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Datasheet for the decision of 25 October 2016

Case Number: T 1592/12 - 3.3.04

Application Number: 00959423.5

Publication Number: 1210115

IPC: A61K39/395, C07K16/32

Language of the proceedings: EN

Title of invention:
Dosages for treatment with anti-ErbB2 antibodies

Patent Proprietor:
Genentech, Inc.

Opponents:
BioGeneriX AG
Stada R & D GmbH
Teva Pharmaceutical Industries Ltd.
Celltrion, Inc.
Sandoz AG
Synthon B.V.

Headword:
Herceptin dosage regimen/GENENTECH

Relevant legal provisions:
EPC Art. 83, 114(2)
RPBA Art. 13(1), 13(3)

Keyword:
Sufficiency of disclosure - main (sole) request (no)

Decisions cited:
T 0609/02, T 0157/03, T 0433/05, T 0601/05

Catchword:

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Case Number: T 1592/12 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 25 October 2016

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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 4 May 2012 revoking European patent No. 1210115 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman B. Claes
Members: R. Morawetz
M.-B. Tardo-Dino

Summary of Facts and Submissions

I. The appeal of the patent proprietor (hereinafter "the appellant") lies against the decision of the opposition division to revoke European patent No. 1210115. The patent in suit, entitled "*Dosages for treatment with anti-ErbB2 antibodies*", was granted in respect of European patent application No. 00959423.5 and claims priority of US 151018P, filed on 27 August 1999 (hereinafter "first priority") and US 213822P, filed on 23 June 2000 (hereinafter "second priority").

Claim 1 as granted read:

"1. Use of the anti-ErbB2 antibody huMab 4D5-8 in the manufacture of a medicament for use in a method for treating a human patient diagnosed with a breast cancer characterized by overexpression of ErbB2, said method comprising the steps of administering to the patient an initial dose of 8 mg/kg of the anti-ErbB2 antibody; and administering to the patient a plurality of subsequent doses of the antibody in an amount that is 6 mg/kg, wherein the doses are separated in time from each other by three weeks."

II. The patent was opposed by six opponents, *inter alia* under Articles 100(b) and 100(c) EPC. The opponents requested revocation of the patent in its entirety.

III. The opposition division decided that the claims of the sole request before it (claims as granted) fulfilled the requirements of Article 123(2) EPC but that the patent failed to meet the requirements of Article 83 EPC in relation to the subject-matter defined in claims 1 and 4.

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

D2 Goldenberg M.M., Clinical Therapeutics (February 1999), vol. 21, pages 309 to 318.

D4 Pegram M.D. *et al.*, Journal of Clinical Oncology (1998), vol. 16, pages 2659 to 2671.

D9 Baselga J. *et al.*, Journal of Clinical Oncology (1996), vol. 14, pages 737 to 744.

D39 Declaration of Jerome A. Moore, dated 8 December 2011.

D40 Declaration of N. "Shasha" Jumbe, dated 8 December 2011.

D54 Herceptin®, Final Labeling Text, 2010, Genentech, Inc.

D57 Declaration of George Grass, dated 11 September 2012

D66 UK High Court judgment [2014] EWHC 1094 (Pat), dated 10 April 2014.

D67 UK Court of Appeal judgment [2015] EWCA Civ 57, dated 6 February 2015.

D68 Declaration of Professor Pater Barrett-Lee, dated 12 August 2016.

D69 Declaration of Professor Alan Vincent Boddy, dated 11 August 2016.

D70 Letter from Genentech Inc. to G.D. Jones, Director, Division of Application Review and Policy, Food and Drug Administration, pages 1 to 9, dated 20 February 2001.

V. In its statement of grounds of appeal the appellant maintained the set of claims as granted as its main request. No auxiliary requests were filed.

VI. Opponents 01 to 06 (hereinafter "respondents I to VI", respectively) filed written replies to the statement of grounds of appeal.

VII. The parties were summoned to oral proceedings and subsequently informed of the board's preliminary opinion in a communication according to Article 15(1) RPBA.

VIII. With letter dated 15 August 2016 the appellant submitted two UK judgments, documents D66 and D67, along with two declarations, documents D68 and D69.

IX. On 8 September 2016 observations by a third party (Article 115 EPC) including document D70 were filed.

X. Respondent IV submitted with letter dated 21 September 2016 a further copy of document D70.

XI. As announced beforehand in writing, respondents I, II, III and V were neither present nor represented at the oral proceedings before the board on 25 October 2016, which in accordance with Rule 115(2) EPC and Article 15(3) RPBA were therefore conducted in their absence. At the end of the oral proceedings the chairman announced the board's decision.

XII. The arguments of the appellant relevant for the present decision may be summarised as follows:

Documents D68 and D69

Declarations D68 and D69 had been provided to ensure that significant points arising from the UK proceedings were not misrepresented in the appeal proceedings.

Document D70

Document D70 was not relevant; it was dated after the filing date of the patent.

Main request

Sufficiency of disclosure - claim 1

The issue was whether the European patent disclosed the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. Carrying out the treatment regimen as defined in claim 1 led to success (see e.g. document D54).

In decision T 609/02 the board had emphasised that the application had to disclose the suitability of the product to be manufactured for the claimed therapeutic application. In the present case, the suitability of Herceptin® for treating breast cancer characterised by overexpression of ErbB2 was well known in the art. It had not been established in decision T 609/02 that a patent had to demonstrate that a new dosage regimen for a known drug worked. The facts in the present case were completely different from those considered in decision T 609/02.

Decisions T 433/05 and T 601/05 confirmed that the pharmaceutical usefulness of an agent could be evident from common general knowledge and that the opposition division's approach based on decision T 609/02 was incorrect. Decisions T 157/03 and T 1262/04 acknowledged that data could be provided subsequent to the filing date.

Paragraphs [0001], [0013], [0016], [0019], [0028], [0034], [0088], [0168], [0203], [0214], [0217] of the patent and the data of example 2 provided sufficient information for the skilled person to carry out the invention. Motivated by the reference to infrequent dosing the skilled person would study the data of example 2. The correct half-life of Herceptin® could be obtained from the data in Table 2 and Figure 3 of the patent, see declarations D39 and D40.

Example 6 provided a detailed protocol for administration of the Herceptin® antibody every three weeks, starting with a loading dose of 8 mg/kg followed by maintenance dose of 6 mg/kg every three weeks (see paragraph [0230]). The patent disclosed that the simulation carried out in example 6 suggested that trough concentration would be 17 µg/ml and thus within the required window for therapeutic efficacy. In addition, paragraph [0233] stated that it was believed that the claimed treatment regimen was effective. The clinical trial described in example 6 had been performed after filing the patent and shown to work.

Motivated by example 6 the skilled person would study the rest of the patent, in particular the data of example 2.

Document D70 did not show that additional data were

needed to ascertain the correct half-life.

XIII. The arguments of the respondents relevant for the present decision may be summarised as follows:

Declarations D68 and D69

Declarations D68 and D69 were not relevant to the issue to be decided and could have been filed earlier. The UK proceedings had ended over 18 months earlier. The appellant had waited until 2 months before the oral proceedings before submitting these two expert declarations. It had given no reasons why they could not have been submitted immediately after the UK trial. In such circumstances, the additional declarations should be considered "late-filed" and not be admitted into the proceedings.

Document D70

Document D70 was relevant to the issue to be decided as it showed that the trial data - Herceptin® (trastuzumab) administered every three weeks in combination with Taxol® (paclitaxel) - used to determine the longer half-life of Herceptin® were not in the patent. The document was not complex and could not come as a surprise to the appellant as it was its own document.

Main request

Sufficiency of disclosure - claim 1

The patent in suit did not disclose any experimental evidence showing that the treatment regimen of granted

claim 1 was actually applied.

It was established case law of the Boards of Appeal in relation to sufficiency of disclosure for second medical use claims that the description had to disclose (at the effective date) the suitability of the product (composition or dosage regimen) for the therapeutic application claimed (see e.g. decision T 609/02), suitability being proven by at least some information in the form of experimental tests, for instance.

Herceptin® was known to be efficacious when administered at a loading dose of 4 mg/kg followed by a maintenance dose of 2 mg/kg every week (in brief 4/2/1). The essential feature distinguishing the claimed invention from the known use of Herceptin® was the different dosage regimen. The specification had to demonstrate that despite the change in dosage regimen, the effect of Herceptin® remained unchanged.

It was part of the skilled person's common general knowledge that a serum trough concentration of at least 10 to 20 µg/ml was necessary for therapeutic efficacy of Herceptin®, that the dosing interval should not be substantially longer than the half-life of the antibody and that the half-life of Herceptin was thought to be around one week.

The patent in suit proposed a high initial dose followed by lower maintenance doses. Moreover, the patent in suit taught that the dosage interval was "*most preferably, 1 week or less*" (see paragraphs [0016] and [0214]). The skilled person would thus have relied on a half-life of one week for assessing the feasibility of the claimed dosing regimen.

The clinical data in the patent related to trials in which the conventional weekly dosing interval had been used, the experimental aspect being the increase in the initial dose (see example 2). The patent in suit provided two data sets, Table 2 and Figure 3. Figure 3 was mentioned once in the patent at the top of page 26 but no significance was attached to the data shown in Figure 3 and the patent did not combine the two data sets.

The skilled person would not have calculated the half-life of Herceptin® anew. The patent in suit contained neither the term "*half-life*" nor any suggestion that the skilled person should reconsider the half-life of Herceptin®.

To calculate the longer half-life from the data of example 2 the skilled person needed more information than that given in the patent, namely that a different model was to be used and that the data were to be combined, see expert evidence D39, D40 and D57 provided by the appellant.

Document D70 showed that to arrive at the longer half-life the skilled person had to rely on data which were in neither the prior art nor the patent.

While example 6 focused on a 3-weekly regimen, Herceptin® was administered in combination with chemotherapy. It was not explained why this regimen should be effective for the treatment of breast cancer or what kind of simulation had been done, e.g. that example 2 was the source of the data for the simulation or whether the simulation was based on a combination with chemotherapy. Since example 6 did not comprise any experimental data, the skilled person could not know

that the trial described in example 6 worked. The skilled person reading example 6 would not have calculated the half-life anew.

The skilled person reading example 6 and aware that the half-life of Herceptin® was one week also had no reason to accept that the claimed regimen was in fact effective. This raised "serious doubts" about the likely success of the claimed dosage regimen.

XIV. The appellant requested that the decision under appeal be set aside and that the patent be maintained as granted.

The respondents requested that the appeal be dismissed.

Reasons for the Decision

1. Respondents I, II, III and V were neither present nor represented at the oral proceedings. The board considered it expedient to conduct the scheduled oral proceedings in their absence in order to reach a final decision in this appeal case. They were treated as relying on their written case in accordance with Rule 115(2) EPC and Article 15(3) RPBA.

Admissibility of declarations D68 and D69

2. The appellant submitted declarations D68 and D69 two months before the oral proceedings took place. They were said to address some of the findings in UK courts in revocation proceedings involving the EP (UK) counterpart of the patent in suit. Respondents I, III, and IV requested that they not be admitted into the proceedings.

3. The board notes that the UK proceedings and the resulting judgments turned on inventive step, whereas the present decision is solely concerned with sufficiency of disclosure (see below, points 14 to 43).

4. Judgment D66 was handed down on 10 April 2014, judgment D67 on 6 February 2015. The appellant has provided no justification for not filing declarations D68 and D69 immediately after the two judgments were pronounced.

5. The board considers that filing the declarations shortly before the oral proceedings has effectively deprived the respondents of a reasonable opportunity to consult their experts and prepare suitable evidence in response.

6. In view of the above, the board concludes that the two declarations D68 and D69 were submitted late, that they do not appear to address the issue to be decided, and that admitting them into the proceedings would be prejudicial to the right to be heard of the respondents.

7. Therefore, the board decided not to admit declarations D68 and D69 into the appeal proceedings (Article 114(2) EPC and Articles 13(1) and (3) RPBA).

Admissibility of document D70

8. Document D70 is a copy of a letter from the appellant to the US Food and Drug Administration (FDA) dated 20 February 2001. Respondents IV and VI requested that it be admitted into the appeal proceedings.

9. The appellant requested that document D70 not be admitted as it was dated after the filing date of the patent in suit and was thus irrelevant for the issue to be decided, *i.e.* sufficiency of disclosure.

10. The board considers that document D70's date does not necessarily disqualify it as evidence. After all, the expert declarations relied on by the appellant in the context of sufficiency of disclosure, *i.e.* declarations D39, D40 and D57, are also dated after the filing date of the patent in suit.

11. Document D70 reports that preliminary data from a clinical trial involving administration of Herceptin® every three weeks in combination with Taxol® indicated that the half-life of Herceptin® was considerably longer than originally determined.

12. The board considered that the question as to which clinical data led to a reconsideration of the half-life of Herceptin® was relevant to the issue to be decided (see below). Moreover, document D70 was not considered to be complex; it was only a few pages long and moreover had been known to the appellant before it was filed in these appeal proceedings.

13. Therefore, the board decided to admit document D70 into the appeal proceedings (Article 114(2) EPC and Articles 13(1) and (3) RPBA).

Main (sole) request

Sufficiency of disclosure - claim 1

14. Independent claim 1 is formulated as a "Swiss-type" claim and relates to the use of the anti-ErbB2 antibody

huMab 4D5-8, commonly known as trastuzumab (Herceptin®), for treating a human patient diagnosed with breast cancer, whereby the antibody is administered at an initial dose of 8 mg/kg followed by maintenance doses of 6 mg/kg every three weeks (in brief 8/6/3).

15. Sufficiency of disclosure requires that the European patent application or European patent disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Articles 83 and 100(b) EPC). According to established case law of the boards of appeal (see decision T 609/02 of 27 October 2004, point 9 of the reasons) where a therapeutic application is claimed in the form of a "Swiss-type" claim, attaining the claimed therapeutic effect is a functional technical feature of the claim. As a consequence, under Article 83 EPC, unless this is already known to the skilled person at the priority date, the application must disclose the suitability of the product to be manufactured for the claimed therapeutic application. In this context, post-published evidence may be taken into account, but only to back up the findings in the patent application and not to establish sufficiency of disclosure on their own.

16. The principles established in decision T 609/02, *supra*, in relation to sufficiency of disclosure of a second medical use claim do not relate only to the factual situation in that specific case, but are accepted to be generally applicable to such claims (see Case Law of the Boards of Appeal of the EPO, 8th edition 2016, section II.C.6.2 and decisions referred to therein).

17. The appellant's argument that for compliance with the requirement of sufficiency of disclosure it suffices that the skilled person can carry out the claimed dosage regimen thus fails.

18. The appellant's further argument that for such compliance it suffices that the suitability of the Herceptin® antibody for treating breast cancer characterised by overexpressing ErbB2 was well known in the art also fails, for the following reasons.

19. In the present case, the technical contribution does not reside in the provision of Herceptin® for treating breast cancer. Indeed, the parties agree that, at the effective date of the patent, Herceptin® was well known to be suitable to treat breast cancer - if given weekly, and more specifically with a dosage regimen of a starting dose of 4 mg/kg followed by weekly doses of 2 mg/kg (in brief 4/2/1).

20. However, the claimed treatment regimen differs from the known treatment regimen in the administration frequency of Herceptin®, *i.e.* every three weeks instead of weekly. From the general principle that the extent of the monopoly conferred by a patent should correspond to, and be justified by, the technical contribution made to the art, it follows that it is the suitability of this different administration frequency to treat breast cancer which needs to be disclosed in the patent for the requirements of sufficiency of disclosure to be met (see also decision T 609/02, *supra*, reasons, point 8).

21. Accordingly, since in the present case the pharmaceutical usefulness of Herceptin® for treating breast cancer is undisputed, decisions T 433/05 of

14 June 2007 and T 601/05 of 2 December 2009, which held that an active agent's pharmaceutical usefulness may be evident from common general knowledge, do not assist the appellant's case.

22. According to established case law, a sufficient disclosure must be made at the effective date of the patent, on the basis of the information in the patent together with the common general knowledge then available to the skilled person (*cf.* decision T 609/02, *supra*, reasons, point 8).

23. The appellant did not dispute that the following facts summarise the common general knowledge of the skilled person before the first priority date of the patent in suit. A serum trough concentration of at least 10 to 20 µg/ml Herceptin® is necessary for therapeutic efficacy in the treatment of breast cancer; the appropriate dosing interval suitable for achieving accumulation of the antibody up to the targeted serum trough concentration should not be substantially longer than the half-life of the corresponding antibody because otherwise no accumulation to the targeted serum trough concentration is achieved; and the half-life of Herceptin® is around one week (see also document D2, page 309, left hand column and right hand column, paragraph bridging pages 312 and 313; document D4, page 2660, left hand column, third paragraph, Table 6; and document D9, page 738, right hand column, 4th paragraph and page 739, right hand column, second paragraph).

24. The patent in suit concerns the treatment of human patients diagnosed with cancer overexpressing ErbB2 wherein the anti-ErbB2 antibody is administered by front loading which has the advantage of increased efficacy by reaching a target serum drug concentration

early in treatment (see paragraphs [0001], [0016] and [0088]). The patent in suit discloses infrequent dosing of anti-ErBB2 antibodies (see paragraph [0001]) but also that the initial dose is separated in time from the first subsequent dose *"most preferably 1 week or less*" (see paragraphs [0016] and [0214]) while paragraph [0028] discloses that the first dose and subsequent doses are separated by about two weeks to about two months. The patent furthermore sets out numerous permutations of possible doses and dosage intervals including the claimed regimen (see paragraphs [0017] to [0024] and paragraphs [0166] to [0172]).

25. Example 1 of the patent in suit provides details for the preparation of the Herceptin® antibody and for combination therapy with chemotherapy. On day 0, patients received a 4 mg/kg dose of Herceptin®, followed by weekly administration of 2 mg/kg antibody (in brief 4/2/1), while chemotherapy was started 24 hours after the initial dose of Herceptin®. The administration frequency of Herceptin® is thus the same as in the prior art, *i.e.* weekly.

26. Also example 2 relates to the 4/2/1 dosing regimen known in the prior art. Table 2 reports Herceptin® anti-ErbB2 antibody trough and peak serum concentrations for the first 8 weeks of treatment, while Figure 3 is a graph of Herceptin® trough serum concentration from week 2 through week 36 of treatment. The patent in suit states with reference to Figure 3 that "*trough serum concentrations tended to increase through week 12 and tended to plateau after that time*" (see paragraph [0198]). The board notes however that no importance is attached to the data shown in Figure 3, nor are these data combined with those of

Table 2.

27. Example 2 mentions one alternative dosing regimen wherein an initial dose of 8 mg/kg is followed by weekly administration of 4 mg/kg Herceptin® (in brief 8/4/1), and notes a significant difference between the Herceptin® trough serum concentration in the responders and non-responders. The patent in suit then concludes that the data disclosed in example 2 indicate "*that front loading of antibody, such that a target serum concentration is reached more quickly, may be associated with improved outcomes*" (see paragraphs [0201] and [0203]).

28. The board concludes from the above that the skilled person, having read the general description of the patent in suit which emphasises weekly administration as most preferred and having studied examples 1 and 2 which likewise apply weekly administration, would rely on Herceptin®'s known half-life of one week to assess the suitability of the claimed dosing regimen. The skilled person would thus have serious doubts that three-weekly administration of Herceptin® would suffice to maintain the serum trough concentration of Herceptin® required for effective treatment of breast cancer (see point 23). Consequently, the suitability of the claimed dosing regimen for the treatment of breast cancer cannot be considered to have been disclosed.

29. The appellant argued that the patent in suit repeatedly emphasised a more infrequent dosing than that known from the prior art. The skilled person would therefore study the data provided in example 2 and understand therefrom that the half-life of the huMab 4D5-8 antibody was sufficiently long for administration once

every three weeks.

30. The board notes however that the half-life of Herceptin® is not mentioned in example 2 or anywhere else in the patent. The most preferred dosing frequency in the patent in suit is disclosed to be weekly, and also the administration frequency of both trials in example 2 is weekly. Weekly administration is in line with a half-life of one week, *i.e.* the half-life of Herceptin® the skilled person was familiar with (see point 23 above).

31. The board further notes that the sole conclusion drawn in the patent in suit as regards example 2 concerns the beneficial effect of front loading in the context of weekly dosing of Herceptin®. However, no conclusions are drawn in the patent in suit from the data depicted in Figure 3, and no pharmacokinetic analysis of the data of Table 2 or Figure 3 is carried out. In these circumstances the board considers that the skilled person had no reason to analyse the data of example 2 with a view to reassessing the half-life of Herceptin®.

32. Therefore, the question whether the skilled person would have recognised that the data in Table 2 and Figure 3 needed to be combined, and a pharmacokinetic model different from the one used in the prior art was required to actually arrive at a half-life of 28 days does not arise. Accordingly, and for the same reasons, declarations D39, D40 and D57 - which merely confirm that an analysis of the data in example 2 yields a half-life of 28 days - do not assist the appellant's case.

33. In view of the above considerations the appellant's main argument fails.

34. The appellant's further argument was based on example 6 of the patent in suit. This is a prophetic example which discloses that the recommended dose of Herceptin® at the relevant date was 2 mg/kg once weekly and proposes that "*Patients will be administered HERCEPTIN® every three weeks instead of weekly, along with paclitaxel (175mg/m^2 every three weeks). Simulation of the proposed treatment regimen suggests that the trough serum concentrations will be 17 mcg/ml, in the range (10-20 mcg/ml) of the targeted trough serum concentrations from previous HERCEPTIN® IV clinical trials. After the first 12 patients the PK parameters will be assessed, if exposure is felt inadequate, then the dose will be increased to 8 mg/kg every three weeks for the remaining 12 patients*" (see paragraph [0227]). The example concludes by stating that "*it is believed that the above treatment regimen will be effective in treating metastatic breast cancer, despite the infrequency with which HERCEPTIN® is administered to the patient*" (see paragraph [0233]).

35. The board notes that the patent in suit does not disclose the nature of the described "*simulation of the proposed treatment regimen*". Moreover, the patent in suit neither explains why the treatment regimen will be effective nor contains data demonstrating the actual performance of the treatment regimen described.

36. The board further notes that the skilled person reading example 6 is however aware that the half-life of Herceptin® is assumed in the art to be around one week, and thus too short to maintain an effective trough serum concentration when Herceptin® is

administered once every three weeks (see point 23 above).

37. The board concludes from the above that the skilled person would thus have serious doubts that three-weekly administration of Herceptin® would suffice to maintain the serum trough concentration of Herceptin® required for effective treatment of breast cancer (see point 23). This has the consequence that the suitability of the claimed dosing regimen for the treatment of breast cancer cannot be considered to have been disclosed by example 6 either.

38. The appellant submitted that "*the skilled person who wanted to carry out the claimed invention would look for the basis for the inventors' stated belief that the treatment regimen will be effective* [note by the board: point 34 above] *which would have motivated analysis of the data of example 2 with consequent appreciation of the longer half-life.*"

39. The board notes however in this context that example 6 does not explain how the simulation of the proposed treatment regimen was done or that it was based on the data of example 2. Also, the proposed treatment regimen of example 6 is a combination therapy of Herceptin® with paclitaxel administered every three weeks, while example 2 relates to a monotherapy with Herceptin® which is administered weekly. Thus, example 2 relates not only to a different dosage regimen but to a different treatment regimen. In the board's judgement, the skilled person thus had no reason to turn to example 2 or to analyse the data of example 2 when faced with the treatment proposed in example 6.

40. Post-published document D70 is considered to corroborate the board's finding in this respect. Document D70 discloses that preliminary data from 15 patients treated with Herceptin® administered every three weeks in combination with Taxol® "*now indicate that the half-life Herceptin® is considerably longer than was originally determined*" (see page 1). The document thus provides evidence that the appellant itself, although in possession of the data of example 2 of the patent in suit and in particular of the data depicted in Figure 3, had only reconsidered the half-life of Herceptin® when analysing the data obtained from the clinical trial proposed in example 6 of the patent in suit. However, these data are neither contained in the patent in suit nor disclosed in the prior art. Accordingly, the appellant's submission that the notional skilled person reading the patent in suit would have realised from the data in its example 2 that the half-life of Herceptin® was considerably longer is also contradicted by the evidence provided in document D70.

41. In conclusion, the board, having regard to the facts and arguments presented to it, decides that the contested patent does not disclose the suitability of Herceptin® for the treatment of breast cancer with the claimed dosage regimen.

42. Under these circumstances, the appellant cannot rely on post-filed evidence such as document D54 (see point 15 above). In this context the board notes that in T 157/03 of 4 January 2005 the deciding board accepted that post-published documents could be used as evidence as to whether the invention was indeed reproducible without undue burden at the relevant filing date (see reasons, point 9). However, as set out above (see

points 15 and 16), the established case law followed by this board requires the suitability of the claimed dosage regimen to be disclosed at the effective date of the patent. Accordingly, the appellant's reliance on decision T 157/03, *supra*, cannot lead to a different conclusion as regards sufficiency of disclosure.

43. The decision of the opposition division as regards insufficiency of disclosure (Article 100(b) EPC) of the subject-matter of claim 1 was correct.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

P. Cremona B. Claes

Decision electronically authenticated