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Datasheet for the decision of 25 June 2013

Case Number: T 0501/09 - 3.3.04

Application Number: 96943576.7

Publication Number: 865448

IPC: C07K 16/32, C07K 16/46, C12N 5/20, C12N 5/10, A61K 39/395

Language of the proceedings: EN

Title of invention:
Apoptosis induced by monoclonal antibody anti-Her2

Patent Proprietor:
Amgen Inc.,

Opponent:
Fresenius Biotech GmbH

Headword:
Apoptosis/AMGEN INC.

Relevant legal provisions:
EPC Art. 108
EPC R. 99(2), 101(1)
RPBA Art. 12(4)

Keyword:
"Admissibility of appeal/patentee - statement of grounds (not filed)"
"Admissibility of appeal/opponent - appeal sufficiently substantiated (no)"

Decisions cited:
G 0009/91, G 0010/91, R 0002/08, T 0220/83, T 0923/92, T 1002/92, T 0015/01, T 1557/05, T 0724/08

Catchword:
Admissibility of appeal, see points 2 to 8

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0501/09 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 25 June 2013

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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 11 December 2008 concerning maintenance of European patent No. 865448 in amended form.**

Composition of the Board:

Chairman: C. Rennie-Smith
Members: R. Morawetz
M. Montrone

Summary of Facts and Submissions

I. The appeals of the patent proprietor (hereinafter "appellant-patentee") and the opponent (hereinafter "appellant-opponent") lie from the interlocutory decision of the opposition division posted on 11 December 2008, whereby European patent No. EP 0 865 448 has been maintained in amended form on the basis of auxiliary request 2.

II. The patent at issue has the title "Apoptosis induced by monoclonal antibody anti-Her2". It was granted on European application No. 96943576.7 which originated from international application PCT/US96/19289 published as WO 97/020858 (hereinafter "application as filed").

Claims 1 and 16 as granted read as follows:

"*1. An anti-Her2 antibody or fragment thereof which induces apoptosis in cells expressing Her2.*

16. A pharmaceutical composition comprising an amount of an antibody of claim 1 sufficient to induce apoptosis in a mixture with a pharmaceutically acceptable adjuvant."

III. The patent was opposed under Article 100(a) EPC 1973 on the ground of lack of inventive step (Article 56 EPC 1973), under Article 100(b) EPC 1973 and under Article 100(c) EPC 1973.

IV. The following documents are referred to in this decision:

(D1) Curiel D, Gene Therapy, vol. 2, page 20 (1995)
(D2) Deshane J et al., J. Invest. Med., vol. 32, page 328A (1995)
(D3) Grim J et al., Cancer Gene Therapy, vol. 1, pages 333-334 (1994)
(D7) Kyakumoto S. et al., Archives of Oral Biology, vol. 39, pages 569-580 (1994)
(D11) Yarden Y. and Ullrich A., Ann. Rev. Biochem., vol. 57, pages 443-478 (1988)
(D12) Fendly B.M. et al., Cancer Research, vol. 50, pages 1550-1558 (1990)
(D13) Vitetta E.S and Uhr J.W., Cancer Research, vol. 54, pages 5301-5309 (1994)
(D14) Wu X. et al., J. Clin. Invest., vol. 95, pages 1897-1905 (1995)
(D15) WO98/17797
(D16) Phillips G.D.L. et al., Cancer Research, vol. 68, pages 9280-9290 (2008)
(D17) Hudziak R.M. et al., Molecular and Cellular Biology, vol. 9, pages 1165-1172 (1989)

V. The opposition division maintained the patent in amended form on the basis of auxiliary request 2 filed by letter dated 01 August 2008.

Claim 1 of auxiliary request 2 reads as follows:

"*1. A pharmaceutical composition comprising an anti-Her2 antibody or fragment thereof which induces apoptosis in cells expressing Her2 in an amount*

sufficient to induce apoptosis in a mixture with a pharmaceutically acceptable adjuvant."

VI. As regards novelty, the opposition division held (see decision under appeal, reasons, point 4.3) that documents (D1) to (D3) could not be seen as providing an enabling disclosure of an anti-Her2 antibody.

VII. As regards inventive step of auxiliary request 2, the opposition division held that the subject-matter of claim 1 involved an inventive step (see decision under appeal, reasons, point 11.3) for the following reasons: "*Document D2 is considered to represent the most relevant state of the art in that it refers to the induction of apoptosis in cancer cell lines using an antibody. D2 is based on transfecting cells with a gene expression construct and intracellular expression of the antibody. The subject-matter of claim 1 differs from the teaching of D2 in that it refers to a pharmaceutical composition already containing the antibody. The underlying objective technical problem may therefore be seen in providing alternative means for inducing apoptosis in Her2 expressing cells. Antibodies to Her2 are known in the art, e.g. from D7. However, from D7 it is not apparent that the anti-Her2 antibody actually induces apoptosis, since apoptosis is not investigated in D7. The morphological changes referred to in D7 can not be interpreted as clearly pointing towards apoptosis. D2 on the other hand is based on an entirely different approach, namely intracellular expression of an antibody from a gene construct. D2 is totally silent as to addition of antibodies produced outside of the cell to the cells in order to induce apoptosis. Therefore, from D2 the*

skilled person does not get any hint that an antibody which is administered to the cells could have an apoptotic effect. Therefore, preparation of a composition containing such antibodies is also not disclosed or even hinted at. Claim 1, as well as claims directly or indirectly dependent therefrom, are thus considered to be inventive within the meaning of Article 56 EPC."

VIII. Finally, the opposition division held that the requirements of Article 83 EPC were also met and argued as follows (see decision under appeal, reasons, point 3.3): "*The application discloses methods for producing (more than one) specific anti-Her2 antibodies which fulfil the functional requirements of claim 1. Detection of apoptosis using a commercially available test is also explicitly disclosed. Therefore, a person skilled in the art clearly gets enough information from the application about how to produce anti-Her2 antibodies, and how to test them for apoptotic activity. The Opposition Division agrees with the Patentee that in view of the specific teaching of the application with regard to e.g. mAb74, together with the skilled persons knowledge of routine procedure for producing antibodies and testing apoptosis, claim 1 is sufficiently disclosed over the whole of the claimed scope.*"

IX. The appellant-patentee filed a notice of appeal on 12 February 2009 and paid the fee for appeal on the same date. No statement of grounds of appeal was filed by the appellant-patentee and the notice of appeal contained nothing that could be regarded as statement of grounds of appeal pursuant to Article 108 EPC.

X. The appellant-opponent filed its notice of appeal on 17 February 2009 and paid the fee for appeal on the same date. With its statement of the grounds of appeal the appellant-opponent filed new documents (D11) to (D15).

XI. By communication dated 15 May 2009, sent by registered letter with advice of delivery, the registry of the board informed the appellant-patentee that no statement of grounds had been filed and that it was to be expected that the appeal will be rejected as inadmissible pursuant to Article 108, third sentence, EPC in conjunction with Rule 101(1) EPC.

XII. In response to the appellant-opponent's grounds of appeal the appellant-patentee filed on 25 September 2009 documents (D16) and (D17) and provided arguments why the claimed subject-matter of auxiliary request 2 was novel, inventive and sufficiently disclosed.

XIII. By a communication dated 17 January 2013 the parties were summoned for oral proceedings to be held on 25 June 2013.

XIV. With a letter dated 21 January 2013 the appellant-patentee requested that the board deny the admission of documents (D11) to (D15) into the proceedings, dismiss the appeal of the appellant-opponent and maintain the patent on the basis of auxiliary request 2.

XV. By a letter dated 23 May 2013 the appellant-opponent provided arguments why documents (D11) to (D15) were not late filed and *prima facie* highly relevant and

asked the board to exercise its discretion and to admit documents (D11) to (D15) into the proceedings.

XVI. Oral proceedings took place on 25 June 2013. At the beginning of the oral proceedings the appellant-patentee agreed that its appeal had to be regarded as inadmissible. In the context of the assessment of the *prima facie* relevance of documents (D11) to (D15) the board asked the appellant-opponent to comment on the public availability of the antibodies referred to in documents (D12) and (D13). After the chairman announced that the board had decided that documents (D11) to (D17) and arguments based thereon were inadmissible, the representative of the appellant-opponent stated that he was confronted for the first time at the oral proceedings by a matter raised by the board (not the other party), namely that documents (D12) and (D13) lacked enablement and he would have been better prepared to deal with this matter if the board had raised it in a preliminary opinion (cf minutes). In a faxed letter dated 28 June 2013 the appellant-opponent’s representative set out his views of the proceedings and concluded, referring to the statement he asked to be recorded in the minutes, that he had made it clear that he made this request for the purposes of review proceedings.

XVII. The appellant-patentee's arguments may be summarised as follows:

Admissibility of the appellant-patentee's appeal

The appeal was inadmissible.

Admissibility of documents (D11) to (D15)

The board should deny the admission of documents (D11) to (D15) into the proceedings. The presentation of these documents for the first time in appeal proceedings was improper in that it misapprehended the stated nature of appeal proceedings as a second instance judicial review. Documents (D11) to (D15) were not previously cited against the patent in the first instance. The appellant-opponent presented arguments against the impugned decision solely on these newly submitted documents. Thus, lack of novelty was alleged over document (D12) and (D13) and lack of inventive step was alleged over the combination of documents (D13) and (D14). The function of the Boards of Appeal was to give a judicial decision upon the correctness of a separate earlier decision (Case Law, 6th edition, 2010, section VII.E.I, pages 821-822). The appellant-opponent's reliance entirely on evidence and arguments derived from documents (D11) to (D15) was not in standing with the principle of appeal proceedings. The appellant-opponent had provided no reason as to why documents (D11) to (D15) submitted with their grounds of appeal, or the arguments based thereon, were not, or could not have been, submitted when auxiliary request 2 was on record in first instance opposition proceedings. By relying on these documents now, the appellant-opponent sought to convert appeal proceedings into an extension of the first instance opposition proceedings.

The subject-matter of claim 1 was identical to the subject-matter of claim 16 as granted. The notion of surprise advanced by the appellant-opponent fell short of credibility and was difficult to accept. If anything,

it was surprising that the appellant-opponent was surprised that the patent was maintained in the absence of any attack. It was not for the appellant-patentee to argue the presence of an inventive step but for the appellant-opponent to advance arguments against the presence of an inventive step. In the proceedings before the department of first instance arguments had only been advanced for claim 1 as granted, see notice of opposition, item VIII, point 4. The attack on claim 1 as granted was based on the known gene therapy approaches and thus irrelevant for the pharmaceutical composition claimed in auxiliary request 2. Accordingly, the appellant-opponent could not have been surprised by the decision of the opposition division. The only relevant question was whether documents (D11) to (D15) could have been presented earlier (Article 12(4) RPBA).

Auxiliary request 2 had been filed 2 months before the oral proceedings before the department of first instance. It was filed to distinguish the extracellular use of the antibodies, i.e. the application to the cell from the outside, from the known intracellular use. The antibody of the present invention induced apoptosis when applied extracellularly which was fundamentally different from the approach taken in the prior art, where antibodies were expressed intracellularly (see response to the notice of opposition, page 6, last paragraph; page 7, last paragraph, page 9, second but last paragraph, page 10, first paragraphs).

There was no need to search for new documents. Documents (D12), (D13), and (D14) were mentioned in the patent specification in paragraphs [006] and [007]. The attack based on different documents which were cited in

the patent amounted to a fresh case and was egregious. That the documents were dealt with in the response of the appellant-patentee did not mean that they were admissible. The concept of submission to further proceedings without contestation was not applicable (cf. decisions T 75/11, T 2102/08).

Documents (D12) and (D13) were not *prima facie* relevant. Claim 1 related to a pharmaceutical composition while documents (D12) and (D13) were argued to disclose an antibody. These documents had to be combined with document (D15) to provide an antibody achieving apoptosis. An antibody inducing apoptosis had not been made available in document (D12). The relevant time point was the publication date of documents (D12) and (D13). Document (D12) provided *in vitro* data only, there was no mention of apoptosis in document (D12). Envisaged uses of the antibodies were immunodiagnostics or immunotherapy with conjugates (page 1156, right hand column). Document (D13) disclosed cell death (generic) but not apoptosis (specific) in the context of antibody 4D5 and only *in vitro* experiments. Document (D11) related to the technical background. Document (D14) was not *prima facie* relevant, because it related to EGFR and not to Her2. Document (D15) was post-filed and post-published and irrelevant. The apoptotic effect of 4D5 had not been described before. Document (D15) made clear that restrictions on the availability to the public of the antibodies existed and would only be removed upon granting of the patent (see page 37, last 2 lines). The application referred to on page 2 of document (D15) had been published before the deposit, which was made in 1990, so antibody 4D5 could not have been deposited in the context of that application. The

scientific publications relied on by the appellant-opponent as showing that antibody 4D5 was publicly available were all authored by persons affiliated with Genentech (the applicant of document (D15)).

Admissibility of documents (D16) to (D17)

These documents had only been submitted to respond to arguments based on documents (D11) to (D15). If documents (D11) to (D15) were not admitted, these documents needed not to be admitted either.

Admissibility of the appellant-opponent's appeal

With documents (D11) to (D15) excluded, there remained nothing in the appellant-opponent's grounds of appeal setting forth any arguments as to why the appealed decision was incorrect. The appeal was thus unsubstantiated and had to be dismissed for this reason alone.

XVIII. The appellant-opponent's arguments may be summarised as follows:

Admissibility of documents (D11) to (D15)

Documents (D11) to (D15) were filed as early as possible and as an appropriate and immediate reaction to the developments and the decision in the first instance. Claim 1 of auxiliary request 2 was based on claim 16 as granted. This claim was attacked in the notice of opposition together with granted claim 1 to which it referred for lacking inventive step. Prior to the oral proceedings before the opposition division the

appellant-patentee did not provide any argument in favour of inventive step of the subject-matter of granted claim 16. Until the oral proceedings it had never been discussed in the opposition proceedings why a claim relating to a pharmaceutical composition comprising an antibody, that *per se* was considered not to be inventive, could be inventive. The appellant-opponent was taken by surprise that the opposition division finally maintained the patent on the basis of auxiliary request 2. Faced with this surprising and unfavourable decision of the opposition division, the opponent was required to search for additional art and to develop corresponding arguments in order to reverse the decision. Hence the earliest opportunity to file a substantiated reaction was the statement of grounds of appeal. The appellant-patentee had nearly four years time to analyse and react on the newly filed documents and arguments. It was in the board's discretion to admit the new documents (Case Law, 6th edition, section VII.C.1.1.2. on page 701).

Documents (D11) to (D15) should be admitted because they were *prima facie* highly relevant. Documents (D12) and (D13) disclosed specific anti-Her2 antibodies that turned out to induce apoptosis as could be seen in document (D15). Document (D15) qualified as expert opinion and disclosed the apoptotic properties of the antibodies made available by document (D12). Document (D13) was novelty destroying because it disclosed the anti-Her2 antibody 4D5 in the context of apoptosis. Document (D15) provided the deposit data for antibodies 7C2, 7F3 and 4D5 on page 37. The deposit of antibody 4D5 had been made in the context of an earlier application, see document (D15), page 2, line 27. The

deposit under the terms of the Budapest Treaty transported the antibody into the public domain. That antibody 4D5 was publicly available could also be derived from the fact that it was mentioned in many scientific publications, cf. decision T 923/92. Document (D14) described the anti-EGFR antibody mAb225 for the treatment of a human colorectal carcinoma cell line. It taught the importance of the ability to induce apoptosis by therapeutical antibodies against EGFR receptors. Hence it was highly relevant for the inventive step of the medical use of an anti-Her2 antibody that induced apoptosis. Document (D11) confirmed the common general knowledge that Her2 and EGFR were related receptor-tyrosine kinases. The appellant-patentee had addressed these documents in its response and had requested only recently not to admit them.

Substantiation of the appellant-opponent's appeal with regard to Article 83 EPC

The opposed patent did not provide any guidance how to obtain further apoptosis inducing anti-Her2 antibodies, besides the specific mAb74 antibody which could be obtained from deposited clone HB-12078.

XIX. The appellant-opponent requested that the decision under appeal be set aside and that the patent be revoked. The appellant-patentee requested that documents (D11) to (D15) filed with the appellant's statement of grounds of appeal and arguments based on those documents be not admitted into the proceedings and that the appeal of the opponent be dismissed.

Reasons for the Decision

Admissibility of the appeal of the appellant-patentee

1. As no written statement setting out the grounds of appeal has been filed, the appeal has to be rejected as inadmissible (Article 108 EPC, third sentence, in conjunction with Rule 101(1) EPC).

Admissibility of the appeal of the appellant-opponent

2. According to established jurisprudence of the Boards of Appeal, the admissibility of an appeal may be assessed *ex officio* at every stage of the appeal proceedings (cf. decision T 15/01, OJ EPO 2006, 153; reasons, point 1), and accordingly also during oral proceedings.

3. The appeal of the appellant-opponent complies with Articles 106 and 107 EPC as well as with the first and second sentence of Article 108 EPC and with Rule 99(1) EPC. This is also not disputed by the appellant-patentee. The admissibility of the appeal therefore depends solely on whether the statement setting out the grounds of appeal complies with Article 108 EPC, third sentence, and Rule 99(2) EPC.

Substantiation of the appellant-opponent's appeal (Article 108 EPC and Rule 99(2) EPC)

4. Article 108 EPC, third sentence, in conjunction with Rule 99(2) EPC stipulates that in the statement of grounds of appeal the appellant shall indicate the reasons for setting aside the decision impugned, or the

extent to which it is to be amended, and the facts and evidence on which the appeal is based. In line with established jurisprudence of the Boards of Appeal this is understood to mean that the arguments have to be clearly and concisely presented to enable the board and the other party or parties to understand immediately **why** the impugned decision is alleged to be incorrect, and on what facts the appellant bases its arguments, without first having to make investigations of their own (Case Law of the Boards of Appeal, 6th edition 2010, section VII.E.7.6.1 and decision T 220/83, OJ EPO 1986, 249).

5. In the present case, the impugned decision held that the claimed subject-matter of auxiliary request 2 was novel, was sufficiently disclosed and involved an inventive step.

6. Regarding the opposition grounds under Article 100(a) EPC (novelty and inventive step), the statement of grounds of appeal of the appellant-opponent relies on documents (D12) and (D13) to raise an objection as regards lack of novelty while lack of inventive step is argued on the basis of documents (D11), (D13) and (D14).

7. Documents (D11) to (D15) were not part of the first instance opposition proceedings but were filed by the appellant-opponent with its statement of the grounds of appeal (see section VI above). The appellant-opponent thus chose to base its argumentation on appeal on new evidence instead of providing reasons why the conclusions of the opposition division as regards Article 100(a) EPC (novelty and inventive step) vis-à-vis the documents on file in the first instance

proceedings were considered incorrect.

8. This board is aware that other Boards of Appeal have found that an appeal based entirely on new evidence, in other words a fresh case, may be admissible when the grounds for opposition have remained the same (see e.g. decision T 1557/05 of 4 May 2007, reasons, point 1.2). However, if this new evidence is subsequently not admitted in the appeal proceedings this has the consequence that the appellant's case on appeal is not substantiated (cf. decision T 1557/05, *supra*, reasons, point 2.13). Jurisprudence of the Boards of Appeal suggests that in this situation the appeal is unallowable. Since the substantiation of the appeal is a requirement for its admissibility, this board considers it appropriate to consider the question whether or not documents (D11) to (D15) should be admitted in the appeal proceedings in the context of the assessment of the admissibility of the present appeal. The appellant-opponent submitted that it made no difference whether the appeal was held inadmissible or had to be dismissed as being unallowable.

Admissibility of documents (D11) to (D15) in the appeal proceedings

9. The appellant-patentee requested not to admit documents (D11) to (D15) in the appeal proceedings. It argued that these documents were late-filed and created a fresh case on appeal.

10. It is settled case law of the Boards of Appeal that the purpose of the *inter partes* appeal procedure is mainly to give the losing party a possibility to challenge the

decision of the opposition division on its merits. Its function is to give a judicial decision upon the correctness of a separate earlier decision taken by the department of first instance. The appeal proceedings are thus largely determined by the factual and legal scope of the preceding opposition proceedings (see decision G 9/91 and opinion G 10/91 of the Enlarged Board of Appeal, OJ EPO 1993, 408 and 420). Given that the aim of opposition-appeal proceedings is to obtain a judicial review of the opposition decision, it follows that the board must as a rule take its decision on the basis of the issues in dispute before the opposition division. It can be directly inferred from the above that the parties have only limited scope to amend the subject of the dispute in second-instance proceedings and this principle is reflected in Article 12(4) RPBA. The appeal proceedings are not about bringing an entirely fresh case (Case Law of the Boards of Appeal, 6th edition 2010, section VII.E.7.6.1 and decision T 220/83, OJ EPO 1986, 249).

11. Article 12(4) RPBA provides that the board has discretion to hold inadmissible facts, evidence or requests which could have been presented or were not admitted in the first instance proceedings. The first question which thus arises in the present case is whether or not documents (D11) to (D15) filed with the statement of grounds of appeal of the appellant-opponent could have been presented in the first instance proceedings.

12. The board notes that claim 1 of auxiliary request 2 corresponds to claim 16 as granted. Independent claims 3, 5, 6, and 9 of auxiliary request 2 correspond to

claims 6, 8, 9 and 14 as granted, respectively. Also the dependent claims find correspondence in the set of claims as granted. This has not been contested by the appellant-opponent. Therefore the claims of auxiliary request 2 relate to subject-matter for which the appellant-opponent could have been expected to substantiate any ground of opposition relied upon within the nine months period referred to in Article 99(1) EPC. Accordingly, the filing of documents (D11) to (D15) cannot be regarded as being justified by the amendments made by the appellant-patentee before the opposition division.

13. The statement of grounds of appeal of the appellant-opponent provides no explanation let alone justification for the filing of new documents (D11) to (D15) on appeal. Only 4 years later the appellant-opponent argued that documents (D11) to (D15) were filed as early as possible and as an appropriate and immediate reaction to the developments and the decision in the department of first instance (see sections XV and XVIII, above).

14. In the board's view, the appellant-opponent's submission "*that until the oral proceedings it had never been discussed in the opposition proceedings why a claim relating to a pharmaceutical composition comprising an antibody that per se was considered not to be inventive, could be inventive*" is not supported by the facts. The opposition division, when finding in favour of inventive step of auxiliary request 2 (see section VII, above), followed in essence the line of reasoning brought forward by the appellant-patentee in the first instance proceedings (see e.g. its response

to the notice of opposition dated 18 March 2005, item VI on page 9 last two paragraphs to page 10, first two paragraphs), namely that the known intracellular expression of an anti-Her2 antibody from a gene construct to induce apoptosis in a cell does not render the extracellular use of an anti-Her2 antibody to induce apoptosis obvious. Thus, the opposition division held that the skilled person would not get any hint from document (D2), which disclosed intracellular expression of an antibody, that an antibody which is administered to the cells could have an apoptotic effect. Therefore, the preparation of a composition containing such antibodies, i.e. the subject-matter of claim 1 of auxiliary request 2, was considered to involve an inventive step.

15. If the appellant-opponent was surprised by the decision of the opposition division, such surprise may be an understandable subjective reaction but such subjective surprise cannot change the fact that the line of reasoning relied on by the opposition division was in the proceedings and was known to the appellant-opponent. Indeed, if the decision under appeal had been based on a line of reasoning unknown to the appellant-opponent, it should have argued that its right to be heard had been violated - which it did not. Moreover, the appellant-opponent did not state that it was surprised by the decision of the opposition division when it filed its grounds of appeal, but only when the admissibility of the documents was challenged by the appellant-patentee. Finally, the board notes that during opposition proceedings before the department of first instance the appellant-opponent raised no objections against auxiliary request 2 under Article 54

EPC (see decision under appeal, reasons, point 10.1) and objected only to claim 3 of auxiliary request 2 under Article 56 EPC but not to claim 1 (see decision under appeal, reasons, points 10.1 and 11.1).

16. Contrary to the position taken by the appellant-opponent, there is normally no need to rely on new documents to revert the impugned decision. Indeed, according to established jurisprudence of the Boards of Appeal the **factual** and legal framework of the appeal should not exceed that of the preceding opposition proceedings (see point 9 above). Accordingly, the board is not persuaded by appellant-opponent's argument that "*Faced with this surprising and unfavourable decision of the opposition division, the opponent was required to search for additional art and to develop corresponding arguments in order to revert the decision*."

17. The new documents (D11) to (D15) and arguments based thereon do not address the reasons underlying the impugned decision, in particular the issue that a claim relating to a pharmaceutical composition comprising an antibody that *per se* was considered not to be inventive, could be considered inventive, but bring about a **fresh case**, tantamount to a new opposition by attacking subject-matter which was present in the claims as granted on the basis of new evidence under Article 54 EPC and 56 EPC. This is also illustrated by the statement in the grounds of appeal that documents (D11) to (D15) are referred to "*to **further** illustrate that the claimed subject-matter is not patentable.*"(emphasis added). It is however not the purpose of *inter partes* appeal proceedings to give the appellant-opponent, who

did not succeed in the proceedings before the department of first instance, a second chance to file an opposition against the patent.

18. As regards the suggested requirement to search for new documents, the board notes that documents (D12), (D13), and (D14) and their disclosure regarding growth inhibitory effects of anti-Her2 mAbs and apoptotic effect of an anti-EGFR mAb were discussed in the patent in suit (see paragraphs [0006] and [0007]). Accordingly, the board is unable to identify any need to search for these documents.

19. As regards the appellant-opponent's contention that the appellant-patentee had four years time to analyse and react on the newly filed documents and arguments the board observes that, in fact, the appellant-patentee as the respondent to the appellant-opponent's case had 4 months to file its reply (Article 12(1)(b) RPBA), which it did (see section XII, above).

20. The board concludes from points 10 to 19 above, that documents (D11) to (D15) could have been presented in the first instance proceedings and that their submission on appeal was not a justified reaction to the opposition division's decision. Thus, the filing of documents (D11) to (D15) was not in due time but late.

21. Pursuant to Article 12(4) RPBA it is in the board’s discretion not to admit these documents. This discretion may be exercised having regard to *inter alia* the degree of relevance of the documents. In the present circumstances, i.e. the filing of a fresh case on appeal based on documents which could have been

presented in the first instance proceedings, and considering that the appellant-patentee requested not to admit these documents in the proceedings the board contemplated exercising its discretion under Article 12(4) RPBA not to admit documents (D11) to (D15) without even considering the relevance of the new evidence (cf. decision T 724/08 of 16 November 2012, reasons, point 3).

22. However, as the relevance of the documents was discussed during the oral proceedings, the board has also taken the relevance of the documents into consideration when exercising its discretion.

23. As to the degree of relevance required for a document to be admitted into the proceedings at a late stage, in accordance with the established case law of the Boards of Appeal such material should be ***prima facie* highly relevant** in the sense that it can reasonably be expected to change the eventual result and is thus highly likely to prejudice the maintenance of the European patent (see e.g. decision T 1002/92, OJ EPO 1995, 605, reasons, point 3.4).

Prima facie relevance of documents (D11) to (D15)

Document (D11)

24. Document (D11) is a review article on growth factor receptor tyrosine kinases and, according to the appellant-opponent, represents the common general knowledge that Her2 and EGFR were related receptor-tyrosine kinases.

25. This common general knowledge is not in dispute. Indeed, the patent in suit acknowledges that Her2 is a member of the epidermal growth factor receptor subfamily, which includes EGFR, see paragraph [0002]. Accordingly, the board is not persuaded that document (D11) is *prima facie* highly relevant.

Documents (D12) and (D13)

26. Document (D12) concerns the characterization of murine monoclonal antibodies reactive to either EGFR or Her2. Three specific anti-Her2 antibodies, termed 7C2, 7F3 and 4D5, were studied for binding specificity and inhibition of cell growth (see page 1552, left hand column, third full paragraph and page 1554, right hand column, first full paragraph). On first examination document (D12) does not disclose the structure of any of these anti-Her2 antibodies but only their arbitrary designations, which disclosure does not put the skilled person in possession of these antibodies. Moreover, on first examination document (D12) also does not disclose that any of the anti-Her2 antibodies induces apoptosis.

27. Document (D13) relates to the use of monoclonal antibodies as agonists in cancer therapy. The authors reviewed evidence supporting the concept that antibodies directed against cell surface molecules on many types of tumor cells can act as ligands, resulting in powerful antitumor effects mediated by signal transduction (see introduction). Document (D13) discloses that antibody 4D5 has been found to induce both cell cycle arrest (CCA) and cell death in erbB-2R overexpressing breast cancer cells (see page 5304, left hand column, second paragraph). The board notes that

erbB-2 is a synonym of Her2. On first examination also document (D13) does not disclose the structure of the 4D5 antibody or that it induces apoptosis.

28. The appellant-opponent submitted that documents (D12) and (D13) were *prima facie* highly relevant as they provided specific anti-Her2 antibodies that turned out to induce apoptosis as could be seen from post-published document (D15).

29. That a disclosure destroys novelty only if the teaching it contains is reproducible is settled case law of the Boards of Appeal (Case Law of the Boards of Appeal, 6th edition 2010, section I.C.2.12), and has not been contested by the appellant-opponent.

30. In the board's judgement, none of the specific antibodies mentioned in document (D12), i.e. antibodies 7C2, 7F3 or 4D5, or in document (D13), i.e. antibody 4D5, can be considered as having been "made available to the public" by the mere fact that documents (D12) and (D13) refer to these antibodies by their arbitrary designations. The board noted during the oral proceedings, that according to established case law of the Boards of Appeal, biological material which is the subject of a scientific publication is not automatically considered as being publicly available (Case Law of the Boards of Appeal, 6th edition 2010, section I.C.1.8.7). This was not contested by the appellant-opponent.

31. The appellant-opponent argued firstly, that document (D15) provided the necessary evidence for the public availability of the antibodies referred to in documents

(D12) and (D13). Thus, document (D15) disclosed that the antibody 4D5 was deposited at the American Type Culture Collection (ATCC) and thus available, because the deposit under the terms of the Budapest Treaty transported it into the public domain. Secondly, it argued that antibody 4D5 had already been deposited in the context of an earlier application cited on page 2, line 27 of document (D15). Thirdly, the appellant-opponent submitted that in line with decision T 923/92 (OJ 1996, 564, reasons, point 43) the antibody 4D5 was publicly available because it was mentioned in several documents referred to in document (D13).

32. The board is not persuaded by any of these arguments. In fact, document (D15) discloses that antibodies 7C2 and 7C3 were deposited at the ATCC on 17 October 1996, while antibody 4D5 was deposited on 24 May 1990 (see page 37, lines 26 to 32). Document (D15) therefore provides evidence that none of the antibodies 7C2, 7F3 and 4D5 had been deposited before the publication date of document (D12), which lies in March 1990, and which is the relevant date for the assessment of its disclosure in the context of Article 54(2) EPC.

33. Document (D13) was published in October 1994, and thus after the deposit date of antibody 4D5. However, document (D15) also states (see page 37, lines 33 to 40) that the deposits at the ATCC were made under the provisions of the Budapest Treaty on the international recognition of the deposit of microorganisms for the purpose of patent procedure and the regulations thereunder. Contrary to the submission by the appellant-opponent, the deposit at the ATCC for patent purposes does not make the deposited antibody publicly

available. Indeed, it can be taken from document (D15) itself, see page 37, lines 36 to 40, that restrictions applied on the availability to the public of the deposited cultures and that these restrictions would only be removed upon granting of the patent corresponding to document (D15). Considering that the filing date of document (D15) is 9 October 1997, no patent could possibly have been granted on the basis of document (D15) prior to the relevant date of document (D13). As regards the further argument that the deposit of antibody 4D5 had been made in the context of an earlier application, the board notes that the publication date of that application is 27 July 1989 (see document (D15), page 2, line 27). This date lies prior to the deposit date of antibody 4D5 with the ATCC, which is 24 May 1990 (see point 32, above). Accordingly, this argument did not persuade the board either.

34. The board concludes that document (D15) cannot be taken to provide evidence for the availability to the public of antibodies 7C2, 7F3 and 4D5 at the publication dates of either document (D12) or document (D13).

35. As regards the third argument, namely that antibody 4D5 was referred to in many scientific publications and hence available to the public, the board takes the following view. The appellant-opponent relied on decision T 923/92, *supra*. The factual situation underlying decision T 923/92, *supra*, differs from the present situation in that in the former case there was a large body of evidence available which showed that the biological material in question was generally available and freely exchanged in the scientific community and that neither secrecy agreements nor

contractual obligations among the research workers restricted the use or dissemination of the biological material. In the present case, the mere reference to antibody 4D5 in several scientific publications is thus not enough to acknowledge its public availability in the absence of corroborating evidence that neither secrecy agreements nor contractual obligations among the authors of these documents and the owners of antibody 4D5 restricted the use or dissemination of the antibody.

36. In the board's judgement it was for the appellant-opponent, who relied on documents (D12) and (D13) to object to the novelty of claim 1 of auxiliary request 2, also to provide the necessary evidence that the antibodies 7C2, 7F3, and 4D5 were indeed available to the public at the relevant dates to allow the board to assess without further investigation (i.e. *prima facie*) the facts relied on to build its case. This the more so since, in the present case, none of the documents relied on by the appellant-opponent before the department of first instance in support of its novelty objection then, was considered by the opposition division to provide an enabling disclosure of an anti-Her2 antibody (see section VI, above). The appellant-opponent ought to have been aware that the enablement of the anti-Her2 antibodies was an issue to be considered when basing its case on documents (D12) and (D13).

37. It is established jurisprudence that in opposition proceedings before the EPO, which are contentious proceedings, each party bears the burden of proof for the facts it alleges (cf Case Law of the Boards of

Appeal, 6th edition 2010, section VI.H.5.1.1). The preservation of judicial impartiality is a paramount requirement in *inter partes* proceedings. Indeed, it is not for the board to make investigations of its own or to alert a party to a possible argument against it. Alerting a party to a possible argument against it and on a ground on which the burden of proof rests on it, in advance of the oral proceedings would amount to a clear violation of the principle of impartiality (Case Law of the Boards of Appeal, 6th edition 2010, section VII.E.5.2). Similarly, the Enlarged Board of Appeal has held that a party is responsible for the conduct of its case and it is for the party to submit the necessary arguments to support its case on its own initiative and at the appropriate time (see decision R 2/08 of the Enlarged Board of Appeal of 11 September 2008, reasons, points 8.5 and 9.10).

38. The board concludes that neither document (D12) nor document (D13) make available anti-Her2 antibodies that induce apoptosis. Accordingly, no case has been made out that documents (D12) and (D13) are *prima facie* highly relevant let alone more relevant than the prior art relied on before the department of first instance.

Document (D14)

39. Document (D14) discloses that mAb 225, an anti-EGFR antibody, induces apoptosis in the human colorectal carcinoma cell line, DiFi, which overexpresses EGFR. The appellant-opponent submitted that this document taught the importance of the ability to induce apoptosis by therapeutical antibodies against EGFR receptors. Hence it was highly relevant for the

inventive step of the medical use of an anti-Her2 antibody that induced apoptosis.

40. The board notes that document (D14) does not mention Her2 (or erbB-2). Moreover, there is no general teaching in document (D14) that antibodies directed against receptor-tyrosine kinases induce apoptosis. The board concludes that document (D14) provides no motivation to replace the anti-EGFR antibody with an anti-Her2 antibody. Accordingly, document (D14) cannot be *prima facie* highly relevant.

Document (D15)

41. Document (D15) is a post-filed and post-published document. The appellant-opponent cited this document as expert opinion which disclosed the apoptotic priorities of the antibodies made available by document (D12).

42. In view of the fact that document (D12) did not *prima facie* make available the anti-Her2 antibodies (see points 26 to 38, above), further evidence relating to their properties is of no relevance. Accordingly, document (D15) is not *prima facie* highly relevant.

Conclusion on prima facie relevance

43. In summary, none of documents (D11) to (D15) is *prima facie* highly relevant in the sense that it could reasonably be expected to change the eventual result and was thus highly likely to prejudice maintenance of the European patent in suit. For this reason and for the reasons set out above (see points 10 to 20), the board decides to exercise its power under

Article 12(4) RPBA not to admit documents (D11) to (D15) in the appeal proceedings. Accordingly documents (D16) and (D17) filed by the appellant-patentee are also not admitted.

44. This has the consequence that the appellant-opponent's case on appeal - at least as regards its submissions under Article 54 EPC and Article 56 EPC in sections C and D.1 to D.3, respectively, of its grounds of appeal loses its factual and evidential basis, i.e. is not substantiated.

45. It therefore remains to be decided whether or not what remains of the appellant-opponent's case on appeal allows the board to understand **why** the decision under appeal should be set aside, in other words why it is incorrect (see point 4, above).

46. On page 2 of the grounds of appeal (see paragraphs 2, 4 and 6) various statements to the effect that the appellant-opponent disagrees with the opposition division's decision as regards auxiliary request 2 can be found, but no reasons are given why the decision was wrong.

47. In section D on page 12 of the grounds of appeal the appellant-opponent submits that the assessment of the opposition division that the claims of auxiliary request 2 fulfil the requirements of Article 56 EPC was erroneous. Starting from the statement in the appealed decision that the subject-matter of claim 1 differed from the teaching of document (D2) in that it referred to a pharmaceutical composition already containing the antibody it is submitted that: "*Yet, from the cited*

prior art already discussed in the opposition proceedings [as well as the additional documents provided herein], it is evident that the use of an anti-Her2 antibody clearly lies in the immunotherapy of cancerous diseases, like in breast or ovarian cancer/carcinomas. Accordingly, the provision of pharmaceutical compositions which comprise such an obvious medical tool can certainly not carry the day for Patentee".

48. In the board's judgement, the argumentation advanced by the appellant-opponent fails to address the reasoning given by the opposition division for acknowledging an inventive step, namely that intracellular expression of an antibody from a gene construct does not render a pharmaceutical composition comprising an antibody which is produced outside of the cell and which has an apoptotic effect when administered to the cells obvious (see section VII, above). It falls thus short of providing any reasons why the decision is erroneous.

49. Finally in section E of the grounds of appeal (see page 16) under the heading "enabling disclosure" the appellant-opponent submits as follows: "*Accordingly, at the most, the opposed patent provided for one antibody, namely mAb74, which is capable of inducing relevant apoptosis in Her2 expressing cells. Hence, the opposed patent does not provide any guidance how to obtain further apoptosis inducing anti-Her2 antibodies, besides the specific mAb74 antibody which can be obtained from deposited clone HB-12078.*"

50. The opposition division had decided that in view of the specific teaching of the application with regard to e.g.

mAb74, together with the skilled person's knowledge of routine procedures for producing antibodies and testing them for apoptosis, claim 1 was sufficiently disclosed over the whole of the claimed scope (see section VIII, above).

51. The board notes that appellant-opponent's submission corresponds in essence to its submission made in its notice of opposition (see paragraphs VI.3. and VI.4.) but fails to provide any arguments **why** the decision under appeal is incorrect on this point, contrary to the provisions of Rule 99(2) EPC.

52. The board concludes from points 45 to 51 above, that none of the passages on pages 2, 12 and 16 of the grounds of appeal, separate or together, explain why the conclusions of the opposition division were wrong.

53. The board concludes that the appellant-opponent's case on appeal is not substantiated contrary to the requirements of Article 108 EPC, third sentence, in conjunction with Rule 99(2) EPC and therefore it has to be rejected as inadmissible (Rule 101(1) EPC).

The appellant-opponent's representative's letter of 28 June 2013

54. The board makes no comment on the substance of the appellant-opponent's representative's letter of 28 June 2013 which was filed after the oral proceedings and thus after the board's decision had been announced. On the procedural point that the representative had made it clear that his request to have a statement recorded in the minutes was made for the purposes of review

proceedings, the board notes that the minutes, which provide a contemporary record of the statement which the representative asked to be minuted, make no mention of review proceedings.

Order

For these reasons it is decided that:

Both appeals are rejected as inadmissible.

The Registrar: The Chairman:

P. Cremona C. Rennie-Smith