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**Datasheet for the decision
of 3 February 2017**

Case Number: T 0950/13 - 3.3.01

Application Number: 04758053.5

Publication Number: 1610780

IPC: A61K31/427, A61K31/506,
A61P35/02

Language of the proceedings: EN

Title of invention:

CYCLIC PROTEIN TYROSINE KINASE INHIBITORS

Patent Proprietor:

Bristol-Myers Squibb Holdings Ireland

Opponent:

APOTEX INC.

Headword:

Dasatinib in the treatment of chronic myelogenous leukemia/
BRISTOL

Relevant legal provisions:

EPC Art. 83, 111(1)

Keyword:

Main request and auxiliary request 1: Sufficiency of disclosure - (no)

Auxiliary request 2a: Sufficiency of disclosure - (yes), plausible technical concept

Appeal decision - remittal to the department of first instance (yes)

Decisions cited:

T 0609/02, T 0157/03, T 1262/04, T 1329/04, T 0578/06

Catchword:



Beschwerdekammern
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European Patent Office
D-80298 MUNICH
GERMANY
Tel. +49 (0) 89 2399-0
Fax +49 (0) 89 2399-4465

Case Number: T 0950/13 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 3 February 2017

Appellant: Bristol-Myers Squibb Holdings Ireland
(Patent Proprietor) Hinterbergstrasse 16
6312 Steinhausen (CH)

Representative: Reitstötter Kinzebach
Patentanwälte
Sternwartstrasse 4
81679 München (DE)

Respondent: APOTEX INC.
(Opponent) 150 Signet Drive
Toronto, Ontario M9L 1T9 (CA)

Representative: Uexküll & Stolberg
Partnerschaft von
Patent- und Rechtsanwälten mbB
Beselerstraße 4
22607 Hamburg (DE)

Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 1 February 2013
revoking European patent No. 1610780 pursuant to
Article 101(3)(b) EPC.**

Composition of the Board:

Chairman A. Lindner
Members: G. Seufert
L. Bühler

Summary of Facts and Submissions

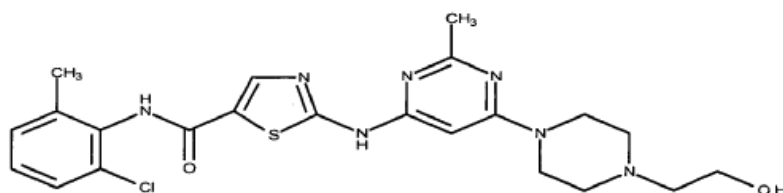
- I. The patent proprietor (appellant) lodged an appeal against the decision of the opposition division revoking the European patent No. 1 610 780.
- II. The present decision refers to the following documents:
- (1) WO 00/62778
 - (2) L. J. Lombardo *et al.*, *Journal of Medicinal Chemistry*, Vol. 47, 2004, pages 6658 to 6661
 - (3) J. Wityak *et al.*, *Bioorganic & Medicinal Chemistry Letters*, Vol. 13, 2003, pages 4007 to 4010
 - (5) E. Buchdunger *et al.*, *Biochimica et Biophysica Acta*, Vol. 1551, 2001, pages M11 to M18
 - (6) T. Kindler *et al.*, *Expert Opinion on Therapeutic Targets*, Vol. 6, No. 1, 2002, pages 85 to 101
 - (7) Highlights of Prescribing Information, SPRYCEL (dasatinib) Tablet for Oral Use, Rev. October 2010
 - (8) Declaration by Dr. A. J. Bridges dated 10 June 2013, submitted by the appellant with the statement of grounds of appeal
 - (9) D. S. Lawrence, J. Niu, *Pharmacol. Ther.*, Vol. 77, No. 2, 1998, pages 81 to 114
 - (10) Ch.-J. Chang, R. L. Geahlen, *Journal of Natural Products*, Vol. 55, No. 11, 1992, pages 1529 to 1560
- III. Notice of opposition was filed by the respondent (opponent) requesting revocation of the patent in suit in its entirety on the grounds of lack of inventive step, insufficiency of disclosure and added matter (Article 100(a), (b) and (c) EPC).

The opposition division decided that claims 2, 4, 9 and 11 of the main request (claims as granted) had no basis in the application as originally filed and that the subject-matter of auxiliary requests 1 and 3 was not sufficiently disclosed. The division considered that, in the absence of any experimental evidence of an inhibitory activity on BCR-ABL protein tyrosine kinase (PTK) and the lack of a coherent theory, which could explain such an effect, substantial doubts existed as to whether the compound dasatinib was suitable for the claimed treatment of chronic myelogenous leukemia (CML). According to the opposition division this lack of sufficiency of disclosure could not be remedied by the post-published evidence (documents (2) and (7)). Auxiliary request 2 was withdrawn at the oral proceedings before the opposition division.

IV. With the statement of grounds of appeal, the appellant filed an amended main request and auxiliary requests 1, 2a, 2b, 3a and 3b. It also submitted document (8).

The main request consist of 6 claims with claims 1 and 4 reading as follows:

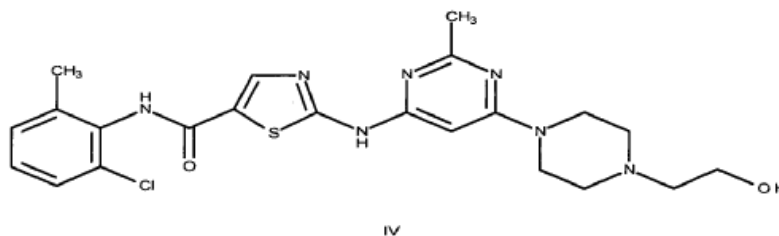
"1. Use of the compound of formula (IV) or a salt thereof:



IV

for the manufacture of a medicament for the oral treatment of cancer, wherein the cancer is chronic myelogenous leukemia (CML)."

"4. Compound of formula IV or a salt thereof:



for use in the oral treatment of cancer, wherein the cancer is chronic myelogenous leukemia (CML)."

Auxiliary request 1 differs from the main request in that the expression "or a salt thereof" in claims 1 and 4 has been deleted.

Auxiliary request 2a differs from the main request in that claims 2 and 5 have been deleted and the remaining claims have been renumbered.

Auxiliary request 2b differs from auxiliary request 2a in that the expression "or a salt thereof" in claims 1 and 3 has been deleted.

Auxiliary request 3a differs from the main request in that it contains only two claims (former claims 1 and 4) and that the cancer has been restricted to CML **"resistant to STI-571"**.

Auxiliary request 3b differs from auxiliary request 3a in that the expression "or a salt thereof" has been deleted.

V. With the reply to the statement of grounds of appeal the respondent maintained its objection of lack of sufficiency of disclosure against all requests and

raised added matter objections against all requests except auxiliary requests 2a and 2b. It also filed documents (9) and (10).

- VI. Further arguments were provided with the appellant's letters of 1 September 2014 and 30 July 2015 and the respondent's letter of 22 December 2014.
- VII. Third party observations filed by Mr Markus Jacobi, a professional representative, were received on 29 November 2016.
- VIII. With letter dated 5 January 2017, the respondent informed the board that it withdrew its request for oral proceedings and would not attend the oral proceedings scheduled for the 3 February 2017.
- IX. The arguments provided by the appellant as far as they relate to the decisive issues of the present decision can be summarised as follows:

- Sufficiency of disclosure

The application clearly taught the suitability of dasatinib in the treatment of CML (see claim 4; page 46, line 39 to page 47, line 3). With regard to the specific disease, it was common general knowledge that BCR-ABL was the single causative abnormality in CML and that inhibition of BCR-ABL kinase was considered to be an effective way to treat CML (see documents (5), page M11, right-hand column, point 2 and document (6), page 94, point 5).

Given the fact that BCR-ABL was known to be the single causative abnormality in CML, the teaching that dasatinib is useful in the treatment of CML was

tantamount to the teaching that dasatinib inhibited BCR-ABL kinase, even though the application does not provide an IC value. The skilled person could easily have verified this activity without undue burden using known and reliable assays, with which he would be familiar (see document (5), page M13, paragraph bridging left- and right-hand column, Table 1). This was confirmed by document (8), points 28, 29 and 36.

At the relevant date of the application it was also widely known in the art that imatinib, a BCR-ABL kinase inhibitor, had been successfully used in the treatment of CML, which provided proof of the concept for the inhibition of BCR-ABL kinase as a working therapeutic strategy in treating CML. The suitability of dasatinib resided in its functional analogy to imatinib as a BCR-ABL kinase inhibitor.

Being told that there was a functional analogy between dasatinib and imatinib in that they both inhibited BCR-ABL kinase was sufficient information for the skilled reader to consider dasatinib's suitability in the treatment of CML to be a plausible teaching. Experimental proof was not required for patentability and post-published documents could constitute evidence that the invention was reproducible without undue burden in cases of a plausible conceptual disclosure. As a consequence, the post-published evidence in the form of documents (2) and (7), which confirmed the BCR-ABL kinase inhibitory activity of dasatinib and its suitability for the oral treatment of CML, could be taken into account.

There were no *prima facie* serious doubts as to the suitability of dasatinib as BCR-ABL kinase inhibitor in the oral treatment of CML. The invention was not

conceptionally new, did not go against prevailing opinion, established theories or natural laws, and was not concerned with the use of compounds yet to be identified, as in T 609/02 on which the opposition division relied. The mere fact that the exemplary assays described in the application did not include a BCR-ABL kinase assay was no reason for doubts, because these assays were described in a generic manner and the skilled person was in a position to set-up assays for these and many other PTKs based on his common general knowledge without requiring a detailed description in the application (see document (8), point 29). The experimental evidence in the application as filed with regard to the inhibition of PTKs other than BCR-ABL kinase was not a reason to doubt the disclosure that dasatinib was suitable in the treatment of CML. It was not unusual for a compound to inhibit more than one PTK as was apparent for example for imatinib. The opposition division in the decision under appeal had incorrectly equated surprise with doubts. Non-obviousness of a technical teaching was, however, not a relevant criterion in the assessment of sufficiency of disclosure.

The respondent's arguments with regard to the alleged broadness of the disclosure, completely disregarded that the application also clearly disclosed the suitability of dasatinib in the treatment of CML.

The application as filed also clearly disclosed the suitability of dasatinib in the treatment of CML, which was resistant to imatinib. As was confirmed by the technical expert, the only plausible explanation for this statement was that dasatinib could inhibit commonly occurring imatinib resistant mutants. The

skilled person would know that resistance could be overcome by using a different inhibitor.

X. The arguments provided by the respondent as far as they relate to the decisive issues of the present decision can be summarised as follows:

- Sufficiency of disclosure

The application as filed disclosed in the introductory section and the summary of the invention (see pages 1, line 18 to page 2, line 29, page 3, line 15 to page 8, line 25) a very broadly defined group of compounds allegedly useful as inhibitors for a wide variety of PTKs associated with a wide variety of oncological and immunological diseases. Moreover, it was known from the prior art that changes in the structure of a PTK inhibitor easily caused loss of activity and that an inhibitor of a specific PTK did not necessarily inhibit other PTKs. In view of these known structure-related changes, as evidenced by document (9) (see pages 87 to 105) and document (10) (see pages 1533 to 1551), and confirmed by the appellant's own post-published document (2) (i.e. dasatinib was shown to be unsuitable for the inhibition of a number of PTKs; compounds according to formula I were shown to have poor oral absorption properties) and document (3) (compounds according to formula I were shown to be inactive), the skilled reader would not have considered it plausible after reviewing the introductory part and the summary of the invention that all compounds of formula (I) were active PTK inhibitors.

A further discussion of medical indications said to be associated with PTKs was provided on pages 42 to 47 of the application. However, no explanation was given

therein as to why the skilled reader should believe that specific members of the large group of compounds of formula I acted as inhibitors of PTKs.

The final section of the description of the application was related to a number of *in vitro* assays. None of these assays contained any data in support of any observed effect. Furthermore, these assays were unreliable, as it was well known in the art (see document (9), pages 82 and 86/87) that it was not possible to mimic *in vitro* the cellular levels of ATP. A compound that showed PTK inhibitory activity *in vitro* was therefore not necessarily potent enough *in vivo*. The information in the assay section also did not provide any guidance as to which, if any, of the compounds of formula I, including dasatinib, showed any activity, let alone any level of activity which would render a compound useful in the oral treatment of CML or any other cancer or disease mentioned in the application. The skilled person was therefore left to guess whether dasatinib at the effective date of the patent in suit showed any PTK inhibitory activity with respect to any kinase, let alone BCR-ABL kinase inhibitory activity. Finally it was apparent from document (2) that at the priority date of the patent in suit, the relevant assays were not part of the common general knowledge.

Based on the prior art knowledge on the variation or loss of PTK inhibitory activity when changing the substitution pattern of an active substance and the variation in the inhibition of different kinases by a given substance, the skilled person would have had serious doubts as to dasatinib's suitability in the treatment of any of the diseases or disorders mentioned in the application, including CML.

It was not disputed that imatinib, a BCR-ABL kinase inhibitor, was known to be suitable in the treatment of CML. However, the structure of imatinib was significantly different from the structure of dasatinib. Taking into account the influence which a change in structure could have on the activity of a compound, no extrapolation from imatinib to dasatinib with regard to the suitability in the treatment of CML was possible.

The application as filed also contained no information which made it plausible that dasatinib was suitable in the treatment of CML resistant to imatinib. According to document (6), several mechanisms of resistance were known. None of them was addressed in the application as filed; nor was any information provided in which of those mechanisms dasatinib might be helpful. In particular, there was no plausible explanation as to why dasatinib, which according to the appellant had the same inhibitory activity as imatinib, would still be active when imatinib had become inactive.

Support for the respondent's arguments concerning sufficiency of disclosure could be found in the case law of the boards of appeal, in particular in the decisions T 609/02 and T 1329/04.

XI. The appellant requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request, or, alternatively, of one of auxiliary requests 1, 2a, 2b, 3a, or 3b, all filed with the statement of grounds of appeal.

XII. The respondent had requested in writing that the appeal be dismissed.

XIII. At the end of the oral proceedings, the decision of the board was announced.

Reasons for the Decision

1. The appeal is admissible.
2. As communicated in advance to the board (see point VIII above), the respondent did not attend oral proceedings, to which it had been duly summoned. The board decided to continue the proceedings pursuant to Rule 115(2) EPC and Article 15(3) RPBA.

Main request and auxiliary request 1

3. Sufficiency of disclosure (Article 100(b) EPC).
 - 3.1 Claim 1 of the main request is directed to the use of dasatinib in the manufacture of a medicament for the treatment of chronic myelogenous leukemia (CML).
 - 3.2 Article 83 EPC stipulates that the patent shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

In relation to claims directed to a second medical use of a compound, it is established jurisprudence of the boards of appeal that Article 83 EPC is complied with if the content of the application as filed or common general knowledge at the relevant date enables the skilled person to prepare the claimed compound or compounds - which was not disputed in the present

case - and the claimed treatment can be achieved in a reliable and reproducible manner. This means that either the application must provide suitable evidence for the claimed therapeutic effect or it must be derivable from the prior art or common general knowledge. Post-published evidence may be taken into account, but only to back-up the findings in the application in relation to the use of the compound(s) as a pharmaceutical (cf. T 609/02, point 9 of the Reasons).

It follows from the above that in the present case the suitability of dasatinib for the treatment of patients with chronic myelogenous leukemia has to be plausible to the skilled person either from the teaching of the application as filed or from common general knowledge at the relevant date.

- 3.3 The application as filed, irrespective of a broader general disclosure in the description, is directed to the use of generically defined compounds in the treatment of specific types of cancer, including CML (see claims 1 and 11), based on the activity of said compounds to inhibit certain protein tyrosine kinases such as SRC, BCR-ABL and c-KIT associated with these types of cancer (see page 46, line 23 to page 47, line 3). Dasatinib is identified as a preferred compound (see page 41, lines 17 to page 42 line 3). Indeed it is the only individual compound that is specifically identified as suitable in the treatment of the claimed types of cancer (see claim 3). Methods for administration of dasatinib, including oral administration, are also disclosed in the application (see page 50, line 9 to page 51, line 9).

3.4 Furthermore, it is clearly disclosed in the application as filed that dasatinib is suitable in the treatment of CML (see claim 4 and page 46, line 30 to page 47, line 3).

The board notes that claim 4 does not explicitly refer to CML, but to a cancer which is sensitive to treatment by an inhibitor of BCR-ABL kinase. It was, however, commonly known in the art at the filing date of the application that the BCR-ABL oncogene is the single causative abnormality in CML and that its gene product (i.e. the protein) is a constitutively activated tyrosine kinase, which is responsible for the malignant transformation (see document (5), page M11, right-hand column, lines 1 to 2 and 13 to 20; document (6), conclusion). BCR-ABL kinase inhibition was seen as an effective way to treat this disease. This was not contested by the respondent or the opposition division.

The board therefore concurs with the appellant that the skilled person would immediately understand that the cancer referred to in claim 4 includes CML. Given the causative link between BCR-ABL and CML, the teaching that dasatinib is useful in the treatment of CML is equivalent to the teaching that dasatinib inhibits BCR-ABL kinase, in accordance with the disclosure on page 46, lines 23 to 30 of the application.

3.5 The board also concurs with the appellant that a person skilled in the art at the filing date of the application was familiar with the fact that CML can indeed be treated by inhibiting BCR-ABL kinase. It was widely known that imatinib (= Gleevec, STI-571), an effective inhibitor of BCR-ABL kinase (see document (5), page M12, left-hand column, last line to right-hand column, line 4; page M13, table 1, entry 3

and 4) has shown excellent clinical results (see document (5), conclusions; document (6), point 4.2.2 and conclusion) and had been approved for the treatment of CML well before the filing date of the present application (see document (6), page 90, left-hand column, lines 3 to 5). None of this was contested by the respondent.

- 3.6 The application does not contain experimental evidence for dasatinib's BCR-ABL kinase inhibitory activity. However, the disclosure of experimental results in the application is not always required to establish sufficiency, in particular if the application discloses a plausible technical concept and there are no substantiated doubts that the claimed concept can be put into practice (see also T 578/06, point 13 of the Reasons).

In view of the considerations in points 3.4 and 3.5 above and the analogy that is drawn to imatinib on page 46, line 30 to page 47, line 3 of the application, the board is satisfied that the application discloses at least a plausible technical concept, namely that dasatinib based on its functional equivalence to imatinib as a BCR-ABL kinase inhibitor is suitable in the treatment of CML. There are no reasons apparent to the board as to why a skilled person would *a priori* regard this teaching as incredible or implausible. As a consequence, the post-published evidence in the form of document (2), which confirms the BCR-ABL kinase inhibitory activity of dasatinib (see table 2, first entry) and therefore merely backs-up the teaching derivable from the application, can be taken into account (see T 609/02, point 9 of the Reasons;

T 578/ 06, points 12 and 15 of the Reasons).

Document (7) also confirms the suitability of dasatinib as a BCR-ABL kinase inhibitor in the treatment of CML.

3.7 In the decision under appeal, the opposition division held that serious doubts as to dasatinib's suitability in the treatment of CML existed. In its opinion, the biochemical properties of dasatinib which had been substantiated in the application on pages 55 to 58 could not be extrapolated to BCR-ABL kinase inhibition. The experimental evidence was therefore unsuitable to demonstrate that dasatinib was suitable for the treatment of CML. Furthermore, after having compared the content of document (1) with the disclosure of the application, the opposition division concluded that the skilled person would have been surprised by the teaching that dasatinib effectively inhibited BCR-ABL kinase.

3.8 The board does not agree.

Pages 55 to 58 describe, in a generic way and without providing any data, assays which can be used to establish the activity of a compound as protein tyrosine kinase (PTK) inhibitor. An assay for testing BCR-ABL (tyrosine) kinase is not included. However, such assays are known in the art (see document (5) page M12, paragraph bridging left- and right-hand column). Furthermore, in the absence of any evidence to the contrary, the board accepts the appellant's argument that methods for testing a compound's ability to inhibit common PTKs, including BCR-ABL, belong to the skilled person's common general knowledge (see document (8), point 29). This is also confirmed by document (10), which refers to ways of screening for

protein tyrosine kinase inhibitors (see page 1530, last paragraph to page 1532, second paragraph).

The board also notes that if it accepted the opposition division's view that the disclosure on pages 55 to 58 was evidence that dasatinib inhibited certain PTKs, it cannot follow the division's conclusion that there are *a priori* serious doubts as to its potential suitability to inhibit BCR-ABL kinase as taught in the application. It is apparently not uncommon for a protein kinase inhibitor to inhibit more than one protein tyrosine kinase. This can be explained by the fact that in all protein tyrosine kinases the ATP binding site and the transfer domains are to a certain extent similar. Thus, inhibitors which compete with ATP for binding in the kinase ATP-binding domain, but which cannot transfer phosphate and therefore prevent the enzyme from working, can do that with a number of kinases (see document (8), point 12; document (9), page 82, point 2). This is illustrated, for example, by the kinase binding profile of imatinib (cf. table 1 of document (5)) and is confirmed in the inhibitory profiles of various compounds in documents (9) and (10).

The board also does not agree with the opposition division's approach to equate non-obviousness with the existence of serious doubts. A technical teaching - in the present case the teaching that dasatinib is suitable for the treatment of CML based on its functional analogy to imatinib as BCR-ABL inhibitor - is not rendered implausible, because it may not have been obvious in view of the prior art.

3.9 In the decision under appeal, the opposition division also relied on T 609/02 and T 1329/04 in support of its

position on sufficiency of disclosure. However, the board judges that the factual situation underlying said decisions differ to such an extent that they are not considered to be relevant the present case.

3.9.1 In T 609/02 the board was confronted with the situation where a drug was claimed for medical treatment comprising as active ingredients compounds which had not yet been structurally defined and where no direct effect had been demonstrated on the metabolic mechanism specifically involved in the diseases (see T 609/02, point 11 of the Reasons). In these circumstances, where the claimed subject-matter "covers limitless and untried downstream developments in relation to yet to be demonstrated molecular mechanisms" the board in T 609/02 judged that the disclosure "amounts to no more than an invitation to set up further research programs for which no guidance is forthcoming". In the present case, a structurally well-defined compound and a plausible concept for its suitability in the treatment of CML has been disclosed (see points 3.3 to 3.6 above).

3.9.2 In T 1329/04 the key issue was whether it was plausible that the claimed polypeptide GDF-9 belonged to the TGF- β superfamily and therefore exhibited the functions contributed to members of this family. The board held that this was not the case because the polypeptide lacked the consensus region common to all family members known in the art and because no evidence was provided that GDF-9 played a role similar to that of TGF- β . As explained in points 3.3 to 3.6 above, in the present case, the board judges that the application at least discloses a plausible concept for the suitability of dasatinib in the treatment of CML.

3.10 The respondent's submissions regarding insufficiency of disclosure are not convincing for the following reasons:

3.10.1 One of the respondent's main arguments was the breadth of the general disclosure in the application as filed and the lack of experimental data showing that compounds according to formula I, including dasatinib, had a direct effect on the mechanism specifically involved in the claimed diseases or disorders. According to the respondent, it was not plausible that all members of formula I were active PTK inhibitors and the skilled person was left to guess whether dasatinib exhibited any PTK inhibitory activity, let alone activity against BCR-ABL kinase (see point X above). In this context, reference was made to prior art documents (9) and (10) and post-published documents (2) and (3), which, according to the respondent, illustrated the effects of structural changes on the PTK activity and showed that a number of compounds falling under the general formula (I) were not active or were not suitable for oral administration.

3.10.2 However, the respondent neglects that the application as filed is directed to the treatment of specific types of cancer based on the inhibition of specific PTKs associated therewith (see point 3.3 above), irrespective of its broad general description, which is to a large extent merely a copy of the description of the prior art document (1). The respondent also disregards that the present application clearly teaches that dasatinib is suitable in the treatment of CML, which is tantamount to dasatinib being a BCR-ABL kinase inhibitor (see points 3.4 to 3.6 above). Hence, contrary to the respondent's view, the skilled person was not left to guess, which of the various PTKs was

inhibited by dasatinib. Accordingly, no further "research program" was necessary in order to carry out the invention. The allegedly observed failure of some compounds according to formula I to inhibit the protein kinase Lck (see document (3), Table 1) or the poor or reduced oral absorption properties of other compounds falling within the scope of formula I is irrelevant in this context. Equally irrelevant is the low activity of dasatinib on certain other PTKs such as HER1 or HER2 kinase (see document (2), Table 2).

The respondent's arguments may have been relevant, if the application had been limited to the general disclosure relied on by the respondent, i.e. the provision of an extremely broadly defined group of compounds for the treatment of a plethora of diseases or disorders based on the inhibition of different types of PTKs with no further guidance at all as to which compounds inhibits which PTK. However, as set out above this is presently not the case.

- 3.10.3 The respondent also questioned the reliability and significance of *in vitro* assays, such as those disclosed on pages 55 to 58. In particular, it was argued that such assays could not be used to predict whether a compound was a potent enough inhibitor *in vivo*, because it was known in the art that it was not possible to mimic, *in vitro*, the cellular level of ATP (see document (9), pages 82 and 86 to 87). Furthermore, the respondent argued that the assays on page 55 to 58 did not contain any actual data.

The board accepts that *in vitro* tests are not absolute proof for a compound's *in vivo* activity. However, this does not lessen the usefulness of such tests in general, in spite of their shortcomings. Furthermore,

absolute proof is not required and the boards have consistently held that for sufficiency of disclosure of a therapeutic use there is no mandatory requirement of *in vivo* data or clinical data. Showing a pharmaceutical effect *in vitro* may be sufficient, if for a skilled person this observed effect directly and unambiguously reflects the therapeutic application. In the present case, it is known that a constitutively active BCR-ABL kinase is the pathogenic principle in CML and its inhibition has been shown as an effective way to treat CML. The inhibition of BCR-ABL kinase by dasatinib as taught in the application and confirmed by document (2) (see point 3.6 above) is therefore sufficient to establish its suitability in the treatment of CML.

- 3.10.4 Concerning the lack of explicit data, the board re-emphasises that in cases where the application discloses a technical concept which is plausible in the light of the common general knowledge at the relevant date, but lacks concrete or tangible proof that the claimed concept can be put into practice, post-published documents may be used as evidence that the invention was indeed reproducible without undue burden at the relevant filing date of the application (see T 1262/04, point 5 of the Reasons; T 157/03, point 9 of the Reasons).
- 3.10.5 The board also does not accept the respondent's argument that post-published document (2) (see page 6660, right-hand column, first complete paragraph) was evidence for the fact that BCR-ABL kinase assays were not available to the skilled person. The board understands the reference to an in-house-kinase selectivity panel as a reference to in-house screening of dasatinib against a number of kinases, and not as evidence for the use of "uncommon" kinase assays.

- 3.10.6 In support of its arguments, the appellant also relied on decisions T 609/02 and T 1329/04. For the reasons set out in point 3.9 above, the board takes the view that these decisions do not support the respondent's case.
- 3.11 Third party observations have been filed by Mr M. Jacobi (see point VII above). While there is no obligation on the board to consider these observations, the board notes that they are essentially identical to the arguments provided by the respondent and the opposition division which have been addressed in points 3.3 to 3.6, 3.9 and 3.10 above.
- 3.12 It follows from the above that the board is satisfied that the subject-matter of claims 1 and 4 of the main request is sufficiently disclosed.
- 3.13 This conclusion, however, does not apply to the subject-matter of claim 2 of the main request, which is directed to the use of dasatinib for the manufacture of a medicament for oral treatment of CML, which is resistant to STI-571 (= imatinib).
- 3.13.1 It was known in the art that primary and secondary resistance to imatinib is a major problem in patients with CML (see document (6), page 90 left-hand column, lines 6 to 13). Several mechanisms of resistance were known including BCR-ABL overexpression, reduced cellular up-take mediated by the multi-drug resistance P-glycoprotein and specific mutations within the ATP-binding site resulting in diminished binding of imatinib (see document (6), page 90, left-hand column, line 14 to right-hand column, line 1; document (5), point 6). The appellant's argument that the reference

to imatinib-resistant CML in the application would be understood by the skilled person as a clear disclosure that dasatinib inhibits mutation forms of BCR-ABL (see document (8), points 29g) and 36) is therefore not accepted.

- 3.13.2 The application as filed contains no information at all, neither in the form of experimental data nor in the form of a plausible technical concept, that dasatinib is suitable in the treatment of those patients with imatinib-resistant CML. The functional analogy to imatinib as BCR-ABL kinase inhibitor is not helpful in this context and cannot explain why dasatinib should be active, when imatinib is, or has become, inactive.
- 3.14 The board therefore concludes that the claimed therapeutic use, i.e. the treatment of CML which is resistant to imatinib, has not been made plausible to the skilled person either from the teaching of the application as filed or from common general knowledge at the relevant date.
- 3.15 Since the board can only decide on a set of claims as a whole, it follows from the conclusion in point 3.14 above that the main request fails on the ground of lack of sufficiency of disclosure pursuant to Article 100(b) EPC.
- 3.16 In auxiliary request 1, claim 2 is directed to the same therapeutic use as claim 2 of the main request. Hence, the same observations and the same conclusion as in points 3.13 and 3.14 above apply, with the consequence that auxiliary request 1 also fails for lack of sufficiency of disclosure pursuant to Article 100(b) EPC.

Auxiliary request 2a

4. Amendments

Auxiliary request 2a differs from the main request in that claim 2 has been deleted. It is identical to auxiliary request 3 underlying the decision under appeal, except for a minor amendment (correct adaptation of dependency) in claim 4.

In the decision under appeal the opposition division held that claims 1 to 4 of auxiliary request 3 complied with Article 123(2) and (3) EPC. The board has no reason to deviate from the opposition division's finding in this respect, which was also not contested by the respondent. The amendment in claim 4 is of no consequence as regards the opposition division's assessment of compliance with Article 123(2) and (3) EPC.

5. Sufficiency of disclosure (Article 100(b) EPC)

Claim 1 of auxiliary request 2a is identical to claim 1 of the main request. For the reasons set out in out in points 3.3 to 3.10 above, the board concludes that the requirement of sufficiency of disclosure is met for the invention as defined in claim 1 of auxiliary request 2a. The same conclusion applies to claim 3, which is directed to dasatinib for use in the oral treatment of CML.

The ground of opposition according to Article 100(b) EPC therefore does not prejudice the maintenance of the patent on the basis of auxiliary request 2a.

6. Remittal

In the decision under appeal the opposition division revoked the patent solely on the grounds of added matter (main request) and lack of sufficiency of disclosure (auxiliary requests). It did not yet decide on the other grounds of opposition relied on by the respondent, that is lack of inventive step. Taking into account that proceedings before the board are primarily intended to review the correctness of the opposition division's decision, the board considers it appropriate to exercise its discretionary power pursuant to Article 111(1) EPC and remit the case to the department for further prosecution.

7. Having come to the conclusion that the invention defined in auxiliary request 2a is sufficiently disclosed and having decided to remit the case, there is no need for the board to decide on auxiliary requests 2b, 3a and 3b.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance for further prosecution

The Registrar:

The Chairman:



A. Wolinski

A. Lindner

Decision electronically authenticated