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# Datasheet for the decision of 22 April 2021

**Case Number:** T 1326/18 - 3.3.02

**Application Number:** 04806748.2

**Publication Number:** 1720853

**IPC:** C07D401/04, A61K31/505

**Language of the proceedings:** EN

**Title of invention:**
NOVEL POLYMORPHIC FORM OF IMATINIB MESYLATE AND A PROCESS FOR ITS PREPARATION

**Patent Proprietor:**
Natco Pharma Limited

**Opponents:**
Onsagers AS
Gizinska-Schohe, Malgorzata

**Headword:**

**Relevant legal provisions:**
EPC Art. 54(3), 56, 83, 123(2), 123(3)
RPBA Art. 12(4)
RPBA 2020 Art. 12(2), 25(2)

**Keyword:**
Amendments - intermediate generalisation
Novelty
Sufficiency of disclosure
Inventive step
Late-filed document
Late-filed auxiliary requests
Late-filed objection
Remittal

**Decisions cited:**
T 0714/00, T 0777/08, T 2007/11, T 2154/11, T 2287/11, T 1684/16

**Catchword:**

Europäisches Patentamt
European Patent Office
Office européen des brevets

**Beschwerdekammern**

**Boards of Appeal**

**Chambres de recours**

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

**Case Number: T 1326/18 - 3.3.02**

# D E C I S I O N
# of Technical Board of Appeal 3.3.02
# of 22 April 2021

| | |
|---|---|
| **Appellant:** (Patent Proprietor) | Natco Pharma Limited<br>"Natco House"<br>Road No. 2<br>Banjara Hills<br>Hyderabad, Andhra Pradesh 500033 (IN) |
| **Representative:** | J A Kemp LLP<br>14 South Square<br>Gray's Inn<br>London WC1R 5JJ (GB) |
| **Appellant:** (Opponent 1) | Onsagers AS<br>P.O. Box 1813 Vika<br>Munkedamsveien 35<br>0123 Oslo (NO) |
| **Representative:** | Onsagers AS<br>Munkedamsveien 35<br>P.O. Box 1813 Vika<br>0123 Oslo (NO) |
| **Appellant:** (Opponent 2) | Gizinska-Schohe, Malgorzata<br>Helmpertstrasse 11A<br>80687 München (DE) |
| **Representative:** | Hoffmann Eitle<br>Patent- und Rechtsanwälte PartmbB<br>Arabellastraße 30<br>81925 München (DE) |
| **Decision under appeal:** | **Interlocutory decision of the Opposition Division of the European Patent Office posted on 20 March 2018 concerning maintenance of the European Patent No. 1720853 in amended form.** |

**Composition of the Board:**

| | |
|---|---|
| **Chairman** | M. O. Müller |
| **Members:** | S. Bertrand |
| | R. Romandini |

## Summary of Facts and Submissions

I. The appeals by the opponents and the proprietor lie from the opposition division's interlocutory decision that European patent No. 1 720 853 in amended form according to the then pending eighth auxiliary request filed on 22 February 2018 met the requirements of the EPC.

II. The patent as granted contained 6 claims, independent claims 1 to 4 of which read as follows:

"1. *An $\alpha_2$ crystalline form of Imatinib Mesylate which has the XRPD characteristics given below*

| Angle 2-Theta | d Value Angstrom | Intensity % |
|---|---|---|
| 4.841 | 18.24057 | 33.6 |
| 10.410 | 8.49070 | 100.0 |
| 11.194 | 7.89775 | 14.2 |
| 11.856 | 7.45827 | 19.9 |
| 12.881 | 6.86709 | 6.8 |
| 13.819 | 6.40328 | 12.9 |
| 14.860 | 5.95663 | 67.7 |
| 16.439 | 5.38788 | 32.4 |
| 17.049 | 5.19665 | 5.6 |
| 17.623 | 5.02870 | 58.6 |
| 18.052 | 4.91000 | 61.6 |
| 18.567 | 4.77491 | 98.8 |
| 19.032 | 4.65925 | 70.2 |
| 19.772 | 4.48657 | 15.3 |
| 21.236 | 4.18055 | 60.8 |
| 21.582 | 4.11431 | 59.4 |
| 22.594 | 3.93217 | 19.7 |
| 23.137 | 3.84112 | 21.8 |
| 23.696 | 3.75172 | 25.0 |
| 24.851 | 3.57993 | 58.6 |
| 26.250 | 3.39226 | 9.1 |
| 27.341 | 3.25932 | 18.7 |
| 28.475 | 3.13204 | 42.4 |
| 31.896 | 2.80347 | 9.0 |
| 32.533 | 2.75005 | 6.6 |
| 43.447 | 2.08117 | 6.4 |

*which is stable at room temperature and even at higher temperatures like 120°C and accelerated stress conditions, and is freely soluble in water.*"

"*2. A process for the preparation of the $\alpha_2$ crystalline form of Imatinib Mesylate of claim 1, the method comprising:*

*suspending Imatinib base in isopropanol;*

*adding methane sulfonic acid at room temperature;*

*maintaining the reaction mixture at a temperature in the range of 40-80°C, for a period in the range of 20-30 minutes; and*

*cooling to 40-45 °C and filtering to obtain the $\alpha_2$ crystal form.*"

"*3. A process for the preparation of the $\alpha_2$ crystalline form of Imatinib Mesylate of claim 1, the method comprising:*

*suspending β polymorphic form Imatinib Mesylate in water and organic solvents like methanol, Isopropyl ether* [sic]*, toluene, cyclohexane and Isopropyl alcohol* [sic]*;*

*distilling off water azeotropically; and*

*cooling and filtering to obtain the $\alpha_2$ crystal form.*"

"*4. A pharmaceutical composition comprising the novel $\alpha_2$ crystalline form of Imatinib Mesylate of claim 1 along with excipient useful for the treatment of chronic myelogenous leukemia.*"

III. The following documents are referred to in the present decision:

D1 WO 99/03584 A1

D2 WO 2004/074502 A2, prior art pursuant to Article 54(3) EPC

D6 Byrn et al., 1995, Pharmaceutical Research, 12 (7), pages 945-954

D8 Liebermann et al, "Pharmaceutical Dosage Forms", 1989, pages 34-41

D12 Gorbitz, expert report of 28 September 2016, table 1 and figures 1-4

D18 WO 03/090720 A1

D21 Gorbitz, notes regarding the cooling conditions in D12, submitted on 21 December 2017

A026 Prof. Michal Piotr Marszall, Declaration of 16.07.2018

A027 WO 01/47507 A2

A028 Remington's Pharmaceutical Sciences, 18th edition, Eds. A.R.Gcnnaro, Mack Publ. Co., 1990, Easton, PA, pages 1633-1665

A029 Copy of information available with EMA regarding marketing authorization of Glivec®

IV. The opposition division came, *inter alia*, to the following conclusions:

- the invention defined in the claims of the main request (patent as granted) was sufficiently disclosed,

- claim 1 of the main request and the first, third and seventh auxiliary requests then on file lacked novelty in view of D2,

- claim 1 of each of the second, fourth, fifth and sixth auxiliary requests then on file did not meet the requirements of Article 123(2) EPC, and

- the claims of the eighth auxiliary request then on file met the requirements of Articles 54, 56 and 123(2) EPC.

V. In its statement setting out the grounds of appeal, opponent 1 contested the reasoning of the opposition division and submitted that the claims of the eighth auxiliary request held allowable by the opposition division did not comply with Article 123(2) and (3) EPC, and the subject-matter of the claims of said request did not involve an inventive step in view of D1 as the closest prior art.

VI. In its statement setting out the grounds of appeal, opponent 2 submitted that claims 2 and 3 of the eighth auxiliary request held allowable by the opposition division did not meet the requirements of Article 123(2) and (3) EPC. It submitted documents A026 to A028. It further submitted that the subject-matter of the claims of said request was not novel over D2 and D18, and did not involve an inventive step in view of D1, D18 or A027 as the closest prior art.

VII. In its statement setting out the grounds of appeal, the patent proprietor submitted that claim 1 of the main request was novel over D2 and involved an inventive step in view of D1 as the closest prior art. It submitted claim sets of the first to eighth auxiliary requests.

VIII. Since the patent proprietor and the opponents are both appellant and respondent in the present appeal proceedings, they are referred to as "patent

proprietor", "opponent 1" and "opponent 2" in the decision.

IX. In its reply to the grounds of appeal, opponent 1 submitted that the claim sets in the second to fifth, seventh and eighth auxiliary requests should not be admitted into the proceedings. It submitted that the claims of the first to eighth auxiliary requests added subject-matter. It further submitted that the subject-matter of claim 1 of each of the main request and the first to fifth auxiliary requests lacked novelty over D2, and that the subject-matter of claim 1 of all the requests did not involve an inventive step in view of D1 as the closest prior art. It submitted document A029 to evidence the suitability of Imatinib Mesylate for the treatment of chronic myelogenous leukemia.

X. In its reply to the grounds of appeal, opponent 2 submitted that claim 1 of each of the first to fourth, sixth and seventh auxiliary requests contravened Article 83 EPC. Claims 1 and/or 2 of the first to eighth auxiliary requests did not meet the requirements of Article 123(2) and (3) EPC. At least claim 1 of each of the first to fifth auxiliary requests and claim 2 of each of the first to third and fifth to seventh auxiliary requests lacked novelty over D2. Claim 1 of each of the first to eighth auxiliary requests lacked novelty in view of D18 or A027.

XI. In its reply to the grounds of appeal, the patent proprietor submitted that documents A026 to A028 should not be admitted into the proceedings. It commented on the objections made by opponents 1 and 2 and made submissions on the admittance of the first to eighth auxiliary requests.

XII. On 10 December 2021, the board issued a communication in preparation for the oral proceedings to be scheduled as requested by the parties.

XIII. By letter of 2 March 2021, opponent 1 withdrew its request for oral proceedings.

XIV. In a further letter dated 15 March 2021, opponent 2 submitted further arguments regarding added subject-matter in claim 2 of each of the first and second auxiliary requests. It also provided submissions on the admittance of the second to fifth, seventh and eighth auxiliary requests and A026, and further arguments on the inventive step of claim 1 of each of the second to eighth auxiliary requests.

XV. Oral proceedings before the board were held on 22 April 2021 by videoconference in the absence of opponent 1, in accordance with Rule 115(2) EPC and Article 15(3) RPBA. Opponent 2 stated that it did not rely on A027 and A028.

XVI. Opponents 1 and 2's case, where relevant to the present decision, may be summarised as follows.

Main request - Novelty

- Even if no XRPD were disclosed in D2, the compound in example 3 of D2 was the $\alpha_2$ crystalline form of Imatinib Mesylate according to claim 1 of the main request, as evidenced by the experimental data of D12. D12 was a reproduction of example 3 of D2. The XRPD of the crystalline form prepared in D12, including the precipitate formed prior to cooling, corresponded to that of the $\alpha_2$ crystalline form of Imatinib Mesylate according to claim 1 of the main request.

First auxiliary request - added subject-matter

- Claim 2 of the first auxiliary request represented an intermediate generalisation between the examples and claim 2 as filed.

- The specific reaction conditions (cooling time, concentrations, reaction temperatures) of the examples were linked with the subsequent cooling to 40-45°C within 45 minutes. These reaction conditions were not reflected in claim 2 of the first auxiliary request.

- The intermediate generalisation was not allowable.

Second auxiliary request - added subject-matter

- The arguments given for the intermediate generalisation in claim 2 of the first auxiliary request applied to claim 2 of the second auxiliary request.

Admittance of the second to fifth, seventh and eighth auxiliary requests

- These requests included second medical use claims and did not represent a reaction to an unexpected conclusion of the opposition division on the auxiliary requests presented in the first instance proceedings.

- Opponent 1 already objected to the novelty of the pharmaceutical composition in the letter of 20 December 2017 in preparation for oral proceedings to be held before the opposition division. In its summons to attend oral proceedings, the opposition division indicated that certain auxiliary requests may possibly not change the factual and legal situation underlying the claims of the main

request. The patent proprietor could not have been surprised by the discussion on the lack of novelty of the pharmaceutical compositions during the oral proceedings before the opposition division.

- By introducing claims that were in the form of a second medical use into said auxiliary requests in appeal proceedings, the opponents had no opportunity to object to such claims before the opposition division and the patent proprietor avoided the opposition division drawing a conclusion on the patentability of such claims. By admitting said auxiliary requests, the patent proprietor would have been given a second chance to overcome the objection of lack of novelty over D2 (Article 12(2) RPBA 2020).

- The second to fifth, seventh and eighth auxiliary requests could have been presented by the patent proprietor in the proceedings at first instance, and since they were not, said requests should not be admitted (Article 12(4) RPBA 2007).

Remittal

- The case should be remitted to the opposition division so that the new auxiliary requests could be reviewed in two instances, should they be admitted.

Third auxiliary request - added subject-matter

- The features "heating the reaction mixture at a temperature in the range of 75-80°C for a period of 30 minutes" found in claim 1 of the third auxiliary request did not meet the requirements of Article 123(2) EPC since the temperature of 75-80°C and the period of 30 minutes were not disclosed in claim 2

as filed or the term "heating at" did not have the same meaning as the term "heated to" found in examples 1 and 2 of the application as filed.

- The cooling temperature was linked to the concentration of the $\alpha_2$ crystalline form of Imatinib Mesylate, i.e. any concentration of the $\alpha_2$ crystalline form of Imatinib Mesylate in the reaction mixture could not be crystallized at a temperature of 40-45°C. Therefore the intermediate generalisation was not allowable.

Fourth auxiliary request

- Added subject-matter

  - Claim 2 of the fourth auxiliary request did not meet the requirements of Article 123(2) EPC since the application as filed did not disclose a process for the preparation of a pharmaceutical composition according to claim 2 of the fourth auxiliary request, defined by a method for the preparation of the $\alpha_2$ crystalline form.

- Extended protection

  - The claims as granted did not claim a process for preparing a pharmaceutical composition, defined by a method for the preparation of the $\alpha_2$ crystalline form. Claim 2 of the fourth auxiliary request referring to such a process therefore did not meet the requirements of Article 123(3) EPC.

- Sufficiency of disclosure

  - The invention defined in claim 1 of the fourth auxiliary request was not sufficiently disclosed since the claim did not define the x-ray wavelength used for repeating the measurement of the XRPD.

- Inventive step

  - D1 related to a crystalline form of Imatinib Mesylate and was the closest prior art. D1 disclosed a pharmaceutical composition comprising the β crystalline form.

  - The distinguishing feature of claim 1 of the fourth auxiliary request was the $\alpha_2$ crystalline form of Imatinib Mesylate.

  - There was no basis in the patent or the data provided by the patent proprietor for assessing that the $\alpha_2$ crystalline form of the claimed composition had any advantageous characteristics compared with the β crystalline form of D1.

  - The objective technical problem was to provide a composition comprising an alternative crystalline form of Imatinib Mesylate.

  - The screening of polymorphic form was part of common general knowledge as evidenced by D6. Therefore, D1 in combination with D6 would have prompted the skilled person to arrive at the claimed pharmaceutical composition comprising the $\alpha_2$ crystalline form of Imatinib Mesylate.

  - It was confirmed by T 2007/11 that screening for solid-state forms of a drug and characterisation of these forms did not require inventive skills.

- The subject-matter of claim 1 of the fourth auxiliary request did not involve an inventive step.

- Admittance of A026

  - The submission of A026 was occasioned by the fact that the opposition division ignored the relationship between the dissolution rate and the particle size. This argument, based on the difference in particle size, was already submitted in the letter in preparation for the oral proceedings before the opposition division.

XVII. The patent proprietor's case, where relevant to the present decision, may be summarised as follows.

Main request - Novelty of claim 1

- There was no single inevitable result of the teaching of example 3 of D2. The manufacturing method in D12 differed from that of D2 and could lead to a solid form of Imatinib Mesylate that was different from that obtained in D2. There was uncertainty as to the similarity of the product produced by D12 to that in example 3 of D2. D2 therefore did not provide a clear and unambiguous disclosure of a compound falling within the scope of the claims of the main request.

- Even if there were a high degree of probability that example 3 resulted in the $\alpha_2$ crystalline form of Imatinib Mesylate, it was not enough to acknowledge that the skilled person repeating example 3 of D2 would inevitably arrive at the compound claimed in the patent.

- D12 reported a small amount of amorphous material. The solid material formed in D12 prior to cooling could be this amorphous material, rather than the claimed $\alpha_2$ crystalline form.

- The $\alpha_2$ crystalline form of Imatinib Mesylate of claim 1 of the main request was novel in view of the disclosure of D2.

First auxiliary request - added subject-matter

- Claim 2 of the first auxiliary request was based on claims 1, 2 and 4 as filed, and examples 1 and 2 of the application as filed.

- The cooling temperature disclosed in examples 1 and 2 of the application as filed, and referred to in claim 2 of the first auxiliary request, was not linked to the other features of the process of preparation of the $\alpha_2$ crystalline form of Imatinib Mesylate disclosed in said examples.

- The intermediate generalisation was allowable.

Second auxiliary request - added subject-matter

- The arguments given for the intermediate generalisation in claim 2 of the first auxiliary request applied to claim 2 of the second auxiliary request.

Admittance of the second to fifth, seventh and eighth auxiliary requests

- The second to fifth, seventh and eighth auxiliary requests were closely related to the auxiliary requests admitted into the first instance proceedings.

- The patent proprietor was taken by surprise by the opposition division's conclusion that D2 disclosed a pharmaceutical composition suitable for the treatment of chronic myelogenous leukemia and comprising the product of example 3 of D2 and a pharmaceutically acceptable excipient. The second to fifth, seventh and eighth auxiliary requests addressed the objection of lack of novelty over D2, as submitted in the statement of grounds of appeal.

- The admission of the requests including second medical use claims did not "shift the whole case" and did not require any significant analysis by any party, since the introduction of second medical use claims only overcame the objection of lack of novelty over D2.

Third auxiliary request - added subject-matter

- The feature "heating at" found in claim 2 of the third auxiliary request had the same meaning as the feature "heating to" found in examples 1 and 2 of the application as filed.

- The reasons given for claim 2 of the first auxiliary request and regarding the intermediate generalisation applied to claim 2 of the third auxiliary request.

Auxiliary request 4

- Added subject-matter

  - The application as filed (page 1, lines 11 and 12) disclosed a process for the preparation of a pharmaceutical composition.

- Claim 2 of the fourth auxiliary request did not introduce subject-matter which extended beyond the content of the application as filed.

- Extended protection

  - According to established case law, a product claim conferred protection to all processes for making that product. Claim 1 as granted embraced the $\alpha_2$ crystalline form of Imatinib Mesylate, with all compositions comprising this crystalline form and all methods for producing the composition comprising this crystalline form.

  - Claim 2 of the fourth auxiliary request, relating to a process for the preparation of a pharmaceutical composition comprising the $\alpha_2$ crystalline form of Imatinib Mesylate thus met the requirements of Article 123(3) EPC.

- Sufficiency of disclosure

  - The opposition division's findings that the claims of the main request met the requirements of Article 83 EPC applied to the claims of the fourth auxiliary request.

- Inventive step

  - D1 disclosed a pharmaceutical composition comprising the β crystalline form of Imatinib Mesylate.

  - The distinguishing feature of claim 1 of the fourth auxiliary request was the $\alpha_2$ crystalline form of Imatinib Mesylate.

- Tables 3 to 6 of the patent showed that the $\alpha_2$ crystalline form of Imatinib Mesylate had stability properties and a solubility higher than that of the β crystalline form of Imatinib Mesylate of D1.

- The objective technical problem was the provision of a pharmaceutical composition containing a crystalline form of Imatinib Mesylate which had balanced properties in terms of high solubility and sufficient stability.

- The teaching of D1 led away from screening any α crystalline form of Imatinib Mesylate, the document mentioning that such crystalline forms were metastable at room temperature, hygroscopic and not suitable for pharmaceutical compositions. Providing the $\alpha_2$ crystalline form of Imatinib Mesylate was not obvious.

- The subject-matter of claim 1 of the fourth auxiliary request involved an inventive step.

- Admittance of A026 and the opponent 2's statement on D1

  - A026 was an experimental report on the dissolution rates of the $\alpha_2$ crystalline form according to the invention and the β crystalline form of Imatinib Mesylate disclosed in D1. The dissolution profile of the different crystalline forms of Imatinib Mesylate, as presented in table 6 of the patent was already discussed at the beginning of the opposition proceedings and was not occasioned by matter first raised in the impugned decision. A026 should not be admitted into the proceedings pursuant to Articles 12(4) RPBA 2007. Admitting A026 would have led to a new

evaluation of the technical data on dissolution rate and an entirely fresh case, contrary to the requirements of Article 12(2) RPBA 2020.

- The opponent 2's statement that the α crystalline form of Imatinib Mesylate disclosed in D1 (bottom of page 2 and figure 1/3 of D1) was not the $\alpha_2$ crystalline form as claimed was only made during the oral proceedings before the board and should not be admitted into the proceedings.

XVIII. The parties' requests relevant for the present decision were the following:

Opponent 1 requested in the written proceedings:

- that the decision under appeal be set aside and the patent be revoked in its entirety,

- that the second to fifth, seventh and eighth auxiliary requests not be admitted into the proceedings, and

- should the board admit any of said auxiliary requests into the proceedings, the case be remitted to the opposition division.

Opponent 2 requested:

- that the decision under appeal be set aside and the patent be revoked in its entirety,

- that A026 be admitted into the proceedings, and

- that the second to fifth, seventh and eighth auxiliary requests not be admitted into the proceedings.

The patent proprietor requested that:

- the decision under appeal be set aside and the patent be maintained as granted,

- alternatively, that the patent be maintained in amended form on the basis of one of the claim sets of the first to eighth auxiliary requests, the sixth auxiliary request implying the dismissal of the opponents' appeals,

- document A026 not be admitted into the proceedings, and

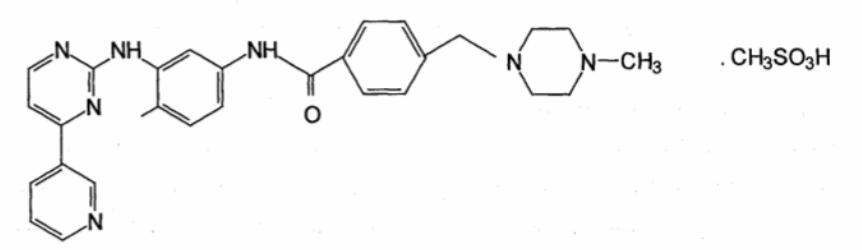
- that opponent 2's request of not admitting the second to fifth, seventh and eighth auxiliary requests into the proceedings not be considered.

## Reasons for the Decision

Main request - patent as granted

1. Claim 1 of the main request (II, *supra*) relates to an $\alpha_2$ crystalline form of Imatinib Mesylate which has the XRPD characteristics given in the claim and is stable at room temperature and even at higher temperatures like 120°C and accelerated stress conditions, and is freely soluble in water.

Imatinib Mesylate has the following chemical formula:



2. Admittance of the objection of lack of novelty based on D18

2.1 Opponent 2 objected to the novelty of the subject-matter of claim 1 of the main request in view of the disclosure of D18 (page 2 of D18).

2.2 The board notes the following:

D18 (page 2, first paragraph) discloses a tablet comprising an Imatinib compound and an excipient. The Imatinib compound is an α or β crystalline form of Imatinib Mesylate (page 2, fourth paragraph).

The objection of lack of novelty based on D18 has not been raised during the first instance proceedings and was not discussed in the impugned decision. The objection was submitted for the first time with the statement of grounds of appeal.

The admittance of the objection based on D18 is thus governed by Article 12(4) RPBA 2007 (cf. the transitional provisions pursuant to Article 25(2) RPBA 2020, the statement of grounds of appeal having been filed before 1 January 2020).

2.3 D18 was relied upon by opponent 2 during the opposition proceedings in the context of obviousness in combination with D1 as the closest prior art (point 6.3 of the notice of opposition). No objection of lack of novelty based on D18 was raised in the notice of opposition or in the letter of 20 December 2017 in preparation to oral proceedings before the opposition division.

Furthermore, opponent 2 did not argue that the objection was submitted in response to facts, objections, arguments or evidence on which the decision

under appeal is based and the board sees no reason that justifies the late filing of the objection.

Consequently, the objection could (and should) have been presented during the first instance proceedings in the sense of Article 12(4) RPBA 2007.

Furthermore, it is the purpose of appeal proceedings to review the opposition division's decision rather than to start a second opposition proceedings (Article 12(2) RPBA 2020). Admitting the objection based on D18 into the proceedings would give opponent 2 a second chance in opposition proceedings to object to novelty over a different document, even if the decision under appeal could not deal with this objection.

The above points were made already in the board's communication under Article 15(1) RPBA and not contested by the opponents.

Therefore, the board decided that the objection of lack of novelty in view of D18 would not be admitted into the proceedings in accordance with Article 12(4) RPBA 2007 and Article 12(2) RPBA 2020.

3. Novelty

3.1 Opponents 1 and 2 objected to the novelty of the subject-matter of claim 1 of the main request in view of example 3 of D2, as evidenced by D12.

3.2 Example 3 of D2 discloses the preparation of Imatinib Mesylate. The Imatinib free base (50 g) was suspended in 500 ml of isopropanol and 9.85 g of methane sulphonic acid was added. The reaction mixture was refluxed for 2 hours, concentrated to about 100 ml volume, cooled and Imatinib Mesylate was isolated. D2 does not disclose any XRPD of the product prepared.

D12 is a document submitted by opponent 1 with its notice of opposition. It is a repetition of example 3 of D2: 1.795 g of the Imatinib free base was suspended in 18 ml isopropanol (2-propanol), 0.354 g of methane sulphonic acid was added dropwise. The mixture was heated to its boiling temperature, whereupon all solid material was dissolved, and then refluxed for 2 hours. The reaction mixture was concentrated to about half of its initial volume, cooled and transferred to a Petri dish. After drying overnight at 65°C, a sample was analysed by XRPD.

The XRPD of the sample of D12 corresponds to the XRPD of the $\alpha_2$ crystalline form of Imatinib Mesylate as defined in claim 1. This is common ground between the parties.

Neither D2 nor D12 gives any details about how cooling was performed.

3.3 The patent proprietor submitted that :

- Which type of solid form of Imatinib Mesylate was obtained depended on the cooling conditions. Since these were not disclosed in example 3 of D2, there was no single inevitable result of the teaching of this example. The manufacturing method of D12 differed from that of D2 and could lead to a solid form of Imatinib Mesylate that was different from that obtained in D2. D2 did not therefore provide a clear and unambiguous disclosure of a compound falling within the scope of the claims of the main request. The repetition of the process for preparing a solid form of Imatinib Mesylate in D12 was uncertain since the exact conditions were not disclosed in D2. The fact that the cooling conditions, which were not disclosed in D2, could

afford a different solid form of Imatinib Mesylate was shown by D8, which taught that a rapid cooling of the composition resulted in an amorphous form.

- Even if there was a high degree of probability that example 3 of D2 resulted in the $\alpha_2$ crystalline form of Imatinib Mesylate, it was not enough to acknowledge that the skilled person repeating example 3 of D2 would inevitably arrive at the compound claimed in the patent.

- D12 reported a small amount of amorphous material. The solid material formed in D12 prior to cooling could be this amorphous material, rather than the claimed $\alpha_2$ crystalline form, as argued by the opponent.

3.4 The board does not agree.

The board acknowledges that cooling with ice (hereinafter "ice cooling") as referred to in D8 may lead to the formation of amorphous Imatinib Mesylate rather than the claimed $\alpha_2$ crystalline form.

However, in example 3, no ice cooling is mentioned, and therefore it can be assumed that ordinary cooling at room temperature was applied. According to the declaration D21, in D12 too, cooling was performed by leaving the reaction mixture to cool at room temperature ("*In my experiment I, after reflux ar approximately 83°C for two hours, left the Erlenmeyer flask to cool a room temperature.*"). Hence, it can be assumed that D12 is a proper repetition of example 3 of D2 and that thus, in the same way as in D12, the claimed $\alpha_2$ crystalline form is obtained in this example too.

This conclusion does not change even if it is assumed that the skilled person would read the step of cooling in example 3 of D2 ("*The reaction mixture was concentrated to about 100ml volume, cooled and the product isolated...*", emphasis added) as implying "ice cooling". More specifically, in D12 a precipitate was already obtained **before** starting cooling, see paragraph 5.b. of D12 ("*During this period a significant amount of material precipitated, Figure 1.*", emphasis added by the board). Hence, in D2 too, a precipitate must form before the start of ice cooling (if any). As submitted by opponent 1's expert of in D21, this precipitate can only be the $\alpha_2$ crystalline form of Imatinib Mesylate. Once formed, there can also be no reason why the subsequent cooling process, whether it is carried out at room temperature or by ice cooling, should change the polymorphic form of the product. Consequently, the formation of the precipitate in D12 and thus example 3 of D2 before cooling represents only one single inevitable result: the formation of $\alpha_2$ crystalline form of Imatinib Mesylate.

With regard to the proprietor's argument that the solid material formed in D12 prior to cooling could be the amorphous material mentioned in D12, the board notes the following: it is stated in D12 that during reflux, i.e. prior to cooling a **significant** amount of material precipitated (point 5c on the first page). This significant amount of material cannot be the amount of the amorphous material mentioned in D12 since the latter amount is defined in D12 to be **small** (point 7 on first page).

3.5 For the reasons given above, the board concludes that the subject-matter of claim 1 of the main request is disclosed in example 3 of D2, as evidenced by D12. The

subject-matter of claim 1 of the main request thus lacks novelty over D2.

4. In view of the above lack of novelty of the subject-matter of claim 1, the main request is not allowable.

First auxiliary request

5. Article 123(2) EPC - Claim 2

5.1 Claim 2 of the first auxiliary request reads as follows:

*"2. A process for the preparation of ~~a novel $\alpha_2$ crystalline form of Imatinib Mesylate~~* ***the pharmaceutical composition of claim 1,*** *~~comprises~~* ***the method comprising:***

*suspending Imatinib base in isopropanol;* *~~and~~*

*adding methane sulfonic acid at room temperature;* *~~and~~*

*maintaining the reaction mixture at a temperature in the range of 40-80°C, for a period in the range of 20-30 minutes;* ***and***

*cooling* ***to 40-45 °C*** *and filtering to obtain the $\alpha_2$ crystal form."* (Emphasis added by the board; struck-through and bold text representing deletions and additions, respectively, compared to claim 2 as filed.)

5.2 Opponent 2 objected that claim 2 of the first auxiliary request introduced subject-matter beyond the content of the application as filed.

5.3 Claim 2 of the first auxiliary request corresponds to claim 2 of the application as filed, except that the process claim is directed to the preparation of the

pharmaceutical composition of claim 1 and the temperature of cooling was specified to be 40-45°C.

Examples 1 and 2 of the application as filed refer to the preparation of the $\alpha_2$ crystalline form. The following temperature is mentioned in the examples: "*and slowly cooled to **40-45°C** during 45 minutes*" (emphasis added). Example 14 discloses the preparation of capsules containing the $\alpha_2$ crystalline form. Example 14 refers to example 1 for the preparation of the $\alpha_2$ crystalline form used for preparing the capsules.

Hence, as submitted by opponent 2, claim 2 of the first auxiliary request represents an intermediate generalisation between claim 2 as filed and the examples of the application as filed.

5.4 According to case law, an intermediate generalisation is in line with Article 123(2) EPC if the extracted feature is not inextricably linked with the other features of the example (see e.g. T 714/00, T 2154/11 and T 2287/11).

5.5 In the case at hand, in order to establish whether the intermediate generalisation is allowable, the question has to be examined as to whether the skilled person could recognise without any doubt from the application as filed that the temperature range **40-45°C** is closely related to the other characteristics of example 1 (i.e. for the preparation of the $\alpha_2$ crystalline form).

This question has to be answered in the affirmative. The "cooling time" during 45 minutes disclosed in examples 1 and 2 of the application as filed is closely related to e.g. the cooling temperature because the effect of cooling not only depends on the temperature but also the time of cooling. More specifically, the

higher the temperature, the shorter the cooling time, and vice versa, to achieve a certain cooling effectiveness and thus crystallisation. Therefore both features are inextricably linked to each other, and for that reason alone, the extraction of the cooling temperature without the cooling time in claim 2 of the first auxiliary request is not allowable.

Furthermore, the temperature of the reaction mixture of 75-80°C disclosed in examples 1 and 2 of the application as filed, i.e. before starting the cooling step, is also linked to the temperature range **40-45°C**, the cooling temperature being dependent on the temperature of the reaction mixture before cooling. The temperature of the reaction mixture (78-80°C) disclosed in examples 1 and 2 of the application as filed is, however, different from the temperature of 40-80°C as mentioned in claim 2 of the first auxiliary request.

The cooling temperature is further linked to the concentration of the $\alpha_2$ crystalline form of Imatinib Mesylate. Not each and every concentration of the $\alpha_2$ crystalline form of Imatinib Mesylate in the reaction mixture can be crystallized at a given temperature of 40-45°C.

Since the cooling temperature on the one hand and the temperature of the reaction mixture of 75-80°C or the initial concentration of the $\alpha_2$ crystalline form of Imatinib Mesylate on the other hand are also inextricably linked to each other, the intermediate generalisation is not allowable for that reason either.

Consequently, claim 2 of the first auxiliary request introduces subject-matter beyond the content of the application as filed, contrary to the requirements of Article 123(2) EPC.

6. For this reason, the first auxiliary request is not allowable.

Second auxiliary request

7. Article 123(2) EPC - Claim 2

Claim 2 of the second auxiliary request essentially corresponds to claim 2 of the first auxiliary request, the only difference being that the feature "pharmaceutical composition of claim 1" in claim 2 of the first auxiliary request was replaced by "pharmaceutical composition **as defined in** claim 1".

Since claim 2 of the second auxiliary request comprises the same feature "cooling to 40-45°C" as claim 2 of the first auxiliary request, the reasons given for claim 2 of the first auxiliary request apply, *mutatis mutandis*, to claim 2 of the second auxiliary request. This was not disputed by the patent proprietor during the oral proceedings.

Hence, claim 2 of the second auxiliary request does not fulfill the requirements of Article 123(2) EPC.

The second auxiliary request is for that reason not allowable.

8. Admittance of the second auxiliary request

During the oral proceedings, it was found that the second auxiliary request was not allowable, and therefore there was no need to decide on its admittance.

9. Admittance of the third to fifth, seventh and eighth auxiliary requests

9.1 Opponents 1 and 2 objected to the admittance of the third to fifth, seventh and eighth auxiliary requests.

9.2 The claims of the third to fifth, seventh and eighth auxiliary requests were submitted with the statement of grounds of appeal. Consequently, the admittance of the claim requests is governed by Article 12(4) RPBA 2007 (statement of grounds of appeal filed before 1 January 2020; cf. the transitional provisions pursuant to Article 25(2) RPBA 2020).

The board notes the following:

- The claims of the third to fifth auxiliary requests are based on the claims of the fourth, fifth, second auxiliary requests and those of the seventh and eighth auxiliary requests are based on the claims of the eighth auxiliary request, all submitted during the proceedings at first instance. The differences between the claims of the third to fifth, seventh and eighth auxiliary requests and the requests submitted during the first instance proceedings are (a) for some auxiliary requests, removal of the XRPD wavelength from claim 1, (b) for some auxiliary requests, cancellation of claim 2 and (c), for all of the third to fifth, seventh and eighth auxiliary requests, revision of claim 1 in the form of a second medical use claim.

- In its notice of opposition (point 6.1), opponent 1 only referred to the lack of novelty of the $\alpha_2$ crystalline form of Imatinib Mesylate, i.e. to the subject-matter of claim 1 as granted, in view of the disclosure of D2.

- In the same way, opponent 2 objected to the novelty of the subject-matter of claim 1 as granted in view of the disclosure of D2 (point 5.2 of its notice of opposition).

- No objection was raised by the opponents in their notice of opposition against the subject-matter of claim 4 as granted relating to a pharmaceutical composition useful for the treatment of chronic myelogenous leukemia.

- In the summons to attend oral proceedings (points 9-11), the opposition division summarised the parties' submissions on the aforementioned objection and did not comment on the novelty of the pharmaceutical compositions according to claim 4 as granted.

- Opponent 2 maintained the objection of lack of novelty of claim 1 as granted in its letter of 20 December 2017 (point 3.4).

- Opponent 1 maintained the objection of lack of novelty of claim 1 as granted in its letter of 21 December 2017 (point 2). It also objected to the novelty of claims of the second, fourth and fifth auxiliary requests then on file directed to a pharmaceutical composition, without arguing on the suitability of the pharmaceutical composition ("useful for the treatment of chronic myelogenous leukemia")(point 4.2 of his letter).

- An objection of lack of novelty of the subject-matter of claim 1 of auxiliary request 7 then on file, relating to a pharmaceutical composition useful for the treatment of chronic myelogenous leukemia, was discussed during the oral proceeding

before the opposition division, based on the disclosure of D2 (point 10 of the minutes).

9.3 Opponent 1 argued that the new auxiliary requests did not address any objections raised by the opposition division.

Opponent 1 and 2 both submitted that, by introducing claims being in the form of a second medical use in said auxiliary requests in appeal proceedings, the opponents had no opportunity to object to such claims before the opposition division and the patent proprietor avoided the opposition division drawing a conclusion on the patentability of such claims. By admitting said auxiliary requests, a second chance would have been given to the patent proprietor to overcome the objection of lack of novelty in view of D2, contrary to the requirements of Article 12(2) RPBA 2020.

Opponent 2 submitted that opponent 1 had already objected to the novelty of the pharmaceutical composition in the letter of 21 December 2017 in preparation to oral proceedings to be held before the opposition division. Furthermore, in its summons to attend oral proceedings the opposition division indicated that certain auxiliary requests may possibly not change the factual and legal situation underlying the claims of the main request. The patent proprietor could not have been surprised by the discussion of the lack of novelty of the pharmaceutical compositions during the oral proceedings before the opposition division.

9.4 The board does not agree with the opponents:

The board observes that the objection of lack of novelty of the claimed **pharmaceutical composition useful for the treatment of chronic myelogenous leukemia** was discussed for the first time during the oral proceedings. The question of whether the feature "useful for the treatment of chronic myelogenous leukemia" was a distinguishing feature was only discussed during the oral proceedings. Consequently, the submission of the third to fifth, seventh and eighth auxiliary requests, of which claim 1 was restricted to a pharmaceutical composition for use in the treatment of chronic myelogenous leukemia to overcome the objection of lack of novelty over D2, is a reasonable response to the late objection and the resulting decision by the opposition division. Therefore, opponent 1's argument that the requests did not address any objections raised by the opposition division is not accepted.

With regard to the argument that the objection of lack of novelty of the pharmaceutical composition was already raised before oral proceedings in its letter of 21 December 2017 in preparation for oral proceedings (point 4.2), opponent 1 mentioned that a pharmaceutical composition comprising the $\alpha_2$ crystalline form of Imatinib Mesylate was not novel over D2 and did not involve an inventive step in view of D1 as the closest prior art; however, it was not argued whether the feature "useful for the treatment of chronic myelogenous leukemia" was disclosed in D2. Whether or not the feature was a distinguishing feature of claim 1 of auxiliary request 7 over the disclosure of D2 was only discussed during the oral proceedings before the opposition division (reasoning given in point 21 of the decision).

Therefore, the claims of the third to fifth, seventh and eighth auxiliary requests could not have been filed during the first-instance proceedings (Article 12(4) RPBA 2007).

Regarding the argument based on Article 12(2) RPBA 2020, the patent proprietor's case does not represent a fresh case. The scope of discussion does not change. Claim 1 of auxiliary request 7 submitted before the opposition division concerned a pharmaceutical composition useful for the treatment of chronic myelogenous leukemia. Recasting the claim as a second medical use on the basis of claim 1 of auxiliary request 7 submitted before the opposition division, i.e. based on the same medical application (treatment of chronic myelogenous leukemia) does not change the scope of discussion.

9.5 Considering the above, the board decided to admit the third to fifth, seventh and eighth auxiliary requests into the proceedings pursuant to Articles 12(4) RPBA 2007 and 12(2) RPBA 2020.

10. Admittance of the opponent 2's request not to admit the second to fifth, seventh and eighth auxiliary requests into the proceedings.

During the oral proceedings, opponent 2 requested not to admit the second to fifth, seventh and eighth auxiliary requests into the proceedings. The patent proprietor objected to the admittance of this request.

Since the second auxiliary request was found non-allowable and the third to fifth, seventh and eighth auxiliary requests were admitted into the proceedings, there was no need to decide on the patent proprietor's

request not to admit opponent 2's request not to admit the auxiliary requests.

11. Remittal

11.1 As set out above, the board admitted the third to fifth, seventh and eighth auxiliary requests into the proceedings. Opponent 1 requested that, should the board admit any of the second to fifth, seventh and eighth auxiliary requests into the proceedings, the case be remitted to the opposition division.

11.2 The board does not see any reason to remit the case to the opposition division. The claims of said requests were recast as second medical use claims to overcome the objection of lack of novelty over D2; however; the second medical use format was not relied on for the assessment of inventive step by the patent proprietor, which was the issue to be decided on if the case were remitted, and does not require any excessive additional analysis by any party. Therefore, recasting the claims as second medical use claims does not represent special reasons in the sense of Article 11 RPBA 2020 to remit the case to the opposition division.

11.3 This position was already contained in the board's communication pursuant to Article 15(1) RPBA and was not contested by the opponent 1.

11.4 The board has therefore decided not to remit the case and to decide on substance, see below.

Third auxiliary request

12. Claim 2 of the third auxiliary request reads as follows:

*"2. A process for the preparation of ~~a novel $\alpha_2$ crystalline form of Imatinib Mesylate~~* ***the pharmaceutical composition of claim 1,*** *~~comprises~~* ***the method comprising:***

*suspending Imatinib base in isopropanol; ~~and~~*

*adding methane sulfonic acid at room temperature; ~~and~~*

*~~maintaining~~* ***heating*** *the reaction mixture at a temperature in the range of ~~40~~* ***75****-80°C, for a period ~~in the range~~ of ~~20-~~30 minutes;* ***and***

*cooling* ***to 40-45 °C during 45 minutes*** *and filtering to obtain the $\alpha_2$ crystal form."* (Emphasis added by the board; struck- through and bold text representing deletions and additions, respectively, compared to claim 2 as filed.)

13. Added subject-matter - Claim 2

13.1 Opponents 1 and 2 objected to the amendment made in claim 2 of the third auxiliary request. A first objection was as regards to the term "heating at" and a second objection related to the intermediate generalisation between claim 2 as filed and the examples of the application as filed.

13.2 Claim 2 of the third auxiliary request does not meet the requirements of 123(2) EPC since the term "heating the reaction mixture at a temperature in the range of 75-80°C for a period of 30 minutes" found in the claim does not have the same meaning as the term "maintaining

the reaction mixture at a temperature in the range of **40-80°C,** for a period in the range of **20-30** minutes" found in claim 2 as filed or as the term "heated **to** 75-80°C for 30 minutes" found in examples 1 and 2 of the application as filed. Firstly, the temperature and the time disclosed in claim 2 as filed (40-80°C and 20-30 minutes) do not correspond to those referred to in claim 2 of the third auxiliary request (75-80°C and 30 minutes). Secondly, "heating to" (examples 1 and 2 of the application as filed) means making warm or hot, e.g. starting from room temperature to a certain temperature. "Heating at" (claim 2 of the third auxiliary request) means to keep a certain temperature constant. The 30 minutes referred to in the examples correspond to the overall time needed for heating the reaction mixture from room temperature to 75-80°C and keeping the reaction mixture at that temperature, meaning that the time during which the reaction mixture is kept at the temperature of 75-80°C is **less than** 30 minutes. Therefore, the time during which the reaction mixture is kept at 75-80°C in claim 2 of the third auxiliary request (i.e. heating the reaction mixture at 75-80°C for 30 minutes) does not correspond to the time during which the reaction mixture is kept at 75-80°C in example 1 or 2 of the application as filed (less than 30 minutes)

Considering the above, the board concludes that the introduction of the term "heating at" into claim 2 of the third auxiliary request does not comply with Article 123(2) EPC.

13.3 Intermediate generalisation

Like claim 2 of the first auxiliary request, the feature "cooling to 40 to 45°C" is based on the disclosure of example 1 or 2. In contrast to claim 2 of

the first auxiliary request, the following additional features were added to claim 2 of the third auxiliary request:

- heating the reaction mixture at a temperature in the range of **75**-80°C (40-80°C in claim 2 of the first auxiliary request)
- cooling to 40-45 °C **during 45 minutes** (no time specified in claim 2 of the first auxiliary request).

As set out in the context of claim 1 of the first auxiliary request, the board is of the view that the cooling temperature is linked to the concentration of the $\alpha_2$ crystalline form of Imatinib Mesylate (5.3, *supra*). Since claim 2 of the third auxiliary request does not refer to the concentration used in the example of the application as filed, the intermediate generalisation is still not allowable.

13.4 For the reasons set out above, claim 2 of the third auxiliary request does not fulfill the requirements of Article 123(2) EPC and the third auxiliary request is not allowable.

Fourth auxiliary request

14. Claims 1-4 of the fourth auxiliary request correspond to claims 1 and 3-5 of the second auxiliary request.

14.1 Claim 2 of the fourth auxiliary request reads as follows:

"2. *A process for the preparation of ~~a novel, stable $\alpha_2$ crystalline form of Imatinib Mesylate which comprises~~* ***the pharmaceutical composition as defined in claim 1, the method comprising:***

*suspending β polymorphic form Imatinib Mesylate in water and organic solvents like methanol, Isopropyl ether, toluene, cyclohexane and Isopropyl alcohol;*

*distilling off water azeotropically; and*

*cooling filtering to obtain the $\alpha_2$ crystal form.*"
(Emphasis added by the board; struck-through and bold text representing deletions and additions, respectively, compared with claim 3 as filed).

Claim 2 of the fourth auxiliary request relates to the preparation of a pharmaceutical composition while claim 3 as filed relates to the preparation of $\alpha_2$ crystalline form of Imatinib Mesylate.

14.2 Opponent 1 submitted that the application as filed did not disclose a process for the preparation of a pharmaceutical composition according to claim 2 of the fourth auxiliary request, defined by a method for the preparation of the $\alpha_2$ crystalline form.

14.3 The board does not agree. As submitted by the patent proprietor, the disclosure of a process for the preparation of a pharmaceutical composition is explicitly disclosed in the application as filed. The passage on page 1, lines 11-12 explicitly refers to "*a process for the preparation of the novel polymorphic form and pharmaceutical compositions containing the novel stable $\alpha_2$ form of Imatinib mesylate and usually employed exepients* [sic]...". Therefore, claim 2 of the fourth auxiliary request is a combination of claim 3 as originally filed and the above passage.

14.4 Considering the above, the board concludes that claim 2 of the fourth auxiliary request meets the requirements of Article 123(2) EPC.

15. Article 123(3) EPC

15.1 Opponents 1 and 2 submitted that claim 3 of the fourth auxiliary request did not meet the requirements of Article 123(3) EPC.

15.2 The board notes that claim 1 as granted relates to the $\alpha_2$ crystalline form of Imatinib Mesylate. As submitted by the patent proprietor, claim 1 as granted confers protection on the compound *per se* and, necessarily, on any composition comprising the compound, and thus the pharmaceutical composition of claim 1 of the fourth auxiliary request, and on any process for the preparation of the pharmaceutical. Thus, claim 2 of the fourth auxiliary request, relating to a process for the preparation of the pharmaceutical composition of claim 1 of the fourth auxiliary request, does not extend the protection conferred by claim 1 as granted and the requirements of Article 123(3) EPC are met.

15.3 This position was already contained in the board's communication pursuant to Article 15(1) RPBA and not contested by the opponents.

16. Sufficiency of disclosure

16.1 Opponent 2 submitted that claim 1 of the fourth auxiliary request was not sufficiently disclosed since the claim did not define the x-ray wavelength used for repeating the measurement of the XRPD peaks defining the $\alpha_2$ crystalline form of Imatinib Mesylate in the claim.

16.2 The board notes the following. The opposition division reasoned in its decision (point 13) why it concluded that the missing indication in a claim of the x-ray wavelength for the XRPD radiation source was not a valid reason for an objection under Article 83 EPC. In

its submission, opponent 2 did not submit why the conclusion of the opposition division would not be correct. In fact, the application as filed identifies the anode and the x-ray wavelength used for measuring the XRPD in figures 1 and 4 ("Anode: Cu - WL1: 1.5406"), as justified by the opposition division.

16.3 This position was already contained in the board's communication pursuant to Article 15(1) RPBA and not contested by the opponents.

16.4 The board concludes that claim 1 of the fourth auxiliary request meets the requirements of Article 83 EPC.

17. Inventive step

17.1 Opponents 1 and 2 objected to the inventive step of claim 1 of the fourth auxiliary request in view of D1 as the closest prior art.

17.2 Closest prior art

The patent aims to provide a polymorphic form of Imatinib Mesylate which is stable under accelerated stress conditions at room temperature or higher and is freely soluble in water for the preparation of pharmaceutical compositions for the treatment of tumors and cancers (see paragraphs [0001], [0003] and [0019] of the patent).

D1 relates to a crystalline form of Imatinib Mesylate, namely the β crystalline form (claim 1 of D1), and the use thereof in a pharmaceutical composition for treating a tumour disease (claim 12 of D1). This represents the same aim as that of the patent in suit. D1 thus provides suitable disclosure of the closest

prior art in the assessment of inventive step of the claimed subject-matter.

17.3 Distinguishing feature

As set out above, D1 discloses the β crystalline form of Imatinib Mesylate. D1 does not disclose the $\alpha_2$ crystalline form of Imatinib Mesylate of claim 1 of the fourth auxiliary request.

The distinguishing feature of claim 1 of the main request is thus the specific crystalline form of Imatinib Mesylate. This was common ground between the parties.

17.4 Formulation of the objective technical problem.

Table 3 of the patent shows the dissolution and stability characteristics of two capsules comprising the $\alpha_2$ crystalline form of Imatinib Mesylate. The table shows that both capsules are stable under 40°±2°C and a relative humidity of 75±5%, or under 25°±2°C and a relative humidity of 60±5%.

Table 4 of the patent relates to a boiling test tube. The $\alpha_2$ crystalline form of Imatinib Mesylate is heated at a temperature of 110 or 120°C for 2, 4 or 6 hours. The only polymorph detected after heating is the $\alpha_2$ crystalline form of Imatinib Mesylate.

Table 5 of the patent sets forth the results of the stability of the $\alpha_2$ crystalline form of Imatinib Mesylate (in a capsule or in bulk) under stress conditions (40°±2°C and a relative humidity of 75±5% for six months). The only polymorph form detected after the test was the $\alpha_2$ crystalline form.

Table 6 of the patent compares the dissolution rate of capsules comprising the $\alpha_2$ crystalline form (according to claim 1) or the β crystalline form (according to D1) at an amount equivalent of 100 mg of Imatinib base (bottom of table 6). Table 6 shows that the release profile of the capsule formulated with the $\alpha_2$ crystalline form is better than the capsule formulated with the β crystalline form after a time of 5, 10, 15, 20 and 30 minutes (61.3, 85.5, 90.5, 92.6, 98.0% for $\alpha_2$ and 32.6, 54.4, 69.4, 78.2, 95.8% for β). A value of 100% dissolution rate is obtained in both cases after 45 minutes.

Based on these results, the objective technical problem is to provide a pharmaceutical composition containing a crystalline form of Imatinib Mesylate, which has balanced properties in terms of high solubility and sufficient stability.

17.5 Obviousness

D1 teaches that the α crystalline form is less thermodynamically stable than the β crystalline form (page 8, second full paragraph).

As submitted by opponent 1, it is expected that, based on the teaching that the α crystalline form is less thermodynamically stable, said form is more soluble than the β crystalline form. The skilled person knows that the most stable crystalline form would need more energy to dissolve and would be less soluble than a crystalline form which is less thermodynamically stable. It can be thus concluded that the improved solubility of the $\alpha_2$ crystalline form disclosed in D1 and thus the $\alpha_2$ crystalline form of claim 1 of AR4 is expected in view of the teaching of D1.

However, D1 does not teach that the α crystalline form is sufficiently stable and suitable for the pharmaceutical composition since it is stated in D1 (bottom of page 2) that the α crystalline form of Imatinib Mesylate "*(...) is hygroscopic. In this form, the crystals* ***are not particularly well-suited to pharmaceutical formulation*** *as solid dosage forms, because their physical properties, for example their flow characteristics, are unfavourable*." (emphasis added). Furthermore, the first full paragraph on page 3 of D1 teaches that "*the β-crystal form is less hygroscopic than the α-crystal form and thus also stores better and is easier to process*". Finally, the second paragraph on page 8 mentions that the α crystalline form of Imatinib Mesylate is metastable at room temperature.

Therefore, these passages in D1 provide teaching that leads away from considering the α crystalline form as a candidate for solving the problem posed.

Consequently, the skilled person would not have investigated the production or the development of an α crystalline form of Imatinib Mesylate, let alone the $\alpha_2$ crystalline form, for solving the objective technical problem.

17.6 Opponents 1 and 2 submitted that the mere provision of a further crystalline form of a known pharmaceutically active compound by means of routine investigations and routine experimentation, i.e. screening for solid-state forms of a drug and characterisation of these forms, did not require inventive skills. They cited decision T 2007/11 to support that claim 1 lacked an inventive step.

According to T 2007/11 (reasons 7.7.1), "*Screening for solid-state forms of a drug and characterisation of these forms is routine practice in the pharmaceutical industry and forms part of the routine task of the skilled person working in the field of drug development, in particular in view of regulatory requirements to provide information on polymorphic, hydrated (solvated) or amorphous forms of a drug*" and "*The mere provision of a further crystalline form of a known pharmaceutically active compound as the result of such routine investigations and routine experimentation does not require inventive skills*".

The case in hand differs from that decision in that the objective technical problem in this case is not that of providing a further crystalline form of Imatinib Mesylate, but that of providing a pharmaceutical composition comprising a crystalline form of Imatinib Mesylate which has balanced properties in terms of high solubility and sufficient stability. In T 777/08, cited in T 2007/11, the board pointed out that "*in the absence of any technical prejudice and in the absence of any unexpected property, the mere provision of a crystalline form of a known pharmaceutically active compound cannot be regarded as involving an inventive step*" (headnote 1)); however, in the case in hand, as set out above, there is no absence of an unexpected property, with the stability of the $\alpha_2$ crystalline form of Imatinib Mesylate for the preparation of pharmaceutical compositions being unexpected. Therefore, the headnote does not apply to the present case.

The fact that the skilled person is taught in the prior art to investigate polymorphs in order to isolate the crystalline form having the most desirable properties is in itself not necessarily sufficient for considering

a specific polymorphic form having a certain desired property to be obvious. An inventive step can only be denied if the prior art contains a clear pointer that it is the claimed subject-matter that solves this problem or if the prior art at least creates a reasonable expectation that a suggested investigation will be successful (see e.g. T 1684/16, point 4.3.4 of the Reasons).

Thus opponents 1 and 2's argument must fail.

17.7 Based on the above considerations, the board comes to the conclusion that, with regard to the cited prior art, it would not have been obvious to the skilled person to isolate the $\alpha_2$ crystalline form of Imatinib Mesylate and to arrive at the pharmaceutical composition as defined in claim 1 of the fourth auxiliary request.

Therefore, the subject-matter of claim 1 and, by the same token, of all remaining claims of the fourth auxiliary request involves an inventive step.

18. Admittance - document, attack and statement relevant for inventive step

18.1 Admittance of the objection of lack of inventive step based on D18 as the closest prior art

Opponent 2 relied on D18 in order to object to the inventive step of the subject-matter of the claims of the fourth auxiliary request starting from D18 as closest prior art. Like the objection of lack of novelty over D18, the attack based on D18 as the closest prior art is entirely new and has not been submitted during the opposition proceedings. It was submitted with the statement of grounds of appeal.

The reasons given for the admittance of the objection of lack of novelty in view of D18 (3.2-3.4, *supra*) apply, *mutatis mutandis*, to the admittance of the objection of lack of inventive step based on D18 as the closest prior art.

Therefore, the board decided not to admit the objection of lack of inventive step based on D18 as the closest prior art into the proceedings pursuant to Articles 12(2) RPBA 2020 and 12(4) RPBA 2007.

18.2 Admittance of A026

18.2.1 A026 was submitted by opponent 2 to dispute the technical effect achieved by the distinguishing feature of claim 1 of the eighth auxiliary request considered by the opposition division in its decision. This also applies to the subject-matter of claim 1 of the fourth auxiliary request. It is an experimental study on the dissolution profile of capsules containing 120 mg of an $\alpha_2$ crystalline form (according to the invention), a β crystalline form (comparative example) or a micronized β crystalline form (comparative example). The capsules of A026 were prepared using the same process and from the same excipients as those of the patent. Table 3 of A026 sets forth the dissolution profile of the three forms of Imatinib Mesylate.

A026 was submitted with the statement of grounds of appeal. Therefore, the admittance of the document is governed by Articles 12(2) RPBA 2020 and 12(4) RPBA 2007.

18.2.2 Opponent 2 submitted in their letter of 15 March 2021 that the submission of A026 was occasioned by the fact that the opposition division ignored the aspect set forth in A026. It was shown in A026 that the dissolution rate depended on the particle size and not

on the crystalline form. They also submitted that the argument based on the effect of the particle size on the dissolution rate had already been submitted in their letter in preparation for the oral proceedings before the opposition division.

18.2.3 In the board's view, the relationship between the particle size of the crystalline form and the dissolution rate is linked to the technical effect achieved by the distinguishing feature of the invention, i.e. the effect achieved by the $\alpha_2$ crystalline form of Imatinib Mesylate.

Table 6 of the patent shows comparative dissolution data of Imatinib capsule formulation containing the $\alpha_2$ crystalline form and the β crystalline form. The submission of A026 does not represent a reaction to data submitted during the opposition or appeal proceedings, but to data already present in the patent. The technical data of A026 which challenges the technical effect, could and should have been submitted with the notice of opposition, and not with the letter in preparation to the oral proceedings before the opposition division, let alone during appeal proceedings.

Furthermore, it is the purpose of appeal proceedings to review the opposition division's decision rather than to start a second opposition proceedings (Article 12(2) RPBA 2020). Admitting A026 into the proceedings would mean exactly that, namely to offer opponent 2 a second go in opposition proceedings. Furthermore, admitting A026 would have led to a new evaluation of the technical data on dissolution rate. As submitted by the patent proprietor, it would have been necessary to discuss and evaluate the results set forth in Table 1 on page 6 of A026, the interpretation of these results,

as disclosed in paragraph 2.3 on pages 15 and 16 of A026, and the newly raised submission that "*(...) for immediate release formulations comparison at 15 min is essential to know if complete dissolution is reached before gastric emptying. Where more than 85% of the drug is dissolved within 15 minutes, dissolution profiles may be accepted as similar without further mathematical evaluation.*" (bottom of page 15 of A026). It would also have been necessary to investigate the discrepancy between the results of A026 and those of the patent. Therefore the admittance of A026 would have led to an entirely fresh case, regarding technical data, to be considered for the first time during the appeal proceedings.

18.2.4 Considering the above, the board decided not to admit A026 into the proceedings pursuant to Articles 12(4) RPBA 2007 and 12(2) RPBA 2020.

18.3 Admittance of opponent 2's statement

During the oral proceedings before the board, opponent 2 stated that the α crystalline form of Imatinib Mesylate disclosed in D1 (bottom of page 2 and figure 1/3 of D1) was not the $\alpha_2$ crystalline form as claimed. This represents an amendment of its appeal case, since it had objected to the novelty of the $\alpha_2$ crystalline form of Imatinib Mesylate in claim 1 as granted in view of the disclosure of D1 (see point 16 of the impugned decision). This implies that opponent 2's position prior to the oral proceedings before the board was that the α crystalline form of Imatinib Mesylate disclosed in D1 was the $\alpha_2$ crystalline form as claimed.

The patent proprietor requested not to admit this statement into the proceedings.

During the oral proceedings the board decided to admit this statement into the proceedings. The subject-matter of claim 1 of the fourth auxiliary request involves an inventive step in view of D1 as the closest prior art, even assuming that D1 discloses the α crystalline form rather than the $\alpha_2$ crystalline form of Imatinib Mesylate, as now argued by opponent 2. The decision on inventive step is in the patent proprietor's favour, and therefore there is no need to give any reason on the admission of opponent 2's statement.

**Order**

**For these reasons it is decided that:**

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to maintain the patent on the basis of the claims according to the fourth auxiliary request, and a description and figures to be adapted thereto.

The Registrar: The Chairman:

N. Maslin M. O. Müller

Decision electronically authenticated