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Datasheet for the decision of 15 October 2015

Case Number: T 2397/11 - 3.3.01

Application Number: 04710031.8

Publication Number: 1597239

IPC: C07D239/94, A61K31/517, A61P35/00

Language of the proceedings: EN

Title of invention:
POLYMORPH OF {6,7-BIS(2-METHOXY-ETHOXY)-QUINAZOLIN-4-YL}-(3E)

Patent Proprietor:
F. Hoffmann-La Roche AG

Opponent:
Teva Pharmaceutical Industries LTD.

Headword:
Erlotinib hydrochloride polymorph/
HOFFMANN-LA ROCHE

Relevant legal provisions:
RPBA Art. 13(1)
EPC Art. 84, 123(3), 54, 111(1)

Keyword:
Clarity (yes)
Extension of protection conferred (no)
Novelty: main, auxiliary request 1 (no);
auxiliary request 2 (yes)
Remittal, auxiliary request 2

Decisions cited:
T 1753/06, T 0296/87, T 0885/02, G 0009/91, G 0010/91, G 0003/14

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Case Number: T 2397/11 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 15 October 2015

Appellant: (Patent Proprietor)	F. Hoffmann-La Roche AG Grenzacherstrasse 124 4070 Basel (CH)
Representative:	Hallybone, Huw George Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Respondent: (Opponent)	Teva Pharmaceutical Industries LTD. 5 Basel Street Petah Tiqva 49131 (IL)
Representative:	Eder, Michael df-mp Dörries Frank-Molnia & Pohlman Patentanwälte Rechtsanwälte PartG mbB Theatinerstrasse 16 80333 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 9 September 2011 revoking European patent No. 1597239 pursuant to Article 101(2),(3)(b) EPC.**

Composition of the Board:

Chairman	A. Lindner
Members:	L. Seymour
	L. Bühler

Summary of Facts and Submissions

I. European patent No. 1 597 239, filed as application number 04 710 031.8, based on the international application published as WO 2004/072049, was granted with the following claim 1:

"1. A crystalline polymorph of [6,7-Bis(2-methoxy-ethoxy)-quinazolin-4-yl]-(3-ethynyl-phenyl)amine hydrochloride which is characterized by an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately

degree 2-theta
5.7
9.7
10.1
11.3
17.0
17.4
18.9
19.6
21.3
22.8
23.6
24.2
24.7
25.4
26.2
26.7
29.3

"

II. The following documents, cited during the opposition/ appeal proceedings, are referred to below:

(1) WO 01/34574

(6) Experimental protocol of repetition of Example 1 of patent in suit, filed by opponent with letter of 6 July 2011

(7) The United States pharmacopeia, USP 25, 2002, pages 2088-2089, section <941>, X-Ray Diffraction

(8) Y-C Tien et al., J. Supercrit. Fluids, 2010, 55, 292 - 299

(9) R A Storey, I Ymén (Eds.), Solid State Characterization of Pharmaceuticals, Wiley 2011, pages 57 and 58 and enlarged copy of Fig. 2.15

III. Revocation of the patent in suit was sought pursuant to Articles 100(b) and 100(a) EPC (lack of novelty and inventive step).

IV. The appeal lies from the decision of the opposition division revoking the patent in suit. The decision was based on a main request (claims as granted), and on three auxiliary requests filed with letter dated 20 May 2011. The subject-matter of claims 1 of the main request and the second auxiliary request was found to lack novelty over document (1). Claim 1 of the first auxiliary request was considered to contravene Article 84 EPC, owing to use of the term "approximately" to describe the relative intensity values introduced into claim 1. The subject-matter of the third auxiliary request, which was limited to process claims, was found to meet the requirements of Articles 123, 54 and 56 EPC, but not of Article 84 EPC, since the description had not been appropriately adapted to render it consistent with the claims.

V. The appellant (patentee) lodged an appeal against this decision, and filed three auxiliary requests with its statement of grounds of appeal.

VI. The respondent (opponent 1) submitted its reply with letter of 4 June 2012.

VII. In a communication sent by the board in preparation for oral proceedings, the issue of novelty was discussed.

VIII. With letter dated 14 September 2015, the appellant filed a main request and auxiliary requests 1 to 4 to replace those previously on file.

Claims 1 of the main request and of auxiliary request 1 are identical, and differ from claim 1 as granted (cf. above point I) in that the term "approximately" is replaced by "±0.2 of the values shown below and which have relative intensities of ±30% of the values shown below", and in the addition of relative intensity values to the table, which now reads as follows:

degree 2theta	relative intensity
5.7	100
9.7	2.7
10.1	3.3
11.3	4.4
17.0	1.2
17.4	1.4
18.9	3.9
19.6	1.2
21.3	2.6
22.8	5.1
23.6	9.0
24.2	3
24.7	2.7
25.4	3.2
26.2	2.2
26.7	1.8
29.3	2

Claim 1 of auxiliary request 2 additionally contains the following feature:

"and characterized by a melting point of 211°C to 214°C".

IX. Oral proceedings were held before the board on 15 October 2015.

X. The appellant's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

The appellant argued that, in accordance with Article 13(1) RPBA, its requests submitted with letter dated 14 September 2015 should be admitted into the proceedings, since they were based on requests previously filed with the statement of grounds of appeal. The respondent's objections raised under Articles 84 and 123(3) EPC related to amendments already present in the latter. The further amendments introduced merely lent additional specificity to the subject-matter claimed.

Document (9) should not be admitted into the procedure in view of its late filing, and lack of relevance.

The features introduced into claims 1 of the main request and auxiliary requests 1 and 2 fulfilled the requirements of Article 84 EPC. The relative intensities of the characteristic peaks as listed therein had been calculated relative to the most intense peak, which was given a value of 100%. This was a well-known parameter that could readily be determined by a skilled person by reference to the X-ray counts of a peak at any given 2θ value. Furthermore, the term

"approximately" had been replaced to recite a margin of error of ±30%. There was only one logical interpretation of this feature, namely, that it related to the respective relative intensity values, such that, for example, a value of 9.0% had a range of 6.3 to 11.7%. The second interpretation advanced by the respondent produced a nonsensical result and would therefore be dismissed by the skilled person. For example, a value of 9.0% could range between +39 and -21%, and would thus include negative values, which were impossible. Therefore, the subject-matter claimed was clear, as a matter of plain English. The issue of whether the claimed features were suitable as distinguishing features over the prior art was a matter to be discussed under the heading of novelty.

The respondent's arguments with respect to Article 123(3) EPC were also not convincing. The fact that the intensities of the smallest peaks could be reduced by 30% did not mean that they dropped below detectable levels.

With respect to the issue of novelty, the question to be decided was whether the definition of polymorph E in claim 1 of the main request and auxiliary request 1, in terms of specific 2θ values and relative intensities, provided an accurate characterisation thereof, distinguishing it over polymorph A as disclosed in document (1) and, in particular, as characterised in Table 2 thereof. From a comparison of said table with the features of present claim 1, it could be readily ascertained that the peaks at 10.1 and 17.4° 2θ were absent in the former. Moreover, the relative intensity values quoted for the peaks of polymorph A differed by more than ±30% from those required by present claim 1. This margin of error took into account any possible

variations in relative intensity owing to preferred orientation of the sample or other variations in equipment and experimental conditions. These differences were therefore significant.

In contrast to the situation considered in T 1753/06, the peaks missing from the X-ray powder diffraction (XRPD) pattern of polymorph A of document (1) were not the weakest peaks that characterised the claimed polymorph. In fact, the peak at 10.1° 2θ was the sixth most intense peak of the seventeen listed. Moreover, in the claim under consideration in that case, no margin of error for the relative intensities had been specified.

According to document (7), every crystal form of a compound produced its own characteristic XRPD pattern; however, the differences between different polymorphs could be relatively minor. The fact that the two diffractograms under consideration in the present case were very similar did not mean that they were identical. It was therefore not appropriate to conclude lack of novelty, as had been done by the respondent, based on a visual comparison of the XRPD patterns. A more reliable basis upon which to make a comparison with the prior art was provided by the tabulated data generated by means of automated systems, based on an objective analysis of the recorded characteristic peaks, normalised to give the largest peak an intensity of 100%.

The respondent's "repetition" of Example 4 of document (1) was not relevant for the examination of novelty because the prior art teaching had not been faithfully followed. Given the differences in the experimental protocol used, especially with regard to

the pivotal choice of solvent, it could not be said that the product obtained by the respondent would be the inevitable result of the prior art teaching. Indeed, it was apparent from the results obtained by the respondent that the experimental conditions had been deliberately chosen to produce polymorph E rather than A. Indeed, as could be seen from the notice of opposition, the melting point of the polymorph obtained by the respondent corresponded to the former rather than the latter.

Contrary to the respondent's suggestion, polymorph A, as disclosed in document (1), and polymorph E, as first disclosed in the patent in suit, were two different crystalline forms of erlotinib hydrochloride, distinguishable through their XRPD patterns, but also through numerous further properties as set out in the patent in suit. The fact that the wrong XRPD diffractogram had been included for polymorph A in the patent in suit did not mean that the remaining data for this form was wrong. Corroboration was provided by document (8), which confirmed the existence of three polymorphs A, B and E of erlotinib hydrochloride, having properties that were entirely consistent with those disclosed in the patent in suit. Therein, polymorphs A and E were disclosed to display very similar XRPD patterns. However, this did not mean that they were identical. The appellant therefore maintained that features defined in claim 1 according to the main request and auxiliary request 1 were to be seen as reliable characterising features in the sense of decision T 296/87.

The respondent had failed to demonstrate beyond doubt that the claimed subject-matter was directly and unambiguously disclosed in document (1).

In claim 1 of auxiliary request 2, polymorph E was additionally characterised by a melting point of 211 to 214°C. In contrast in the patent in suit and in document (8), polymorph A had been found to have a lower melting point. Accordingly, the subject-matter of auxiliary request 2 was novel over document (1).

The appellant argued that the appropriate further course of action with respect to auxiliary request 2 would be remittal, in view of the fact that there had been no discussion on the inventive step with respect to product claims in the decision under appeal. Moreover, an additional sufficiency objection had been raised by the respondent for the first time during oral proceedings before the board, and the appellant should be given the possibility of having the admissibility and allowability of this new line of argumentation to be considered at two instances. No undue legal uncertainty arose for third parties in the present case, since erlotinib hydrochloride enjoyed SPC protection until March 2020, for example, based on SPC/GB06/008.

XI. The respondent's arguments, insofar as they are relevant to the present decision, can be summarised as follows:

With reference to the criteria set out in Article 13(1) RPBA, the respondent argued that, in order to be admitted, the appellant's requests, which had only been filed one month prior to oral proceedings, should at the very least be *prima facie* allowable. This criterion was not fulfilled in the present case, since all the appellant's requests suffered from deficiencies of lack of clarity, in particular, owing to the introduction of

features relating to relative intensities from the description into the main request and auxiliary requests 1 to 3. These amendments additionally gave rise to objections under Article 123(3) EPC. Therefore, the appellant's requests should not be admitted into the proceedings.

With respect to the question of admissibility of document (9), the respondent argued that this was not complex, and was not being introduced as prior art, but only as textbook evidence of common general knowledge, further illustrating the large variations in intensities of XRPD peaks resulting from preferred orientation effects.

Amended claim 1 of the main request did not comply with the requirements of Article 84 EPC owing to the introduction of the relative intensity values. It was generally known that the intensity of peaks could vary considerably even for the same sample, as a result of factors such as sample preparation, preferred orientation effects, background noise, and the software employed to analyse the data. Such parameters could not therefore be viewed as a reliable means for properly distinguishing one polymorph from another. This was particular true of the present case where substantial overlap of peaks and considerable noise was observed in the XRPD diagram. Moreover, the feature allowing a variation in relative intensities of ±30% was unclear, since two possible interpretations of said feature could be envisaged, namely, a variation of ±30% for each individual intensity value, or an absolute variation of ±30% based on the strongest reference peak. In view of the significant magnitude of possible variation, both readings were to be seen as technically meaningful. Negative intensity values theoretically

resulting from the second interpretation would naturally be excluded by the person skilled in the art. The existence of two incompatible interpretations of the feature of ±30% was contrary to the requirements of Article 84 EPC. Corresponding objections applied to the respective claims 1 of auxiliary requests 1 and 2.

Irrespective of the meaning attributed to the feature of ±30%, this allowed peaks, particularly those of lowest intensity, to disappear below a threshold value for being recognised as such. Therefore, this amendment led to a broadening of the subject-matter claimed, contrary to the requirements of Article 123(3) EPC.

On the issue of novelty of the subject-matter of claim 1 of the main request and auxiliary request 1, the respondent pointed to the XRPD data for Form A of erlotinib hydrochloride, as disclosed in document (1), and argued that this displayed all the peaks claimed to be characteristic for Form E. Contrary to the appellant's allegations, the peaks at 10.1 and 17.4° 2θ were not absent in the diffractogram for Form A reproduced in Figure 2 of document (1). Indeed, they were clearly discernible, in the case of the former, as a shoulder of the main peak. Moreover, the skilled person would always compare the entire XRPD patterns in order to establish whether two forms were the same. In the present case, an overlay demonstrated that the XRPD pattern for Form A according to document (1) closely matched that disclosed for Form E in Figure 1 of the patent in suit. Accordingly, there could be no doubt that the claimed Form E of the opposed patent lacked novelty over Form A of document (1). This approach was consistent with that taken in decision T 885/02.

The claimed relative intensities for the observed peaks could not alter this conclusion, since these values were known to be intrinsically unreliable. Substantial variations were known to occur as a result of extrinsic factors, in other words, influences that were independent of the crystalline structure of the compound in question, such as artefacts of measurement. Moreover, in the present case, substantial overlap of peaks was observed, and this introduced an additional source of error in establishing these values. Finally, the peak at 5.7 was very large compared to the remaining peaks, and any variation therein would have an inordinate effect on the relative intensity values obtained. Therefore, the relative intensities could not be considered to constitute a reliable distinguishing feature in the sense of decision T 296/87. This was also in line with the considerations set out in decision T 1753/06.

The respondent emphasised that it had never argued that polymorph E as claimed was the inevitable result of a repetition of Example 4 of document (1). Since there was already a clear and unambiguous disclosure therein of a novelty-destroying crystalline form of erlotinib hydrochloride, it was sufficient to demonstrate that its preparation had been described in an enabling manner. With its adaptation of said example on a lab scale and with the suggested solvent for obtaining pure Form A, the respondent had demonstrated that this was the case. Furthermore, the respondent had also repeated Example 1 of the patent in suit, and found the respective crystalline forms to be indistinguishable, not only based on the comparison of the two XRPD diffractograms, but also with respect to a number of other physicochemical parameters. This experimental

evidence further confirmed that the subject-matter claimed was not novel.

The respondent did not object to the admission of document (8) into the proceedings. The methods used therein for the recrystallisations of Form B erlotinib hydrochloride were unrelated to those employed in the patent in suit, and the products produced had been labelled as Forms A and E, with reference to the patent in suit and a family member of document (1). No firm basis had been provided for this assignment. Therefore, contrary to the contention of the appellant, the results in document (8) could not be used to corroborate the reliability of the data provided in the patent in suit. At best, its disclosure supported the respondent's case that the claimed subject-matter lacked novelty. As was the case for the patent in suit, the authors of document (8) had been unable to distinguish between the polymorphs designated as Forms A and E based on their XRPD patterns. It must therefore be concluded that these were one and the same. The differences in the other properties, such as melting point and dissolution profile, could be explained by the differences that were unrelated to crystal structure, such as the differences in crystal shape and size, and purity.

With respect to claim 1 of auxiliary request 2, the respondent acknowledged that, in view of the fact that the feature introduced relating the melting point of the claimed polymorph had already been present in granted claim 5, it was not open to objection under Article 84 EPC, in accordance with Enlarged Board of Appeal decision G 3/14. It could be derived from Example 5 of the patent in suit that the value

introduced related to onset temperatures obtained by differential scanning calorimetry (DSC).

However, the subject-matter claimed lacked novelty over document (1). No convincing evidence had been provided that the claimed combination of features could be used to distinguish the claimed subject-matter from Form A according to document (1). In particular, no melting point had been disclosed in document (1), and the data in the patent in suit for Form A was to be disregarded as a whole, in view of the erroneous XRPD data. The appellant could have provided additional experimental evidence to dispel these doubts, but had chosen not to do so. For the reasons previously given, document (8) could not be relied upon to corroborate the data provided in the patent in suit. Moreover, the alleged differences in melting point were very small, and could not reliably be said to distinguish crystalline forms, particularly in view of the fact that mixtures of forms were also covered, as could be seen from claim 5. In this context, the respondent expressed its intention to raise an objection of lack of enablement against this claim.

The respondent further argued, with respect to auxiliary request 2, that remittal for further prosecution would not be justified. Since all the required facts and arguments were on the table for deciding on inventive step, in the form of the experimental evidence contained in the patent in suit, the board should hear the entire case. Remittal would lead to unacceptable further delays in bringing the case to a close, contrary to the desirability of procedural economy and legal certainty for third parties. The respondent’s interests in this respect were legitimate, for example, in view of an ongoing

nullity action against the part of the patent in suit having effect in Germany.

XII. The appellant (patentee) requested that the decision under appeal be set aside and that the case be remitted to the opposition division for further prosecution with respect to the issue of inventive step on the basis of the main request or auxiliary requests 1 to 3, all filed with letter dated 14 September 2015.
Alternatively, the appellant requested that the decision under appeal be set aside and the patent be maintained in the following version:

Description: pages 2 to 5 attached as Annex 3 to the minutes of the oral proceedings before the opposition division, and pages 6 to 8 as granted; and

Claims: No. 1 to 5 of auxiliary request 4 filed with letter dated 14 September 2015.

The respondent (opponent) requested that the appeal be dismissed. The respondent further requested that the board should decide on the appeal without remittal.

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. *Admission pursuant to Article 13(1) RPBA*

2.1 *Appellant's requests filed with letter dated 14 September 2015 (main, auxiliary requests 1-4)*

The requests under consideration were filed one month prior to oral proceedings before the board. The main request and auxiliary requests 1 to 3 are based on auxiliary request 1 filed with the statement of grounds of appeal, in accordance with Article 12(1)(a) RPBA. The amendments highlighted by the respondent were already present in the latter, and objected to in detail under Article 84 EPC in the respondent's reply of 4 June 2012 (see point II.3), pursuant to Article 12(1)(b) RPBA. Therefore, *prima facie*, the amendments in question do not represent an amendment to the appellant's case, in the sense of Article 13(1) RPBA, since they do not raise new issues which were not previously present in the initial submissions of the parties. Moreover, they cannot be seen as introducing complexity into the proceedings or hampering procedural economy.

The further amendments undertaken in the main request and auxiliary requests 1 to 3 were of a straightforward nature, and were not objected to by the respondent in its submission on admissibility.

Finally, it is noted that auxiliary request 4 is identical to the third auxiliary request underlying the decision under appeal (cf. above point IV).

Under these circumstances, the board decided to admit the appellant's requests filed with letter dated 14 September 2015 into the proceedings.

2.2 *Document (9)*

Document (9) was filed during oral proceedings before the board. No reason was given by the respondent for filing a new document at such a late stage in the proceedings. Moreover, the publication date thereof was long after the priority date of the patent in suit, rendering it *prima facie* unsuitable for providing evidence of the common general knowledge at the relevant time. Consequently, the board decided not to admit document (9) into the proceedings.

3. *Main request*

3.1 *Clarity (Article 84 EPC)*

In claim 1 as granted (cf. above point I), the claimed polymorph of erlotinib hydrochloride is characterized by defining the position of specific peaks in the XRPD pattern, expressed as 2θ values. Claim 1 of the main request mainly differs from this granted claim in the additional characterisation of the peaks by means of their respective relative intensities, coupled with a variation in the values given of ±30%. Since these additional features were not present in the claims as granted, it must be examined whether said amendment introduces non-compliance with Article 84 EPC.

As set out in document (7), which reflects common general knowledge in the field of X-ray diffraction analysis of crystalline materials, relative intensity is one of the parameters commonly employed to characterise an XRPD pattern, and is calculated based on the ratios of the intensity of each peak of interest relative to the intensity of the strongest maxima in the diffraction pattern (cf. document (7), page 2088, left-hand column, first paragraph; page 2089, right-hand column, last paragraph, second sentence).

Therefore, this is to be regarded as a standard parameter, the meaning of which would be clear to the skilled person.

The respondent criticised that relative intensities were not only determined by the structural factors intrinsic to the the polymorph itself, but also extrinsic factors, such as sample preparation, preferred orientation effects, background noise, and the software employed. Indeed, it can be derived from document (7) that, even when the patterns are generated on the same equipment and under the same conditions, "relative intensities between sample and reference may vary considerably" (see document (7), page 2089, right-hand column, last paragraph; cf. also page 2088, right-hand column, third paragraph; page 2089, left-hand column, second paragraph of "Test Preparation"). However, the fact that relative intensity is subject to a certain amount of variability does not mean that it is meaningless as a feature characterising the underlying XRPD pattern, nor does document (7) suggest that it is so. This feature clearly defines the subject-matter for which protection is sought. Whether or not, based on the facts of the case, it can serve to delimit the subject-matter claimed from that of the prior art is an issue regarding novelty rather than clarity (see point 3.3 below).

The respondent raised a further objection under Article 84 EPC, arguing that two plausible, but incompatible interpretations existed for the feature "±30%", namely, that this could relate to each individual intensity value defined, or be seen as an absolute value based on the strongest reference peak. However, the board cannot agree that the latter interpretation makes technical sense, since it would

result in negative intensity values for all but one of the claimed peaks. Even if, as argued by the respondent, the skilled person would exclude these negative values, this would effectively allow said peaks to disappear into insignificance, leaving only a single peak, thus negating the purpose of the relative intensity values in describing the underlying XRPD pattern. Accordingly, the skilled person would rule out the second interpretation advanced by the respondent as not making technical sense.

It is therefore concluded that the amendments introduced into claim 1 do not result in a lack of clarity to the subject-matter claimed.

3.2 *Article 123(3) EPC*

In the present case, claim 1 of the main request contains a limitation as to the relative intensities of the peaks, which was not present in claim 1 as granted.

The peaks of lowest intensity as recited in claim 1 have a relative intensity of 1.2 (cf. above point VIII). In view the claimed margin of ±30%, the lower end of the range for this value can be calculated at 0.84. No evidence was provided by the respondent that this was to be seen as lying below a threshold value which would no longer allow the corresponding peaks to be detected. Consequently, it cannot be accepted that the feature of ±30% allows said peaks to disappear, thus extending the protection conferred.

Consequently, the requirements of Article 123(3) EPC are met by the claims according to the main request.

3.3 Novelty

3.3.1 As outlined above in point 3.1, present claim 1 relates to a polymorph of erlotinib hydrochloride characterised by a list of XRPD peaks at specified diffraction angles and relative intensities.

In accordance with established case law of the boards of appeal, a chemical substance is held to be new if it differs from a known substance in a reliable parameter (cf. e.g. T 296/87, OJ EPO 1990, 195, headnote).

The question to be decided in the present case is therefore whether the subject-matter claimed is novel over Form A as disclosed in document (1).

3.3.2 In their submissions, the parties relied on the following evidence:

(i) Patent in suit, paragraphs [0031] to [0033], and Figures 1 and 3;

(ii) Document (1), Example 4, Table 2 and Figure 2;

(iii) Opponent's repetition of Example 1 of patent in suit, and characterisation of the product (see notice of opposition, page 13, point 23, and corresponding figures and tables; see also document (6));

(iv) Opponent's repetition of Example 4 of document (1) and characterisation of the product (see notice of opposition, page 12, point 22, and corresponding figures and tables);

and

(v) Document (8).

Note: Enlarged versions of the figures referred to above in items (iii) and (iv) can be found annexed to the minutes of the oral proceedings before the opposition division, and were also resubmitted by the respondent with its letter dated 17 August 2015.

3.3.3 In the patent in suit, paragraph [0031], document (1) is cited as providing methods of obtaining polymorphs A and B of erlotinib hydrochloride, and paragraph [0032] discloses the synthesis of Form E, which is in accordance with the invention. In paragraph [0033], the experimental conditions employed in the XRPD measurements are disclosed, and Figures 1, 3 and 5 show the corresponding data for Forms E, A and B, respectively, as three distinct diffractograms.

However, as demonstrated by the respondent by means of an overlay of Figure 3 of the patent in suit and Figure 2 of document (1) (see Figure 1 of notice of opposition), the former cannot be reconciled with the latter. This was not disputed by the appellant. Therefore, *a priori* the XRPD data provided in the patent in suit cannot serve to confirm the novelty of the claimed subject-matter over Form A as disclosed in document (1).

The appellant therefore chose to rely in its submissions on novelty on the XRPD data for Form A disclosed in document (1), and highlighted the differences between the values listed in claim 1 and those disclosed in Table 2 of document (1). In particular, the appellant submitted that the required peaks at 10.1 and 17.4° 2θ were absent in said Table 2. However, it can be seen from Figure 2 of document (1), and also its overlay with Figure 1 of the patent in suit (see Figure 2 of notice of opposition), that the

peaks at 10.1 and 17.4° 2θ are in fact present in the former, whereby the peak at 10.1° 2θ is merely incompletely resolved. It must therefore be concluded that all the peaks specified in present claim 1 are also observed for Form A in accordance with document (1).

The appellant further argued that the relative intensities as defined in claim 1 could be seen as a reliable distinguishing feature, since the corresponding values in Table 2 of document (1) all exhibited relative intensities lying outside the defined margin of ±30%. However, as explained in the third paragraph of point 3.1 above, it is common general knowledge that relative intensities are particularly vulnerable to experimental conditions. Therefore, under the present circumstances, where the appellant has chosen to rely on a comparison of data collected under different experimental conditions, the appellant's contention that the differences in relative intensities are to be seen as a reliable distinguishing feature over the prior art, rather than an artefact of the method of measurement, must be regarded as an unsupported assertion. Consequently, the parameter relating to relative intensities cannot be acknowledged as a novelty-rendering feature in the present case.

It follows from the above that the subject-matter of claim 1 lacks novelty over Form A as disclosed in document (1).

In view of this conclusion, it was not necessary to discuss the data listed above in point 3.3.2, items (iii) and (iv) (see, however, point 5.2.4 below).

3.3.4 The appellant's further arguments in favour of novelty of the claimed subject-matter are not considered to be convincing:

The appellant argued that the burden of proof rested on the respondent to establish that the claimed subject-matter was directly and unambiguously disclosed in document (1). However, in the present case, it is the appellant who is challenging the decision of the first instance and seeking to establish novelty by introducing a parameter that was not present in the claims as granted, and it is he who therefore has to show that the relative intensities tabulated in the claim are to be seen as a reliable distinguishing feature over the prior art.

Moreover, the board cannot agree with the appellant that the assessment of novelty should be based on the data tabulated, and the complete XRPD data ignored. Such an approach would allow novelty to be acknowledged for identical polymorphs only because different peaks had been selected for listing.

Document (8) referred to by the appellant as corroborating evidence cannot serve to establish the novelty of the subject-matter of claim 1, since, owing to scale and poor quality, the XRPD data provided therein in Figure 3 cannot resolve any of the issues raised above in point 3.3.3, regarding the question as to whether any differences between the diffractograms of polymorphs A and E are reliably and correctly reflected in the claims.

3.3.5 Finally, it is noted that the analysis put forward above in point 3.3.3 is consistent with the approach adopted in the cited decisions T 885/02 and T 1753/06

in making an assessment, based on the facts of the case, as to whether the features defined in the claims could be regarded as suitable distinguishing features:

In decision T 885/02, the claimed polymorph was *inter alia* defined by means of a non-limitative list of IR peaks in a frequency region that was found not to be characteristic; these parameters were therefore considered to be unsuitable for distinguishing the polymorph in question from that of the prior art, and novelty was denied (see Facts and Submissions, point III, and Reasons, points 3.4.10 to 3.4.13).

In decision T 1753/06, claim 1 of the main request related to a polymorph characterised by a list of XRPD peaks, defined in terms of their scattering angles, *d* spacings, intensities and relative intensities (see Facts and Submissions, point IV). Based on the evidence available to them with respect to the claimed polymorph (simulated and experimentally obtained XRPD diagrams), the board first examined the extent to which the parameters as defined in said claim could be regarded as being reliable distinguishing features (see Reasons, points 4.5.1 to 4.5.3). Based on this assessment, the board concluded that, as long as the position of the peaks in an XRPD diagram were substantially identical to the values specified in the patent or in the reference diagrams, the variations concerning weak peaks or overlap or resolution of peaks, as well as the deviation in the intensity of peaks, could not be seen as being indicative of the formation of a different crystalline form (see Reasons, points 4.5.4). In this case too, novelty was ultimately denied (see Reasons, points 4.5.5 to 4.18).

3.3.6 Consequently, the main request is rejected for lack of novelty of the subject-matter of claim 1.

4. *Auxiliary request 1*

Since claim of auxiliary request 1 is identical to that of the main request, the assessment presented above in point 3 applies equally to this request.

5. Auxiliary request 2

5.1 *Articles 84 and 123(3) EPC*

The conclusions set out above in points 3.1 and 3.2 apply *mutatis mutandis*. Indeed, the respondent did not raise any additional objections in this respect. Therefore, the amendments introduced do not give rise to objections under Articles 84 or 123(3) EPC.

5.2 Novelty

5.2.1 As outlined above in point VIII, present claim 1 additionally contains the feature "and characterized by a melting point of 211°C to 214°C", and it must now be decided whether the claimed combination of features can be considered to render the subject-matter of claim 1 novel over Form A of document (1).

5.2.2 In document (1), no melting points are disclosed. Therefore, on the basis of the information provided in document (1) alone, it cannot be concluded whether the defined melting point differs from that of the prior art Form A.

5.2.3 In the patent in suit, Form A, obtainable according to the methods of document (1), is disclosed to have a

melting point (T_{onset}, obtained by DSC) of 205 to 208°C (see paragraphs [0031] and [0035]). This value is clearly distinguishable from the range of 211 to 214°C now claimed.

However, in view of the discrepancy between the patent in suit and document (1) with respect to the XRPD diffractogram included for Form A (cf. above point 3.3.3, second paragraph), the respondent argued that the remaining data in the former for Form A should be disregarded as lacking reliability. The appellant countered that this data was sound, and referred to document (8) as corroborating evidence.

Document (8) is a scientific article relating to the recrystallization of erlotinib hydrochloride using supercritical antisolvent processes, with the stated aim of obtaining the prior art form A, since polymorphs B and E were protected by patents; reference is made in this context to a US family member of document (1) (reference [18]), and the international application on which the patent in suit is based (reference [19]) (see page 293, right-hand column, last paragraph). In the same passage, it is disclosed that the XRD patterns for Forms A and E are very similar, and that "the only obvious difference between these two forms is their melting temperatures". Starting with Form B, under various experimental conditions, two different polymorphic forms were obtained, which were classified as Forms A or E according to their DSC T_{onset} values (see Table 2). The values listed in Table 2 are consistent with the ranges specified in the patent in suit (paragraph [0035]). Moreover, in Figure 5 of document (8), it can be seen that Form A has the fastest dissolution rate, followed by Form E, which is

consistent with the order disclosed in the patent in suit (see paragraphs [0006] and [0037]).

The respondent contested the use of document (8) to support the appellant's case. However, the board does not consider its arguments to be convincing:
As set out above, the basis provided in document (8) for the assignment was the DSC T_{onset} temperatures, which are consistent with those disclosed in the patent in suit. The respondent's assertion that any differences observed were attributable to factors that were unrelated to the crystal structure was not supported by any concrete arguments or evidence. There is therefore no reason to doubt the conclusions of the authors of document (8) that, in addition to Form B, two distinguishable Forms A and E exist (see page 294, right-hand column, last two sentences, and Table 2). The submission of the respondent that Forms A and E as disclosed in document (8) are one and the same is therefore not considered to be tenable.

Consequently, document (8) confirms that three polymorphs of erlotinib hydrochloride exist having properties consistent with those provided in the patent in suit. In the absence of evidence to the contrary, the board therefore sees no reason to doubt the information disclosed in the patent in suit that Form A obtainable in accordance with the method of document (1) can be distinguished by means of its melting point from Form E as as defined in claim 1.

5.2.4 The respondent challenged this conclusion with reference to the results of its own repetitions of Example 1 of the patent in suit and Example 4 of document (1) (see items (iii) and (iv) in point 3.3.2 above).

From the XRPD, ^{13}C solid-state NMR, FT-IR, and DSC T_{onset} data presented in the notice of opposition, page 14 to 19, it is evident that the product of these two sets of experiments are identical.

However, the board notes that it is a generally applied principle for concluding lack of novelty that there must be a direct and unambiguous disclosure in the state of the art which would inevitably lead to subject-matter falling within the scope of the claim. Where gaps in experimental detail exist, these may be filled by the skilled person with his common general knowledge using conventional techniques within reasonable limits, provided that the choices made are not material to the end results (see, for example, T 1753/06, in particular, Reasons, points 4.11, 4.13, 4.16.1, and 4.17).

In the present case, in its reworking of Example 4 of document (1), the respondent did not adhere to the protocol as disclosed on page 47, lines 22 to 35 (cf. Annex filed by the appellant with letter of 3 July 2015). The difference particularly highlighted by the appellant was the replacement of acetonitrile with isopropanol as one of the solvents. Since the solvent system is known to be a potential factor in determining the polymorph obtained, it must be concluded that the respondent's repetition is unsuitable for demonstrating to the required standard of proof that a polymorph exhibiting all the features of claim 1 is the inevitable result of carrying out the protocol disclosed in Example 4 of document (1).

Contrary to the contention of the respondent, it is not considered to be sufficient for denying novelty to

demonstrate that a product having an XRPD pattern and melting point falling within the scope of claim 1 can be obtained when working within the general teaching of document (1), since it cannot be inferred therefrom that the same product would also result from a faithful reproduction of the protocol explicitly disclosed. In the present case, the passage on page 48, lines 1 to 8, of document (1) provides a general indication of several modifications of the solvent system favouring Form A, but does not provide direct and unambiguous instruction as to how these are to be implemented.

Hence, the objection of lack of novelty based on document (1) must fail.

5.2.5 Therefore, the board concludes that the subject-matter of claim 1, and, by the same token, that of the remaining claims 2 to 12, which all refer back thereto, is novel.

6. *Remittal*

Having so decided, the Board has not taken a decision on the whole matter.

In accordance with decisions G 9/91 and G 10/91 (OJ EPO 1993, 408 and 420, in particular, reasons, point 18), the purpose of the appeal proceedings *inter partes* is primarily to give the losing party the possibility of challenging the decision of the opposition division. Therefore, the boards will normally favour remittal if essential questions regarding the patentability of the claimed subject-matter have not yet been examined and decided by the opposition division.

In the present case, the decision under appeal did not address the issue of inventive step for the requests comprising product claims (cf. above point IV, main request and auxiliary request 1 and 2). Moreover, in the written submissions of the parties during the appeal proceedings, the issue of inventive step was only briefly addressed. Finally, at oral proceedings before the board, the respondent raised a new line of argumentation with respect to the sufficiency of disclosure of claim 5 of auxiliary request 2.

In view of the above, the board was not convinced that the respondent's desire for procedural economy and legal certainty should outweigh that of the appellant for a complete consideration of outstanding issues at two instances.

Consequently, the board finds it appropriate to exercise its discretion under Article 111(1) EPC and remit the case to the opposition division for further prosecution on the basis of auxiliary request 2.

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 on the basis of the claims of auxiliary request 2 filed with letter dated 14 September 2015.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated