 (US)
Representative:	Wilkinson, Marc George Avidity IP Broers Building Hauser Forum 21 JJ Thomson Ave Cambridge CB3 0FA (GB)
Respondent: (Patent Proprietor)	Bristol-Myers Squibb Company Route 206 and Province Line Road Princeton, NJ 08543 (US)
Representative:	Vossius & Partner Patentanwälte Rechtsanwälte mbB Siebertstrasse 3 81675 München (DE)
Party as of right: (Opponent 2)	CABINET CAMUS LEBKIRI 25 Rue de Maubeuge 75009 Paris (FR)

Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 22 July 2010 concerning maintenance of the European Patent No. 1292619 in amended form.**

Composition of the Board:

Chairman M. Wieser
Members: P. Julià
J. Geschwind

Summary of Facts and Submissions

I. European patent no. 1 292 619, based on European patent application 01 941 978.7 and filed as International patent application PCT/US2001/018257 (published as WO 2001/094413; hereinafter "*the application as filed*"), was opposed by two parties on the grounds set forth in Articles 100(a), (b) and (c) EPC. The opposition division considered the Main Request and Auxiliary Request 1 to contravene Article 54 EPC. Auxiliary Request 2 was considered to fulfil the requirements of the EPC. All requests were filed on 30 June 2010 at the oral proceedings before the opposition division.

II. An appeal was lodged by opponent 01 (appellant). With the statement of Grounds of Appeal, the appellant filed new documentary evidence (documents D52-D65).

III. In reply thereto, the patentee (respondent) filed new Auxiliary Requests I to XV and documentary evidence (D66-D75). The respondent requested that documents D58 and D59 were not admitted into the appeal proceedings and, if they were admitted, that the case be remitted to the department of first instance for further prosecution.

IV. With letter of 19 April 2011, the appellant filed further submissions ("*Declaration of Professor Christopher Rudd*" and annexes; document D76).

V. With letter of 21 July 2011, the respondent requested the board not to consider these new submissions.

VI. With letter of 16 August 2011, the appellant submitted further arguments to admit documents D58/D59 and D76 into the appeal proceedings.

VII. No submissions were filed by opponent 02 (party as of right).

VIII. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) annexed to Summons to oral proceedings, the parties were informed of the board's preliminary, non-binding opinion on the issues of the case.

IX. In reply to this communication, the respondent maintained its Main Request (set of claims upheld by the opposition division) and filed new Auxiliary Requests I to VI to replace all previous Auxiliary Requests.

X. The appellant did not reply to the board's communication.

XI. With letter dated 11 May 2015, opponent 02 informed the board that it would not be represented at the oral proceedings.

XII. Oral proceedings were held on 21 July 2015. During these proceedings, the respondent withdrew its Main Request and made Auxiliary Request I its new Main Request.

XIII. Claims 1 and 4-5 of the **Main Request** read as follows:

"1. A nucleic acid molecule or a nucleotide sequence selected from the group consisting of:

(a) a nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 11 or 13;

(b) a nucleic acid molecule encoding the amino acid sequence consisting of amino acids 1 to 465 of SEQ ID NO: 7;

(c) a nucleic acid molecule encoding a B7-related polypeptide comprising the amino acid sequence of SEQ ID NO: 11 which is altered to incorporate one polymorphism in the amino acid sequence;

(d) a nucleic acid molecule encoding a B7-related polypeptide comprising the amino acid sequence of SEQ ID NO: 13 which is altered to incorporate one polymorphism in the amino acid sequence;

(e) a nucleotide sequence comprising polynucleotides encoding amino acids 1 to 698 of SEQ ID NO: 9;

(f) a nucleotide sequence comprising polynucleotides encoding amino acids 2 to 698 of SEQ ID NO: 9;

(g) a nucleotide sequence comprising polynucleotides encoding amino acids 69 to 698 of SEQ ID NO: 9;

(h) a nucleotide sequence comprising nucleotides 1 to 2094 of SEQ ID NO: 8;

(i) a nucleotide sequence comprising nucleotides 4 to 2094 of SEQ ID NO: 8;

(j) a nucleotide sequence comprising nucleotides 205 to 2094 of SEQ ID NO: 8;

(k) a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 6, 10, 12 or PTA-1993;

(l) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence encoded by the DNA contained in PTA-1987 or PTA-1988;

(m) nucleic acid molecule which is complementary to the sequence of the nucleic acid molecule according to any one of (a) to (k); and

(n) a nucleotide sequence encoding an extracellular domain of an amino acid sequence selected from the group consisting of SEQ ID NO: 7, 11 and 13 and a nucleotide sequence encoding an Fc domain of immunoglobulin G.

4. A polypeptide encoded by the nucleic acid molecule according to (a) to (i), (l) and (n) of claim 1 or by the nucleic acid molecule of SEQ ID NO: 10 or 12.

5. An antibody that binds to the polypeptide according to claim 4, wherein said antibody blocks the activity of immune or inflammatory response cells."

Claims 2 and 3 are directed to a vector and host cell comprising the nucleic acid of claim 1. Claim 6 relates to a hybridoma cell producing the antibody according to claim 5. Claim 7 refers to the products of claims 1 and 3-5 for use as a pharmaceutical. Claims 8-9 and 11-12 relate to methods of identification and diagnosis using the products of claims 1 and 4-5. Claim 10 is directed to the use of the products of claims 1 and 3-5 for the preparation of a pharmaceutical composition.

XIV. The following documents are cited in this decision:

D1: WO 01/18204 (publication date: 15 March 2001);

D2: US 60/183,578 (18 February 2000);

D10: J. Henry et al., Review Immunol. Today, June 1999, Vol. 20, No. 6, pages 285 to 288;

D39: Open Biosystems. Clone information. incl. Annex as filed by opponent 01/appellant on 15 January 2009;

D58: WO 01/18021 (publication date: 15 March 2001);

D59: US 60/200,346 (filing date: 28 April 2000).

XV. Appellant's arguments, insofar as they are relevant to the present decision, may be summarized as follows:

Admissibility of the Main Request

The Main Request was filed as Auxiliary Request I one month before the oral proceedings and thus, it was late filed. Although filed in reply to the board's communication, it intended to overcome objections that had been in the proceedings from the very beginning. Since it did not overcome these objections, the Main Request did not simplify the proceedings.

Main Request
Article 100(c) EPC

Annex B of the patentee/respondent's submissions filed on 19 August 2009 showed the fragment 1-465 to contain not only the BSL2/B7-H3 extracellular domain (ECD) but also other domains. Likewise, the legend of Figure 3B of the application as filed referred to this fragment as containing the ECD but not equating it to the ECD. Nowhere in the application as filed was the ECD

individualized as such. Claim 9 of the application as filed referred to fusion proteins comprising the ECD but no exact values/positions defining this domain were given therein, nor were these values disclosed in the application as filed. The fragment 1-465 could not be associated to the references in the application as filed to soluble forms of BSL2/B7-H3, since this fragment was disclosed as a mere arbitrary fragment among many other possible fragments available to the skilled person. Thus, the reference to fragment 1-465 in claim 1(b) of the Main Request was taken out of context in the claim and had no formal basis in the application as filed. Moreover, this objection applied to all claims dependent on claim 1(b), such as claim 5 directed to antibodies raised against fragment 1-465. The case law referred to in the board's communication did not apply to the present case. Contrary to the cases underlying the cited decisions where the specific values/positions were identified, in the present case such identification was missing.

New arguments/objections under Article 123(2) EPC

There was no basis in the application as filed for the feature "*one polymorphism*" in claims 1(c) and 1(d). The term "*one*" was disclosed only as part of "*one or more*" and, as shown on page 36 of the application as filed, the presence of "*one or more polymorphisms*" was linked to an intended purpose (enhance BSL2/B7-H3 stability/ reactivity) that was not present in claims 1(c) and 1(d). This objection had already been raised in the opposition procedure.

Finally, anti-BSL2/B7-H3 antibodies were described, on page 78 of the application as filed, as "*specifically react*[ing]" with the BSL2/B7-H3 antigen. This

requirement had been omitted in claim 5, which constituted an unallowable extension of the subject-matter as originally filed.

Admissibility of a new objection under Article 123(3) EPC

Whereas in the context of the application as filed the feature "*one polymorphism*" was clear and not open to interpretation, this feature was taken out of context and open to interpretation in claims 1(c) and 1(d). In these claims, this feature could be understood as allowing the presence of at least one polymorphism. The scope of these claims was accordingly broader than the scope of the corresponding granted claims that was limited by a specific degree of identity. Although this objection was raised for the first time in the oral proceedings before the board, it was highly relevant and should therefore be considered.

Article 100(a) EPC (Article 54 EPC)
Claims 1(k) and 1(m) and claim 2

The Incyte Genomics clone 4616811 (designated in the patent BSL2-4616811, carried on plasmid pINCY:BSL2-4616811 and deposited as ATCC PTA-1993) was a commercially available clone from the LIFESEQ database. This clone contained sequence SEQ ID NO: 6 which encoded sequence SEQ ID NO: 7, as shown in Example 1 of the patent. Evidence was on file, including document D39 and the statements of the patent itself, that established the public availability of the LIFESEQ database and the Incyte Genomics clone 4616811.

Claim 1(b) and claim 5

The BSL2/B7-H3 amino acid/nucleic acid sequences were disclosed in Figure 3 of document D1. The structure of BSL2/B7-H3 was disclosed in detail, with identification of its domains and a hydrophobicity plot analysis in Figure 5. The BSL2/B7-H3 transmembrane domain was identifiable and both, the BSL2/B7-H3 cytoplasmic and extracellular domains, were identifiable in this figure. As shown by an expanded copy of Figure 5, submitted at the oral proceedings, the ECD was identical to the fragment 1-465 in claim 1(b). Document D1 disclosed anti-BSL2/B7-H3 antibodies, in particular antibodies blocking the co-stimulation of T-cells, which were useful for treating autoimmune diseases. Thus, the functional feature given in claim 5 was anticipated by document D1.

Although document D2 did not contain the complete disclosure of document D1, the BSL2/B7-H3 amino acid/ nucleic acid sequences and the hydrophobicity plot analysis were disclosed in Figures 1 and 4 of document D2. References were made to the BSL2/B7-H3 structure, including the transmembrane domain and the four Ig-like domains within the ECD (Figure 3), which anticipated the subject-matter of claim 1(b). BSL2/B7-H3 was identified in document D2 as a member of the B7 family. Members of the B7 family were known, as disclosed in document D2 and exemplified in document D10, to have costimulatory T-cell activity. Thus, antibodies of therapeutic interest for treatment of autoimmune disease were antagonist antibodies with the functional feature cited in claim 5. Indeed, the skilled person knew that there were only agonist and antagonist antibodies and, depending on the intended use, the appropriate antibodies were selected. Thus, the disclosure of document D2 was identical to that of document D1, although in an implicit manner.

Admissibility of documents D58/D59

Documents D58/D59 were filed with the Grounds of Appeal, at the earliest stage of the appeal proceedings. They were known to the respondent more than four years before the oral proceedings and, in this sense, were not late filed. The documents were filed in direct reply to the amendment, i.e. the introduction of the functional feature into claim 5, introduced into claim 5 at the oral proceedings before the opposition division. Thus, the first possibility to react to this amendment was with appellant's Grounds of Appeal. Also in this sense, documents D58/D59 were not late filed. These documents were highly relevant which was the overriding criterium for admitting them into the proceedings. It was against the public interest not to admit highly relevant documents into the appeal proceedings and to maintain a non-valid patent. The contents of documents D58/D59 were not complicated and their relevance was easily established. Indeed, claim requests were on file showing that the respondent had already taken them into account.

Remittal to the first instance

Documents D58/D59 were filed at the earliest stage of the appeal proceedings. The respondent had ample opportunity to prepare its case, react to these documents and, if appropriate, change its claim requests. Indeed, claim requests were on file intending to overcome objections based on these documents. It was not in the public interest, four and a half years after the onset of the appeal procedure, to further delay the proceedings and to remit the case to the first instance for further prosecution. There was no absolute right

for remittal and a patentee could not, always and in all cases, rely on it.

XVI. Respondent's arguments, insofar as they are relevant to the present decision, may be summarized as follows:

Admissibility of the Main Request

The Main Request was based on the request upheld by the opposition division which had been in appeal proceedings from the beginning. Amendments introduced into the Main Request, made in reply to the board's communication, were straightforward (deletion of a claim directed to cell lines and the change of dependency of the antibody claim to exclude antigens encoded by complementary nucleic acid sequences).

Main Request
Article 100(c) EPC

The fragment 1-465 was individualized, as such, in the application as filed and identified as containing the ECD of BSL2/B7-H3, as described in the legend of Figure 3B. The skilled person would have recognized this fragment as a preferred soluble fragment of BSL2/B7-H3. The more so, since in Example 4 of the application as filed, this fragment was used for constructing a fusion protein and was equated to the ECD of BSL2/B7-H3. The amino acid sequence corresponding to this fragment could be identified within the sequence of the fusion protein shown in Figure 4B. Since fragment 1-465 had a basis in the application as filed, there was also a basis for claim 5, directed to antibodies raised against this fragment.

New arguments/objections under Article 123(2) EPC

The objections related to the feature "*one polymorphism*" and to the omission of the feature "*specifically react*" were raised at the oral proceedings, i.e. at the latest possible stage of the appeal proceedings. Although the feature "*one polymorphism*" was discussed at first instance, the decision of the opposition division on this issue, as stated in the board's communication, was not contested by the appellant. The appellant did not reply to this communication. As for the omission of the feature "*specifically react*", according to the case law of the Boards of Appeal (cf. T 189/01 of 15 June 2004), the notion of specificity was inherent to the nature of antibodies and therefore, it was inherent to the antibodies defined in claim 5. In any case, the objection was never raised before and its introduction at the oral proceedings before the board should not be admitted.

Admissibility of a new objection under Article 123(3) EPC

The feature "*one polymorphism*" was not taken out of context in claims 1(c) and 1(d). When these claims were read in a reasonable manner, this feature had the same meaning as in the application as filed, namely the incorporation of only one, single polymorphism into the amino acid sequences. In any case, this objection was raised for the first time at the latest possible stage of the appeal proceedings and referred to an amendment that had been introduced into the claims at the beginning of the opposition proceedings. The objection should not be admitted into the appeal proceedings.

Article 100(a) EPC (Article 54 EPC)
Claims 1(k) and 1(m) and claim 2

The Incyte Genomics database was not publicly available and, in the post-published document D39, only an expressed sequence tag (EST) of 255 nucleotides was disclosed but not the sequences cited in claims 1(k) and 1(m). Two LIFESEQ databases were provided by Incyte, a free database containing only a limited number of sequences and a proprietary database containing more sequences but subjected to confidentiality. Claims 1(k) and 1(m), relating to sequences SEQ ID NO: 6 and 7 and to PTA-1993, were not anticipated by Incyte Genomics clone 4616811. Even if the Incyte Genomics database had been available, the specific clone 4616811 could not have been retrieved without the corresponding sequence at hand. There was no annotation on this EST sequence informing a skilled person that it encoded a polypeptide of the B7 family. According to the case law (cf. T 18/09 of 21 October 2009, T 301/87 of OJ EPO 1990, page 335), neither the library nor the EST sequence, if publicly available, anticipated claims 1(k) and 1(m).

Claim 1(b) and claim 5

Figure 5 of document D1 showed the hydrophobicity plot analysis for the full-length sequence of BSL2/B7-H3. There was no disclosure of any BSL2/B7-H3 fragment in this analysis, let alone of the specific fragment 1-465. The structure of BSL2/B7-H3 was defined only in a general manner and there was no disclosure of the positions defining the BSL2/B7-H3 transmembrane domain. This disclosure was also not derivable from appellant's expanded copy of Figure 5. Position 465 was not identified as the last position of a fragment

containing the ECD nor was position 466 identified as starting the BSL2/B7-H3 transmembrane domain, other positions (467, 468, etc.) were also possible. Thus, the fragment 1-465 cited in claim 1(b) was not disclosed in document D1. The BSL2/B7-H3 function/ activity was not characterized in document D1, which referred only to a general modulation of immune responses. References to therapeutic antibodies were given in a general manner, without characterizing the antibodies as antagonist or agonist antibodies. Indeed, the activity of an antibody depended on the nature of the antigen used for their production, i.e. either the complete BSL2/B7-H3 or only fragments thereof, such as a BSL2/B7-H3 fragment containing only the ECD, which was not even disclosed in document D1. Thus, document D1 did not anticipate antibodies with the functional feature cited in claim 5.

Document D2 contained less information than document D1. The reference to a therapeutic use of BSL2/B7-H3 for treating patients suffering from autoimmune disorders contradicted the identification of BSL2/B7-H3 as a member of the B7 family, since members of this family were known to have a costimulatory T-cell activity. The general reference in document D2 to antibodies for use in therapeutic methods was not a disclosure of antibodies with the functional feature cited in claim 5. These claimed antibodies were a particular sub-group of antibodies which was not derivable from document D2.

Admissibility of documents D58/D59

Documents D58/D59 clearly related to members of the B7 family as seen from their title and they could have been easily retrieved and filed at an earlier stage of

the proceedings. The amendments introduced into claim 5 at the oral proceedings before the opposition division were no excuse for the late-filing of these documents, since claims referring to (increased/decreased) BSL2/B7-H3 activity were already present in the set of granted claims and in all claim requests filed at first instance proceedings. The relevance of this activity for therapeutic uses was known to a skilled person. If documents D58/D59 were admitted into the appeal proceedings, they rendered the case more complex, raised new issues and required a remittal to the first instance, which all went against the need for procedural economy.

Remittal to the first instance

Although there was no absolute right to two instances, in the circumstances of the present case, this right should be accepted by the board. The delay in the proceedings arose from the late-filing of documents D58 and D59. As a reaction, the respondent had filed auxiliary requests as fall-back positions, since it was aware that it had no absolute right to two instances. However, it was not fair to be punished for the precautionary filing of auxiliary requests and to be deprived from arguing and discussing their merits before the opposition division. The filing of auxiliary requests could not put the respondent in a worse position than if it had not filed them.

XVII. The appellant requested that the decision under appeal be set aside and that the patent be revoked.

XVIII. The respondent requested that the decision under appeal be set aside and that the patent be maintained on the basis of the Main Request filed at the oral proceedings

before the board. The respondent further requested that documents D58/D59 not be admitted into the appeal proceedings and, if they were admitted, that the case be remitted to the department of first instance for further prosecution.

XIX. No requests were on file from opponent 02, party as of right.

Reasons for the Decision

Admissibility of the Main Request

1. The Main Request, filed as Auxiliary Request I in reply to the board's communication pursuant to Article 15(1) RPBA, addresses issues raised in this communication, in particular by deleting subject-matter related to cell lines comprising the disclosed nucleic acid molecules and to polypeptides encoded by the complementary sequences of these nucleic acid molecules (cf. points 14.3 and 18 of the board's communication). The deletion of this subject-matter is a straightforward amendment that simplifies the issues of the appeal proceedings and is in line with the need for procedural economy.

2. Apart from these amendments, the Main Request is identical to Auxiliary Request II upheld by the opposition division, which was maintained by the respondent, as its former Main Request, in reply to appellant's Grounds of Appeal and to the board's communication.

3. The board, in exercising its discretion under Article 114(2) EPC and Article 13(1) RPBA, admits the Main Request into the appeal proceedings.

Article 100(c) EPC

4. Claim 1(b) is directed to "*a nucleic acid molecule encoding the amino acid sequence consisting of amino acids 1 to 465 of SEQ ID NO: 7*" (cf. point XIII *supra*), i.e. to a specific fragment of the BSL2/B7-H3 sequence disclosed in the application as filed.

Figure 3A shows the nucleotide sequence of the BSL2-4616811 clone (SEQ ID NO:6) and, in the legend of this figure, the predicted domains are characterized in further detail by indicating the positions that define the translation initiation (121-123), signal peptide cleavage site (204-205), transmembrane domain (1516-1587) and translation termination signal (1723-1725) (cf. page 10, lines 8-15 of the application as filed). Figure 3B shows the predicted amino acid sequence of said BSL2-4616811 clone (SEQ ID NO:7) and, in the legend of the figure, it is stated that "*amino acids (**1-465**) contain the predicted ECD*" (cf. page 10, lines 15-17). Figures 4A-4B illustrate the nucleotide and predicted amino acid sequences of the BSL2-4616811-Ig fusion construct. In the legend of Figure 4B, it is stated that the "*amino acids **1-465** contain the native sequence of BSL2-4616811* [and] *amino acids 466-698 contain the Fc domain of human IgG*" (cf. page 11, lines 1-12). In Example 4, describing the construction of the BSL2-4616811-Ig fusion construct, it is explicitly stated that "[t]*o construct the BSL2-4616811-Ig plasmid, the BSL2-4616811 extracellular domain was PCR amplified*" (cf. page 110, lines 18-20 and page 113, lines 4-7). Thereby, the amino acid fragment 1-465 is explicitly equated to the ECD of the BSL2-4616811 clone.

In the light of this disclosure, the board considers that a skilled person would identify, in a direct and unambiguous manner, the specific amino acid fragment **1-465** (comprising or being the ECD of the BSL2-4616811 clone) as a preferred "*soluble form*" of BS2/B7-H3, as also explicitly indicated in the application as filed itself by stating "[a] *soluble, secreted recombinant B7-polypeptide includes the extracellular domain of the polypeptide*" (cf. page 34, lines 8-11).

In line with the case law of the Boards of Appeal, the disclosure in a Figure of amino acid positions defining a protein domain amounts to an implicit disclosure of said domain and renders it available to the skilled person (cf. T 27/04 of 20 May 2005, points 5-6 of the Reasons; T 1120/01 of 14 July 2003, point 2 of the Reasons).

5. Thus, there is a basis in the application as filed for the subject-matter of claim 1(b) (Article 123(2) EPC).

6. There is also formal basis in the application as filed for antibodies raised against "*portions*" or "*fragments*" of the disclosed BSL2/B7-H3 as well as for antibodies recognizing "*peptides derived from the B7-related polypeptides*" (cf. *inter alia*, page 8, lines 1-5, page 34, lines 17-21, page 41, line 1 to page 42, line 4). The "*soluble forms*" and, more particularly, "[a] *soluble, secreted recombinant B7-polypeptide* [which] *includes the extracellular domain of the polypeptide*" (cf. page 34, lines 8-11), are among the preferred "*portions*", "*fragments*" and "*peptides*" according to the invention. With regard to the preferred antibodies, the application as filed explicitly refers to those antibodies that "*block the activity of immune or inflammatory response cells*

(e.g., T-cells)" (cf. page 8, lines 1-7 and page 78, lines 1-3).

7. Thus, also claim 5 has a basis in the application as filed (Article 123(2) EPC).

New arguments/objections under Article 123(2) EPC

8. At the oral proceedings before the board, the appellant raised two further objections under Article 123(2) EPC, the first objection concerns the feature "*one polymorphism*" in claims 1(c) and 1(d) and the second concerns the omission of the feature "*specifically reacts*" to characterize the antibodies in claim 5.

8.1 The objection related to the feature "*one polymorphism*" had already been raised at first instance and the opposition division decided that it was not relevant (cf. page 1, under the heading "*Discussion on Art. 123(2) EPC*" in the "*Minutes of the oral proceedings before the opposition division*" and page 3, point b) of the decision under appeal). As noted by the board in point 13 of its communication, this decision was not contested by the appellant in the statement of Grounds of Appeal. The appellant did not reply to the board's communication. Thus, this objection was raised and brought to the board's attention, for the first time in the entire appeal procedure, at the oral proceedings.

8.2 The objection concerning the omission of the feature "*specifically react*" for characterizing the claimed antibodies was never raised at first instance, even though claim 5 as granted read "*an antibody that binds to the polypeptide according to claim 4*". There is thus no decision of the opposition division on this issue. This objection had also not been raised in appellant's

statement of Grounds of Appeal. The appellant did not reply to the board's communication, wherein the scope of the appeal proceedings was explicitly defined. The objection was brought to the board's attention, for the first time during the entire appeal procedure at oral proceedings.

9. According to Article 12(2) RPBA, the statement of Grounds of Appeal shall contain appellant's "*complete case*". The new objections raised by the appellant at the oral proceedings are an amendment to its case, submitted at the latest possible stage of the appeal proceedings. According to established case law of the Boards of Appeal such late filing is not in line with the actual purpose of appeal proceedings (cf. *inter alia*, T 1069/08 of 8 September 2011, point 28 of the Reasons; T 1621/09 of 22 September 2011). The board, in exercising its discretion under Article 114(2) EPC and Article 13(1) RPBA, does not admit appellant's new objections under Article 123(2) EPC into the appeal proceedings.

Admissibility of new objection under Article 123(3) EPC

10. The feature "*one polymorphism*" had been introduced into claims 1(c) and (d) in a set of claims filed by the patentee/respondent on 30 April 2010, in preparation for the oral proceedings before the opposition division. At these oral proceedings, none of the opponents, including opponent 01/appellant, raised an objection under Article 123(3) EPC against this feature. There is thus no decision of the opposition division on this issue.

11. In appellant's statement of Grounds of Appeal, no objections were raised under Article 123(3) EPC. The

board, in its communication pursuant to Article 15(1) RPBA, referred to the scope of the appeal proceedings and, in an explicit manner, to the issues decided by the opposition division which were not contested by the appellant (cf. points 7 and 13 of the board's communication). The appellant did not reply to this communication.

12. The objection was brought to the board's attention, for the first time during the entire procedure at the oral proceedings, i.e. at the latest possible stage of the appeal proceedings. According to established case law of the Boards of Appeal (cf. point 9 *supra*) such late filing is not in line with the actual purpose of appeal proceedings. The board, in exercising its discretion under Article 114(2) EPC and Article 13(1) RPBA, does not admit appellant's new objection under Article 123(3) EPC into the appeal proceedings.

Article 100(a) EPC; Article 54 EPC

Claims 1(k) and 1(m), claim 2

13. According to Example 1 of the patent, Incyte Genomics clone 4616811 belongs to the Incyte Genomics Library ID No. BRAYDIT01. This clone was identified using Incyte Genomics template 252899.8 which, according to Example 1, is a consensus EST sequence, representing a mRNA transcript (cf. page 33, paragraphs [0190]-[0191] of the patent). Document D39 shows a partial EST sequence which, according to the appellant, anticipates claim 1(k) as far as it relates to SEQ ID NO: 6 (the nucleic acid sequence of the BSL2-4616811 clone disclosed in the patent; Figure 3A) and to the deposited PTA-1993.

14. There is however no evidence on file showing that the nucleic acid sequences of the Incyte Genomics clone 4616811 or the Incyte Genomics template 252899.8 (or template 252899.6 cited in Example 1) were identified as encoding a member of the B7 family. As it is the case for many EST sequences, document D39 only discloses a partial sequence, not annotated and completely uncharacterised. There is thus no reason for the board to depart from the established case law on EST sequences, stating that their mere existence in a large collection of clones is not seen as a form of implicit disclosure (cf. T 18/09 of 21 October 2009 from this board in a different composition; see points 10-14 of the Reasons).

15. Contrary to the opposition division, the board decides that the availability of the Incyte Genomics clone and templates is not relevant in the present case since, even if available, their presence in a general library, among other clones and EST sequences, does not represent a clear and direct disclosure of the specific nucleic acid sequence of claim 1(k) and/or the deposited PTA-1993, which is required to be considered for the assessment of novelty (Article 54 EPC).

Claim 1(b)

16. Document D1, representing state of the art according to Article 54(3) EPC, is published on 15 March 2001 and claims four different priorities. The patent was filed on 6 June 2001 and is entitled to its first priority date 6 June 2000 (US 209811). The findings of the opposition division as regards the entitlement of the patent to the claimed priority have not been contested by the appellant (cf. page 5, point 2 of the decision under appeal; point 7 of the board's communication).

The third priority document of document D1 (US 60/183,578; designated as document D2 in the appeal procedure) has a filing date of 18 February 2000, i.e. before the priority date of the patent. Therefore, for the assessment of novelty the contents of document D2 are relevant.

16.1 Claim 1(b) refers to a nucleic acid molecule encoding the amino acid sequence consisting of amino acids 1 to 465 of SEQ ID NO: 7, i.e. the extracellular domain (ECD) of BSL2/B7-H3.

The objection under Article 54(3) EPC based on document D1 against claim 1(b) had not been raised in the appellant's statement of Grounds of Appeal, even though the opposition division decided in the patentee/ respondent's favour on this issue (cf. page 6, last paragraph to page 7, second paragraph of the decision under appeal), but only at the oral proceedings before the board, i.e. at the latest possible stage of the appeal proceedings. In line with the case law referred to in point 9 *supra*, the board, in exercising its discretion under Article 114(2) EPC and Article 13(1) RPBA, does not admit appellant's new objection under Article 54(3) EPC into the appeal proceedings.

16.2 However, with a view to the further reasons given in this decision with regard to the novelty of the subject-matter of claim 5 in the light of the disclosure in document D1, the board gives the following evaluation of the arguments presented by the appellant in this respect:

16.3 The predicted amino acid sequence of the "*B7-like protein*" is shown in Figure 3 of document D1 and in Figure 1 of document D2. The amino acid sequence is

identical to that of the BSL2/B7-H3 disclosed in the patent. Documents D1 and D2 describe also the structure of the protein, namely the presence of four Ig-like domains (Figure 3 of document D2) followed by a transmembrane domain and a 44 amino acid cytoplasmic domain (cf. paragraph bridging pages 25-26 in document D1; page 2, first full paragraph in document D2). However, there is no disclosure in the two documents of the exact length and of the amino acid positions defining the transmembrane domain. The hydrophobicity plot analysis of the BSL2/B7-H3 protein is shown in Figure 5 of document D1 and in Figure 4 of document D2. Although the transmembrane domain is identifiable from this analysis, the exact positions defining this domain are not derivable. There is no disclosure that the specific position **465** is the last residue of a fragment comprising/being the ECD of BSL2/B7-H3. This is also not, directly and unambiguously, derivable from the expanded Figure 5 provided by the appellant at the oral proceedings.

Claim 5

17. Claim 5 refers to an antibody that binds to the polypeptide according to claim 4 and blocks the activity of immune or inflammatory response cells (cf. point XIII *supra*).

17.1 The polypeptides referred to in claim 4 are encoded by the nucleic acid molecule according to (a) to (i), (l) and (n) of claim 1, i.e. the BSL2/B7-H3 splice variants of SEQ ID NO: 11 or 13 (and altered sequences incorporating one polymorphism), the amino acid fragment 1-465 of the full-length amino acid sequence SEQ ID NO: 7 and fusion constructs of this sequence with the Fc domain of human IgG (SEQ ID NO: 9). None of

the BSL2/B7-H3 splice variants are disclosed in documents D1/D2 and, as shown in point 16.3 *supra*, the amino acid fragment 1-465 is not disclosed in documents D1/D2.

17.2 None of the polypeptides referred to in claim 4 is used in documents D1/D2 to raise antibodies. Antibodies are defined in document D2 only in a very general manner, namely as "*bind*[ing] *immunospecifically to any of the proteins of the invention*". This includes fragments of the disclosed protein (cf. page 2, last paragraph and page 3, last sentence of document D2). However, contrary to document D1 which explicitly identifies "*regions ... useful for designing epitopes or selecting antigens*" (i.e. the hydrophilic regions identifiable from Figure 5; cf. page 6, lines 8-10 and 14-19 and page 31, lines 20-28 of document D1), no specific fragments are identified in document D2.

17.3 Nevertheless, it is evident from the amino acid sequences of all these polypeptides that all share the same or very similar ECD sequences (four Ig-like domains in the full-length BSL2/B7-H3 sequence) or parts thereof (two Ig-like domains in the BSL2/B7-H3 splice variants) and that they all have identical or very similar linear epitopes. Therefore, it cannot be excluded that antibodies raised against the full-length BSL2/B7-H3 sequence disclosed in documents D1/D2 may have the same properties than the antibodies raised against the polypeptides defined in claim 4, i.e. there may be an overlap between the antibodies raised against the polypeptides of claim 4 and the antibodies raised against BSL2/B7-H3 disclosed in documents D1/D2.

17.4 However, within this overlapping group of antibodies, there are antibodies antagonising and antibodies

agonising the activity of the specific antigen used (which might not be the same activity for all antigens), as well as neutral antibodies with neither an antagonist nor an agonist effect on said activity. Since the antibodies of claim 5 are required to have a specific activity, namely to "*block the activity of immune or inflammatory response cells*", a further selection within the group of possibly overlapping antibodies is made. The claimed subgroup of antibodies is not directly and unambiguously derivable from the general reference in document D2 to "*the generation of antibodies ... for use in therapeutic ... methods*", even when account is taken of the general disorders/ diseases referred to in this document, namely "*for treatment of patients suffering from infectious diseases, cancers, autoimmune disorders and complications associated with graft vs host disease in organ transplantation*" (cf. page 3, three last sentences of document D2).

17.5 Thus, the board, in view of the disclosure in document D2, finds that document D1, with regard to the here relevant parts, is not entitled to its third priority date (US 60/183,578; 18 February 2000). Therefore, for the subject-mater of claim 5, document D1 does not belong to the state of the art under Article 54(3) EPC.

18. Consequently, the Main Request is novel over the disclosure in document D1 (Article 54(3) EPC).

Admissibility of documents D58/D59 into the appeal proceedings

19. The functional feature characterizing the claimed antibodies as blocking the activity of immune or inflammatory response cells, was introduced during the oral proceedings before the opposition division in

order to overcome an objection raised under Article 54 EPC. The introduction of this feature was acknowledged by the opposition division to define the selection of a particular group of antibodies from those already disclosed in the prior art, which rendered the claimed antibodies novel over this prior art (cf. page 10, point 2; page 11, point 1 of the decision under appeal).

20. It is arguable whether this newly introduced functional feature is directly related to the activity mentioned in several method-claims as granted, such as "*increasing or decreasing T-cell activity*" and "*increased immune cell activity*" (granted claims 11 and 12, respectively), and whether or not documents D58/ D59, therefore, could have been submitted earlier.

Fact is that said functional feature was not present in granted claim 5 directed to anti-BSL2/B7-H3 antibodies and that the introduction of the feature constituted a substantial amendment of the claimed subject-matter.

The first opportunity for the appellant to react to such a substantial amendment was with its statement of Grounds of Appeal.

The filing of document D58 and its priority document D59 with the Grounds of Appeal is a direct reply to the amendment introduced into granted claim 5 at the oral proceedings before the opposition division.

21. The statement setting out the Grounds of Appeal has been filed more than four years before the oral proceedings before the board, which gave the respondent plenty of time to study the two documents and to react accordingly.

The board, in its communication pursuant to Article 15(1) RPBA, had already referred to documents D58/D59, although not in detail in view of the pending discussion on their admissibility into the appeal proceedings, and had acknowledged their *prima facie* relevance (cf. point 17.4 of the board's communication).

The respondent, in reply to the Grounds of Appeal and to the board's communication, has filed Auxiliary Requests that obviously take into account the disclosure in documents D58/D59.

22. In the light of the circumstances of the present case, in particular considering the filing of documents D58/D59 as direct reply to amendments introduced at oral proceedings before the opposition division and the *prima facie* relevance of these documents for assessing novelty, the board, exercising the discretion given to it under Article 114(2) EPC and Article 12(4) RPBA, decides to admit documents D58/D59 into the appeal procedure.

Remittal to the opposition division for further prosecution

23. Documents D58/D59 are *prima facie* relevant and, as a consequence, it cannot be excluded that the respondent might loose relevant embodiments of the subject-matter claimed.

24. The board acknowledges that it would not be fair to the respondent that the filing of Auxiliary Requests at an earlier stage of the appeal proceedings influences the board's decision on a remittal of the case and to deprive the respondent of the possibility to defend his

case in the light of a newly introduced and *prima facie* relevant document before two instances.

Since the board decided in appellant's favour and, based on the particular circumstances of the present case, decided to admit documents D58/D59 into the procedure, it is also fair, based on the very same particular circumstances, to grant the respondent's request for a remittal to the opposition division for further prosecution.

25. The board decides to remit the case to the opposition division for further prosecution (Article 111(1) EPC).

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 on the basis of claims 1 to 12 of the Main Request filed at the oral proceedings before the board.

The Registrar: The Chairman:

S. Sánchez Chiquero M. Wieser

Decision electronically authenticated