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Datasheet for the decision of 11 November 2021

Case Number: T 2407/17 - 3.3.01

Application Number: 10746795.3

Publication Number: 2400847

IPC: A61K31/4166, C07D233/74, C07D233/84

Language of the proceedings: EN

Title of invention:
SPECIFIC DIARYLTHIOHYDANTOIN COMPOUNDS

Patent Proprietor:
Medivation Prostate Therapeutics LLC

Opponents:
Actavis Group PTC ehf
LEK Pharmaceuticals d.d.
Generics [U.K.] Limited

Headword:
N-Desmethyl enzalutamide/MEDIVATION

Relevant legal provisions:
EPC Art. 84, 54, 56
RPBA 2020 Art. 13(2)
RPBA Art. 12(4)

This datasheet is not part of the Decision
It can be changed at any time and without notice

Keyword:
Clarity - main request (yes)
Novelty - main request (yes)
Inventive step - all requests (no)

Decisions cited:
G 0001/92

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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 2407/17 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 11 November 2021

Appellant 1: (Opponent 1)	Actavis Group PTC ehf Reykjavikurvegi 76-78 220 Hafnarfjordur (IS)
Representative:	Elkington and Fife LLP Prospect House 8 Pembroke Road Sevenoaks, Kent TN13 1XR (GB)
Appellant 2: (Opponent 2)	LEK Pharmaceuticals d.d. Verovskova 57 1526 Ljubljana (SI)
Representative:	Maiwald Patent- und Rechtsanwaltsgesellschaft mbH Elisenhof Elisenstraße 3 80335 München (DE)
Appellant 3: (Opponent 3)	Generics [U.K.] Limited Station Close Potters Bar Herfordshire EN6 1TL (GB)
Representative:	FRKelly 27 Clyde Road Dublin D04 F838 (IE)
Respondent: (Patent Proprietor)	Medivation Prostate Therapeutics LLC 235 East 42nd Street New York, NY 10017 (US)
Representative:	J A Kemp LLP 80 Turnmill Street London EC1M 5QU (GB)

Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 29 August 2017 concerning maintenance of the European Patent No. 2400847 in amended form**

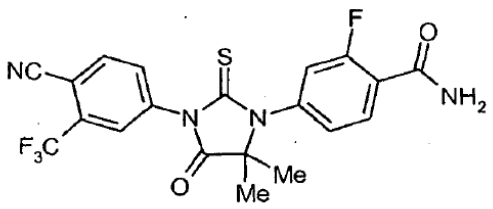
Composition of the Board:

Chairman A. Lindner
Members: J. Molina de Alba
M. Blasi

Summary of Facts and Submissions

I. The decision under appeal is the opposition division's interlocutory decision that European patent No. 2 400 847 in the version of the main request pending before it, and the invention to which it relates, met the requirements of the EPC.

The request held allowable by the opposition division contains seven claims, all of which refer to compound MII, which has the following chemical formula.



MII ,

Claim 1 concerns a pharmaceutical composition comprising MII or a pharmaceutically acceptable salt or solvate of it, and a pharmaceutically acceptable carrier.

Claim 2 concerns compound MII or a pharmaceutically acceptable salt or solvate of it, for use in a method of treatment of an individual.

Claim 3 concerns the compound of claim 2 for use in the treatment of prostate cancer.

Claim 4 concerns the use of compound MII or a pharmaceutically acceptable salt or solvate of it, in

the manufacture of a medicament for the treatment of an individual.

Claim 5 concerns the use according to claim 4 in the manufacture of a medicament for the treatment of prostate cancer.

II. The following documents are referred to in the present decision.

D1	WO 2006/124118
D5	US 2008/0139634
D6	EMA assessment report on Xtandi (enzalutamide), dated 25 April 2013
D10	Furra A., Drug Discovery Today, 2006, 11(3/4), pp. 133-142
D13	FDA assessment report on Xtandi (enzalutamide), dated 22 August 2012
D19	Experimental report filed with the letter dated 31 March 2017
D19a	Experimental report filed with the letter dated 12 May 2017
D20	Testa B., The Metabolism of Drugs and Other Xenobiotics, 1995, pp. 203-234
D21a	Experimental report from Prof Košmrlj dated 19 December 2017
D21b	Report of analysis from the Kemijski Inštitut (Ljubljana) dated December 2017

III. Three oppositions had been filed against the patent on the grounds that the claimed subject-matter lacked novelty and inventive step and was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Article 100(a) and (b) EPC).

In the decision under appeal, the opposition division decided, among other things, that:

- D19 and D19a should not be admitted
- it could not be inferred from decision G 1/92 that MII was publicly available merely because it was a metabolite of compound RD162' in Dl, let alone that MII had the therapeutic activity of RD162'
- starting from D1 and considering the experimental data in the patent and post-published document D6, the objective technical problem was the provision of a therapeutically useful agent with similar receptor activity and improved pharmacokinetics
- as the compounds in Dl were highly sensitive to structural modifications, the solution proposed in the claims of the main request was inventive

IV. Each of opponents 1 to 3 (appellants 1 to 3, respectively) filed an appeal requesting that the decision be set aside and that the patent be revoked in its entirety.

With its statement of grounds of appeal, appellant 2 filed documents D21a and D21b as new evidence to show that MII was inevitably obtained as a side product in the preparation of Example 56 of D1.

V. In its reply to the statements of grounds of appeal, the patent proprietor (respondent) requested that the appeals be dismissed. It also filed the claims of auxiliary requests 1 to 5, which were identical to those filed in the opposition proceedings on 31 March 2017.

VI. In preparation for the oral proceedings, scheduled according to the parties' requests, the board issued a preliminary opinion and drew attention to issues that might be debated at the oral proceedings.

VII. By a letter dated 3 June 2021, the respondent reacted to the board's preliminary opinion and filed the claims of a new main request and six auxiliary requests. Auxiliary requests 2 to 6 are identical to auxiliary requests 1 to 5 filed with the reply to the statements of grounds of appeal, respectively.

The main request differs from the request held allowable by the opposition division in that claim 2 specifies that the method of treatment is for therapy.

Claim 1 of auxiliary request 1 is identical to claim 3 of the request held allowable by the opposition division.

Claim 1 of each of auxiliary requests 2 to 4 is identical to claim 1 of the request held allowable by the opposition division.

Claim 1 of auxiliary request 5 concerns the pharmaceutical composition in claim 1 of the request held allowable by the opposition division for use in a method of treatment of prostate cancer.

Claim 1 of auxiliary request 6 is identical to claim 5 of the request held allowable by the opposition division.

VIII. Oral proceedings were held before the board on 11 November 2021. At the end of the oral proceedings, the board announced its decision.

IX. The appellants' arguments, where relevant to the present decision, can be summarised as follows.

Documents D21a and D21b should be admitted into the appeal proceedings. They were filed with appellant 2's statement of grounds of appeal as a direct response to the decision under appeal. The documents showed that compound MII was not novel because it was inevitably formed as a side product in the preparation of compound RD162' in Example 56 of D1. This objection had been raised and supported with experimental evidence (D19 and D19a) during the opposition proceedings. However, at oral proceedings, the opposition division decided not to admit D19 and D19a because they allegedly contained deficiencies. D21a and D21b overcame the alleged deficiencies.

The main request should not be admitted into the appeal proceedings. It was intended to correct a wrong format of claim 2 as first medical use claim at a late stage of the appeal proceedings. Furthermore, the format of the amended claim was still wrong and raised clarity issues.

Claim 2 of the main request was unclear. It seemed to define a first medical use, but its wording did not comply with the format required by Article 54(4) EPC: it read "for use in a method of treatment of an individual for therapy" instead of "for use in therapy".

D1 anticipated the subject-matter of claims 2 and 3 of the main request (appellant 1's statement of grounds of appeal, point 4.2). It disclosed compound RD162' and its use against prostate cancer. Compound MII was a

metabolite of RD162'. Thus, it was formed *in vivo* when RD162' was administered for the treatment of prostate cancer. This meant that MII could be detected and analysed. Hence, in accordance with decision G 1/92, D1 made MII available to the public. Furthermore, the therapeutic effect of MII was also disclosed because the skilled person would have observed that MII had the same activity as its parent drug RD162'.

The subject-matter of the main request did not involve an inventive step starting from D1, especially from compound RD162' (Example 56 and Table 5). The difference between the claimed subject-matter and the teaching of D1 was that the carbamoyl group of MII was demethylated. The respondent had not proved that this difference produced any technical effect. In fact, the IC_{50} values of MII and RD162' in post-published document D6 (page 18, penultimate paragraph and page 19, penultimate paragraph) indicated that MII was inferior to RD162' as an inhibitor of the human androgen receptor (AR). MII had no improved pharmacokinetic properties either. The passages in D6 (page 34, last paragraph to page 35, paragraph 3) cited by the respondent in relation to the higher free fraction and AUC of MII related to *in vitro* test results and had been taken out of context. Reading the passages in their entirety, D6 taught that *in vivo* MII and RD162' had an equivalent pharmacokinetic profile. Furthermore, D6 did not contain pharmacokinetic data following the administration of MII in the same conditions as RD162'. The data in D6 did not allow comparing the pharmacokinetics of MII and RD162'. Consequently, the objective technical problem was providing a further compound suitable for the treatment of prostate cancer.

Even if the technical problem was not providing a further compound but a compound therapeutically equivalent to RD162', MII remained an obvious solution. This derived from D1 itself and the common general knowledge depicted in D10 and D20. D1 (Tables 5 and 6) showed that N-demethylation of compounds RD131 and RD134 gave the respective compounds RD130 and RD133, which had a therapeutic effect equivalent to their parent compounds. No example in D1 showed that N-demethylation resulted in a loss of activity. The general statement in D1 (paragraph [00196]) that small structural changes of the compounds could lead to large changes in their therapeutic effect did not relate specifically to N-demethylation. In contrast, D10 (page 135, right-hand column, paragraph 2; sentence bridging pages 135 and 136; and Table 1) and D20 (page 204, paragraphs 1 and 2) presented common general knowledge specifically related to N-demethylation. They taught that N-demethylated compounds retained the activity of their N-methylated analogues. The passages in D10 cited by the respondent (page 135, left-hand column, paragraph 1 and page 136, left-hand column, paragraph 1) referred to exceptions to this common general knowledge.

X. The respondent's arguments, where relevant to the present decision, can be summarised as follows.

Documents D21a and D21b should not be admitted into the appeal proceedings. They could and should have been filed during the opposition proceedings. Moreover, they were not suitable for demonstrating that MII was obtained as a side product in Example 56 of D1.

The main request should be admitted. It was filed in response to the board's observation in its preliminary

opinion (point 12.1, last sentence) that the method of treatment in claim 2 was not specifically therapeutic. This issue had not been raised before. Furthermore, the request did not amend the respondent's case since, until the board's preliminary opinion, the opposition division and the parties had considered the method of claim 2 to be therapeutic.

Claim 2 of the main request was clear. It was directed to a first medical use in line with Articles 54(4) and 53(c) EPC. Any skilled person in the art would understand its meaning.

The subject-matter of claims 2 and 3 of the main request was novel. D1 did not disclose MII. The skilled person was not aware that MII could be produced from RD162', let alone that it had therapeutic activity. The fact that MII was a metabolite of RD162' did not imply that it could be analysed within the meaning of G 1/92 and that it was publicly available.

The subject-matter of the main request was inventive starting from D1. MII differed from RD162' in D1 in that its carbamoyl group was demethylated. The effect associated to this difference was an improvement of the pharmacokinetic profile while maintaining the pharmacological effect on AR. The improved pharmacokinetics of MII was derivable from D6 (page 34, last paragraph to page 35, paragraph 3), which stated that MII had a higher free fraction and AUC than RD162'. The pharmacological activity of MII on AR was reported in the patent (Tables 8 and 12). D6 (page 19, last paragraph) and D13 (page 31, last paragraph), which concluded that this activity was equivalent to that of RD162'. The specific IC_{50} values for MII and RD162' in D6 (page 18, penultimate paragraph and page

19, penultimate paragraph) could not be compared because they did not belong to the same test. Thus, the objective technical problem to be solved was providing a therapeutically useful agent with similar receptor activity and improved pharmacokinetics.

Even if the board did not acknowledge the superior pharmacokinetic properties of MII, MII was not an obvious solution. First, the skilled person had multiple ways of modifying RD162', and the cited prior art did not point particularly at N-demethylation. Second, the skilled person had no expectation of success that N-demethylation of RD162' would give a compound with an equivalent pharmacological effect. D1 taught (paragraph [00188]) that the substituents on the aryl ring carrying the carbamoyl group were important for determining activity. In addition, it noted (paragraph [00196]) that small structural changes in the compounds could result in large changes in their therapeutic performance. This was also the general teaching of D10 (page 133, paragraph bridging the columns and page 136, left-hand column, lines 1 to 7), which explicitly referred to the loss of activity of venlafaxine after N-demethylation. Therefore, the skilled person could not have expected MII to exhibit pharmacological activity equivalent to that of RD162'.

XI. The parties' final requests, as far as relevant to the present decision, were the following.

- The appellants requested that the decision under appeal be set aside and that the patent be revoked in its entirety.

- The respondent requested that the patent be maintained in amended form on the basis of the

claims of the main request, implying that the appeals be dismissed, or, alternatively, that the patent be maintained in amended form on the basis of the claims one of auxiliary requests 1 to 6, all filed with the letter dated 3 June 2021.

Reasons for the Decision

1. The appeal is admissible. It meets the requirements of Articles 106 to 108 and Rule 99(2) EPC.

2. *Admittance - documents D21a and D21b*

D21a and D21b were filed by appellant 2 with its statement of grounds of appeal. In its reply to the statements of grounds of appeal, the respondent requested that these documents not be admitted into the appeal proceedings. As the statement of grounds of appeal was filed before entry into force of RPBA 2020, the relevant provision is Article 12(4) RPBA 2007 (see Article 25(2) RPBA 2020).

By filing D21a and D21b, appellant 2 intended to substantiate a lack of novelty objection based on the allegation that MII was inevitably obtained as a sub-product in the preparation of RD162' according to Example 56 of D1. Appellant 2 had raised this objection in its notice of opposition (paragraph 9). However, in its communication issued in preparation for the oral proceedings (point 3), the opposition division considered that, in the absence of supporting evidence, the objection was speculative. Appellant 2 then filed document D19 on the final date for making written

submissions under Rule 116 EPC and D19a shortly before the oral proceedings. The opposition division disregarded both D19 and D19a (decision, point 3.1) for being late filed and because they were not conclusive - they did not exactly reproduce the experimental conditions of Example 56 of D1.

In its statement of grounds of appeal (point V.2), appellant 2 did not contest this aspect of the opposition division's decision. Instead, it filed D21a and D21b as new evidence which allegedly overcame the deficiencies in D19 and D19a.

It is apparent from this sequence of events that appellant 2 could and should have properly substantiated its lack of novelty objection at the outset of the opposition proceedings. It had an additional opportunity to do so in response to the opposition division's preliminary opinion before the oral proceedings. However, appellant 2 also missed this opportunity because the evidence filed (D19 and D19a) did not exactly reproduce the conditions of Example 56 of D1 and could not show that compound MII was necessarily obtained as a sub-product.

Therefore, the board held D21a and D21b inadmissible pursuant to Article 12(4) RPBA 2007.

3. Admittance - main request

The respondent filed the claims of the main request in response to the board's remark in its preliminary opinion (point 12.1, last sentence) that the method of treatment of claim 2 of the main request then on file was not therapeutic.

In the board's view, exceptional circumstances concurred which justified the filing of the claims of the main request in hand. In view of the outcome of the assessment of inventive step in relation to this request (point 6.7 below), the board does not need to give more details for its decision to admit the request pursuant to Article 13(2) RPBA 2020.

4. Clarity - claim 2 of the main request

Claim 2 of the main request relates to compound MII or a pharmaceutically acceptable salt or solvate of it for use in a method of treatment of an individual for therapy.

At the oral proceedings before the board, appellant 1 argued that the feature "for therapy", which was not in the granted claims, rendered claim 2 unclear. This was because the claim seemed to relate to a first medical use, but its wording was not in line with the one derivable from Article 54(4) EPC: a first medical use claim should read "for use in therapy" rather than "for use in a method of treatment of an individual for therapy".

Article 54(4) EPC establishes that Article 54(2) and (3) EPC do not exclude the patentability of any substance or composition, comprised in state of the art, for use in a method referred to in Article 53(c) EPC, provided that its use for any such method is not comprised in the state of the art. As noted by the respondent at the oral proceedings before the board, claim 2 relates to a method of treatment excluded by Article 53(c) EPC, namely a method for treatment of the human or animal body by therapy. Therefore, the respondent was entitled to seek

protection under Article 54(4) EPC. The board does not agree with appellant 1 that Article 54(4) EPC requires the use of a specific wording. Moreover, the wording of claim 2 raises no doubts that it concerns a first medical use.

Therefore, claim 2 is clear and complies with Article 84 EPC.

5. *Novelty over D1 - claims 2 and 3 of the main request*

D1 (abstract and paragraph [0001]) is directed to the use of diarylthiohydantoin compounds for the treatment of hormone refractory prostate cancer. A preferred compound of D1 is RD162' (Example 56 and the table on page 104).

It was undisputed that MII is a metabolite of compound RD162'. This was also acknowledged in the patent (paragraphs [0004] and [0009]).

Appellant 1 submitted (statement of grounds of appeal, point 4.2) that the use of RD162' in D1 for treating prostate cancer anticipated the subject-matter of claims 2 and 3 of the main request. This was because the administration of RD162' resulted in the formation of MII *in vivo*. Given that MII could be detected and identified in the body of the treated patient and that it could be found to be active against prostate cancer, MII and its therapeutic use were implicitly disclosed in accordance with decision G 1/92 of the Enlarged Board of Appeal (OJ EPO 1993, 277).

The board disagrees. In decision G 1/92, the Enlarged Board of Appeal held that the chemical composition of a product is state of the art when the product as such is

available to the public and can be analysed and reproduced by the skilled person (G 1/92, Headnote 1 and Reasons 1.4). This principle does not apply to the case in hand because MII does not meet the precondition that it must be available to the public: although MII is formed *in vivo* when RD162' is administered to a patient, there is no evidence on file showing that MII was ever detected before the filing date. Hence, the skilled person was not aware of the existence of MII and could neither analyse its chemical composition and structure nor reproduce it. Consequently, the therapeutic use of MII was not disclosed either.

Therefore, the subject-matter of the main request meets the requirements of Article 54 EPC.

6. Inventive step - main request

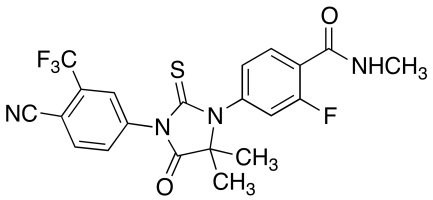
6.1 The patent invention (paragraphs [0004] and [0009]) is based on the identification and study of the metabolites of compound RD162', an active ingredient useful in treating prostate cancer disclosed in D1 (Example 56). In post-published literature, RD162' is also known as MDV3100 or by its common name enzalutamide (see, for instance, D6, page 12, last paragraph and page 14, paragraph 1).

The patent discloses (Examples 1 to 4) the isolation, identification and quantification of two main metabolites of RD162', namely MI and MII. Like RD162', MII is an effective antagonist of AR (Examples B2 and B4). Therefore, MII is believed to be suitable for the treatment of prostate cancer.

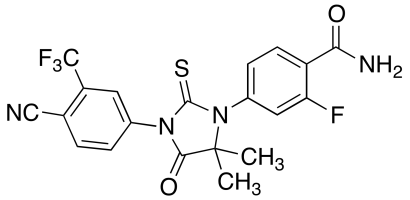
6.2 The parties agreed that D1 is a feasible starting point for the assessment of inventive step. The board shares this view.

D1 concerns (paragraph [0001]) the synthesis of diarylthiohydantoin compounds and their use for treating refractory prostate cancer. A preferred compound in D1 is RD162' (paragraph [0024] and Example 56), which was found to be a strong AR antagonist (paragraphs [00177], [00179] and [00180]; Table 5; and Figures 21A and 21B). RD162' was classified in the group called "Tier 1", which contains the compounds that are much better in treating prostate cancer than the reference drug bicalutamide.

6.3 It was undisputed that the subject-matter of the main request differs from the teaching of D1 in that the active ingredient is MII rather than RD162'. As shown in the formulae below, the structure of MII differs from that of RD162' in that its carbamoyl group is demethylated.



RD162'



MII

6.4 The appellants disputed the technical effect brought about by this difference. They referred to the data in the patent and post-published documents D6 and D13.

D6 and D13 are reports from regulatory agencies on the commercial product Xtandi, used for the treatment of metastatic castration-resistant prostate cancer. The

active ingredient of Xtandi is RD162' (D6, page 14, paragraph 1). D6 and D13 also refer to metabolite M2. The parties did not contest that M2 is metabolite MII in the patent.

6.4.1 The respondent put forward that the patent (Tables 8 and 12), D6 (page 19, penultimate paragraph) and D13 (page 31, last paragraph and table bridging pages 31 and 32) showed that MII was an AR antagonist equivalent to RD162'. In addition, it could be inferred from D6 (page 34, last paragraph to page 35, paragraph 3) that MII had pharmacokinetic properties superior to RD162'.

In contrast, the appellants maintained that, in view of D6 (page 18, penultimate paragraph and page 19, penultimate paragraph), MII was not as good an AR antagonist as RD162'. Regarding the pharmacokinetic profile, D6 did not contain any suitable comparison between MII and RD162' because it did not contain any tests following oral administration of MII. Moreover, D6 concluded (page 35, paragraphs 1 to 3 and page 31, paragraph 1) that, *in vivo*, MII and RD162' had similar pharmacokinetic properties.

6.4.2 With respect to the effect of MII as an AR antagonist, the board agrees with the respondent that the evidence on file allows concluding that MII is equivalent to RD162'. The patent shows (Tables 8 and 12) that MII binds to AR and that it has antagonistic but no agonistic effect. This is confirmed in D6 (page 19, penultimate paragraph) and D13 (page 31, last paragraph and table bridging pages 31 and 32), which conclude that, on the basis of their experimental data, MII and RD162' have similar AR binding affinity and inhibitory activity.

The appellants pointed to the specific IC_{50} values for AR nuclear translocation disclosed in D6 (page 18, penultimate paragraph and page 19, penultimate paragraph), namely 1.9 µM for RD162' and 3.2 µM for MII. On this basis, the appellants contended that MII was a poorer AR inhibitor. This argument is not convincing. The IC_{50} values were taken from different passages in D1, and it is uncertain whether they were obtained under the same conditions. Therefore, there are doubts as to whether they may be compared. As correctly noted by the respondent, D13 (table bridging pages 31 and 32) contains data that may be compared and shows the opposite - RD162' has a slightly higher IC_{50} than MII (0.130 µM vs 0.120 µM). The board considers that the decisive point in D6 and D13 is that, in both cases, the regulatory authorities, considering the available evidence, concluded that MII and RD162' are equivalent AR signalling inhibitors.

6.4.3 In relation to the improved pharmacokinetic properties alleged by the respondent, the board agrees with the appellants that D6 does not demonstrate any improvement.

The respondent referred to the sentences in D6 (page 35, paragraphs 1 and 3) stating that MII has a higher free fraction and AUC than RD162'. However, as noted by the appellants, these sentences do not allow concluding that MII has improved pharmacokinetics. On the one hand, the sentences were taken out of context and limited to observations *in vitro*. The sentences following the cited ones indicate that the difference in free fractions *ex vivo* was much smaller than *in vitro* and that there was no difference in the average patient at steady state, i.e. *in vivo*. On the other hand, the AUC data in D6 are based on the

administration of RD162'. D6 contains no data following the administration of MII. Hence, the data in D6 are not suitable for comparing the pharmacokinetics of MII and RD162'; they merely reflect the contribution of metabolite MII to the total efficacy and safety of RD162'. Therefore, there is no evidence on file showing that MII has superior pharmacokinetic properties.

6.5 Thus, the objective technical problem to be solved by the main request is providing an equivalent compound for the treatment of prostate cancer.

The board is satisfied that MII is a suitable solution to that problem (see points 6.4.2 and 6.4.3).

6.6 The issue of obviousness hinges on whether the skilled person would have contemplated N-demethylation as a suitable modification of RD162' to solve the problem posed. In other words, whether the skilled person would have expected N-demethylation of RD162' to yield a compound with therapeutic properties equivalent to those of RD162'.

6.6.1 In light of common general knowledge, the board agrees with the appellants that this question has to be answered in the affirmative.

D20 is a textbook on the metabolism of drugs which represents common general knowledge. In its introduction to the enzymatic cleavage of N-C bonds (page 204, first and second paragraphs), it conveys the general principles that N-demethylation is the simplest case of oxidative N-C cleavage, that it involves the loss of a small group and that, usually, the N-demethylated compounds retain the pharmacological activity of their parent compounds. This principle is

also taught in review D10, which teaches (page 135, right-hand column, paragraph 2 and sentence bridging pages 135 and 136) that minor structural modifications that involve simple reactions, such as N-demethylation, result in compounds that to some degree maintain the activity of the parent compound. This teaching was confirmed in D1 (Tables 5 and 6): N-demethylation of RD131 and RD134 gave RD130 and RD133, respectively. The N-demethylated compounds were classified within the same level of activity as their respective parent compounds - RD130 and RD131 were in the group "Tier 1", and RD133 and RD134 were in the group "Tier 2".

Thus, the board is persuaded that the skilled person would have been prompted to N-demethylate RD162' in the expectation of obtaining a compound with equivalent therapeutic properties.

6.6.2 The respondent's argument that the skilled person would not have expected the N-demethylated compound to retain the therapeutic properties of RD162' is not convincing.

D10 affirms (sentence bridging pages 135 and 136) that it is not surprising that compounds having significant structural similarities have the same biochemical action. It is true that immediately after this sentence, D10 notes that, nevertheless, minor structural modifications can result in loss of potency or modification of the mode of action of the parent drug. It even gives an example (venlafaxine) in which N-demethylation results in a loss of activity. However, in line with the disclosure of D20 (page 204, paragraph 1), the general teaching of D10 is that of the first sentence. The continuation is rather intended to cite exceptions to the general rule.

The respondent also referred to the general warning in D1 (page 114, paragraph [00196]) that what might appear to be a small change in the structure of a compound could result in a large change in the therapeutic effect. As examples, D1 mentions the defluorination of RD162 (Tier 1) to give RD161 (Tier 2) and the insertion of a methylene group in RD162 (Tier 2) to give RD149 (Tier 4). This general warning, however, was not particularly directed to N-demethylation and cannot counter the common general knowledge depicted in D20. Moreover, as outlined above, a comparison of the activity of compounds RD130, RD131, RD133 and RD134 in D1 confirms that N-demethylated compounds retain the level of pharmacological effect of their parent compounds.

6.7 For these reasons, the board holds that the subject-matter of the main request does not meet the requirements of Article 56 EPC.

7. Auxiliary requests 1 to 6

The respondent did not provide arguments particularly directed to the auxiliary requests. At the oral proceedings before the board, it stated that it did not wish to make any additional submissions in relation to those requests.

All of the auxiliary requests contain claims concerning the use of MII for the treatment of prostate cancer. For the reasons put forward in relation to the main request, that use is obvious too. Hence, none of the auxiliary requests is allowable for reasons of lack of an inventive step (Article 56 EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated