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**Datasheet for the decision
of 25 September 2023**

Case Number: T 2345/17 - 3.3.04

Application Number: 04762858.1

Publication Number: 1670440

IPC: A61K31/56, A61K31/57, A61K9/20

Language of the proceedings: EN

Title of invention:
HRT FORMULATIONS

Patent Proprietor:
Novo Nordisk Health Care AG

Opponents:
Actavis Group PTC ehf
Generics [UK] Ltd (trading as Mylan)

Headword:
HRT Formulations / NOVO NORDISK

Relevant legal provisions:
EPC Art. 56
RPBA Art. 12(4)

Keyword:
All requests - inventive step - (no)

Decisions cited:

T 1323/17



Beschwerdekammern

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Case Number: T 2345/17 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 25 September 2023

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Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
4 August 2017 concerning maintenance of the
European Patent No. 1670440 in amended form**

Composition of the Board:

Chair M. Pregetter
Members: S. Albrecht
 M. Blasi

Summary of Facts and Submissions

- I. European patent No. 1670440 ("the patent") was granted with 28 claims.
- II. Opposition proceedings were based on the grounds for opposition under Article 100(a) EPC for lack of novelty and lack of inventive step, and under Article 100(b) and (c) EPC.
- III. The following documents, cited during the opposition proceedings, are referred to below:
 - D13: US 4,826,831
 - D29: R.J. Harwood *et al.*, "Hydroxypropyl Methylcellulose", Handbook of Pharmaceutical Excipients, 2nd edn., 1994, 229-32
 - D31: F.W. Goodhart, "Lactose", Handbook of Pharmaceutical Excipients, 2nd edn., 1994, 252-61
 - D32: B. Farhadieh, "Starch", Handbook of Pharmaceutical Excipients, 2nd edn., 1994, 483-8
 - D33: J. Schirmer, "Talc", Handbook of Pharmaceutical Excipients, 2nd edn., 1994, 519-21
 - D34: L. V. Allen *et al.*, "Magnesium Stearate", Handbook of Pharmaceutical Excipients, 2nd edn., 1994, 280-2
 - D35: N.R. Poola, "Triacetin", Handbook of Pharmaceutical Excipients, 2nd edn., 1994, 534-5
 - D39: R.J. Harwood *et al.*, "Hydroxypropyl Cellulose", Handbook of Pharmaceutical Excipients, 2nd edn., 1994, 223-8
- IV. The opposition division decided that, as amended in the form of auxiliary request 1 and the invention to which it related, the patent met the requirements of the EPC. The decision was based on a main request and an

auxiliary request (auxiliary request 1). The main request was the patent as granted. The set of claims of auxiliary request 1 was filed with a letter of 30 September 2016.

Claim 1 of auxiliary request 1 reads as follows.

"1. A pharmaceutical formulation containing low concentrations of estradiol and norethindrone acetate (NETA) comprising 0.5 mg of estradiol, optionally as a hydrate thereof, 0.1 mg of NETA or the corresponding amount of norethindrone (NET) or a corresponding amount of an ester or a salt of NET, and a cellulosic binder."

In its decision, the opposition division held *inter alia* that the subject-matter of claim 1 of the main request lacked inventive step over document D13 as the closest prior art. By contrast, the subject-matter of claim 1 of auxiliary request 1 would not have been obvious starting from the same closest prior art. Claim 1 of this request differed from claim 1 of the main request in that it required the presence of a cellulosic binder. This difference gave rise to improved stability, as evidenced by the respondent's comparative experimental data filed with its letter of 30 September 2016. The objective technical problem was therefore the provision of a composition with improved stability. The solution proposed by claim 1 would not have been obvious, since the cited prior art did not provide the skilled person with any pointer towards the claimed binder.

V. Opponent 2 ("appellant") lodged an appeal against the opposition division's decision.

VI. In its statement of grounds of appeal, the appellant requested that the decision under appeal be set aside and that the patent be revoked in its entirety. The appellant further requested a refund of the appeal fee, because the opposition division had committed two substantial procedural violations.

VII. In its reply to the statement of grounds of appeal, the patent proprietor ("respondent") requested that the appeal be dismissed and that the patent be maintained as amended in the form of auxiliary request 1 underlying the decision under appeal (i.e. current main request). In the alternative, the respondent requested that the patent be maintained in amended form on the basis of one of the sets of claims of auxiliary requests 2 to 7 filed on 30 September 2016 before the opposition division, which it resubmitted with the reply to the statement of grounds of appeal and which became current auxiliary requests 1 to 6 respectively.

Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the claimed formulation additionally comprises a cellulosic coating.

Claim 1 of auxiliary request 2 differs from claim 1 of the main request in that the following passage is added at the end of the claim.

"for treating a progestogen-responsive syndrome by administering daily to a patient in need of such treatment the pharmaceutical formulation."

Claim 1 of auxiliary request 3 incorporates the limitation of claim 1 of auxiliary request 1 and further specifies that the cellulosic binder is hydroxypropyl cellulose, that the cellulosic coating is

hydroxypropyl methylcellulose and that lactose, maize starch, talc, magnesium stearate and glycerol triacetate must be present in the formulation.

Claim 1 of auxiliary request 4 differs from claim 1 of auxiliary request 3 in that it specifies the amounts of hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose, maize starch, talc, magnesium stearate and glycerol triacetate.

Claim 1 of auxiliary request 5 reads as follows.

"1. A pharmaceutical formulation containing low concentrations of estradiol and norethindrone acetate (NETA) comprising 0.5 mg of estradiol, optionally as a hydrate thereof, and 0.1 mg of NETA, 37.5 mg of lactose monohydrate, 37.5 mg of maize starch, 3.2 mg of hydroxypropyl cellulose, 0.8 mg of talc and 0.4 mg of magnesium stearate."

Claim 1 of auxiliary request 6 is directed to a dispenser comprising unit dosage forms of a pharmaceutical formulation in accordance with claim 1 of the main request.

- VIII. Oral proceedings before the board were set, as requested by the parties, and were scheduled for 25 July 2022.
- IX. In a letter dated 17 March 2022, the appellant withdrew its request for a refund of the appeal fee and the associated objection that the opposition division had committed two procedural violations.

- X. In a letter dated 31 March 2022, opponent 1 ("party as of right") informed the board that it would not be attending the oral proceedings.
- XI. Likewise, in a letter dated 22 April 2022, the respondent informed the board that it would not be attending the oral proceedings.
- XII. In a communication under Article 15(1) RPBA issued on 5 May 2022 ("communication"), the board informed the parties that it agreed with the appellant's position that the subject-matter of claim 1 of the main request and that of each of auxiliary requests 1 to 6 would have been obvious in light of the closest prior art, document D13, taken in combination with common general knowledge. Furthermore, the board expressed the intention to cancel the oral proceedings within the appropriate time frame, and to continue the proceedings in writing.
- XIII. Subsequently, the board cancelled the oral proceedings and informed the parties that it would issue a decision in due course.
- XIV. The appellant's written case, where relevant to the present decision, may be summarised as follows.

Main request - claim 1 - inventive step

The opposition division was incorrect to take the respondent's comparative experimental data, filed on 30 September 2016, into account when formulating the objective technical problem. These data were based *inter alia* on the use of polyvinyl pyrrolidone (Polyvidon™ VA 64) as the comparative binder. The respondent had provided no justification for selecting

this unusual binder, which was not mentioned in the closest prior art, document D13. The respondent's data were thus irrelevant, and the objective technical problem was merely the provision of a further formulation. The solution proposed by the subject-matter of claim 1 would have been obvious in the light of document D13 taken in combination with common general knowledge.

Admittance of auxiliary requests 1 to 6 into the proceedings (Article 12(4) RPBA 2007)

These requests should be not admitted into the proceedings, since they had not been substantiated.

Auxiliary requests 1 to 6 - claim 1 - inventive step

Starting from document D13 as the closest prior art, the objective technical problem remained the same as for claim 1 of the main request. The additional features of claim 1 of each of auxiliary requests 1 to 6 were trivial solutions to this problem that did not involve an inventive step. The excipients recited in claim 1 of auxiliary requests 1, 3, 4 and 5 were known from the common general knowledge, as evidenced by documents D29, D31 to D35, and D39. The use recited in claim 1 of auxiliary request 2 likewise formed part of the common general knowledge. The dispenser referred to in claim 1 of auxiliary request 6 was a standard way to present any formulation.

- XV. The respondent's written case, where relevant to the present decision, may be summarised as follows.

The opposition division's inventive step findings and analysis, set out on sheets 19 to 21 of the decision under appeal, were correct.

- XVI. The appellant's and the respondent's requests, where relevant to the present decision and as understood by the board, are as follows.

The appellant requests that the decision under appeal be set aside and that the patent be revoked. The appellant further requests that the sets of claims of auxiliary requests 1 to 6, filed as auxiliary requests 2 to 7 on 30 September 2016 before the opposition division and resubmitted with the reply to the statement of grounds of appeal, not be admitted into the proceedings.

The respondent requests that the appeal be dismissed and that the patent be maintained as amended in the form considered allowable by the opposition division (main request), or, in the alternative, on the basis of one of the sets of claims of auxiliary requests 1 to 6 filed as auxiliary requests 2 to 7 on 30 September 2016 before the opposition division and resubmitted with the reply to the statement of grounds of appeal.

- XVII. The party as of right did not file any requests or make any submissions on substance in the appeal proceedings.

Reasons for the Decision

1. The appeal is admissible.

2. Main request - claim 1 - inventive step
(Article 56 EPC)

The closest prior art

- 2.1 In the decision under appeal (see sheet 19, last paragraph), the opposition division considered document D13 to be the closest prior art. This was not contested by the parties.
- 2.2 This document (see column 3, lines 14 to 15 in combination with column 7, line 30) discloses a method of hormonally treating menopausal disorders comprising administering a combination of estradiol and NETA. The unit dosage for estradiol is between 0.5 and 2 mg/day, preferably 1 mg/day (see column 5, Table 1A). The unit dosage for NETA is between 0.1 and 1 mg/day, preferably 0.20 mg/day (see column 6, Table 1B).

Distinguishing features vis-à-vis document D13

- 2.3 It is common ground that the formulation recited in claim 1 differs from document D13
- (a) in terms of the specific amounts of estradiol and NETA, i.e. 0.5 mg and 0.1 mg respectively ("distinguishing feature (a)"), and
 - (b) in the presence of a cellulosic binder ("distinguishing feature (b)").

Objective technical problem and solution

- 2.4 The objective technical problem is to be formulated on the basis of the technical effects that the

distinguishing features provide over the closest prior art.

Distinguishing feature (a)

- 2.5 As noted by the opposition division (see impugned decision, sheet 20, second paragraph) and not contested by the respondent, the specific amounts of estradiol and NETA that are claimed have not been shown to provide any technical effect vis-à-vis document D13.

Distinguishing feature (b)

- 2.6 During the opposition proceedings, the respondent filed comparative data to demonstrate that a cellulosic binder improved the storage stability of NETA (see letter dated 30 September 2016, page 4, penultimate paragraph to page 5, sixth full paragraph).
- 2.7 These data ("respondent's data") stem from an experimental study comparing the stability under storage of four film-coated tablets. Details of the tested tablets are set out in Example 1 of the patent and that of the application as filed. Each tablet contains 0.517 mg of estradiol hemihydrate, 0.100 mg of NETA, 37.5 mg of lactose monohydrate, 37.5 mg of maize starch, 0.800 mg of talc, 0.400 mg of magnesium stearate and 3.20 mg of a binder (see paragraph [0039] of the patent; page 7, lines 3 to 6, of the application as filed). The tablets differ from each other in the type of binder used, i.e. polyvinyl pyrrolidone (Polyvidon™ VA 64) and hydroxypropyl cellulose (Klucel™ EF), and in the amount of the film coat (see paragraphs [0040] and [0041] of the patent; page 7, line 7 to the end of the page, of the application as filed).

- 2.8 The tablets were packaged and subsequently stored for 6 months at $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and $75\% \pm 5\%$ relative humidity. At 0, 3 and 6 months after the start of the study, the tablets were subjected to assay analysis using HPLC to detect NETA and estradiol. Differences in formulations were evaluated by comparing the degradation rates of NETA.
- 2.9 The opposition division admitted the respondent's data into the proceedings and found that these showed the alleged improvement of NETA stability as a result of the cellulosic binder (see paragraph spanning sheets 20 and 21 of the impugned decision). The opposition division took note of the appellant's counter-arguments, including its submission that the respondent's stability tests did not provide a comparison with the closest prior art (document D13); but it dismissed these as unsubstantiated (see impugned decision, sheet 20, third and fourth paragraphs).
- 2.10 According to the established case law of the boards of appeal, if comparative tests are chosen to demonstrate an inventive step on the basis of an improved effect over a claimed area, the nature of the comparison with the closest state of the art must be such that the alleged advantage or effect is convincingly shown to have its origin in the distinguishing feature of the claimed invention compared with the closest state of the art (see also Case Law of the Boards of Appeal, 10th edition 2022, I.D.4.3.2).
- 2.11 To be of relevance in demonstrating that a technical improvement is achieved in comparison with the closest state of the art, the variant of the closest prior art selected as a reference (or comparative) example for

the comparative test must be representative of the closest prior art. This means that the effect shown to be caused by the distinguishing feature in the context of the comparative test must also be expected to take place within the framework of the closest prior art despite the existence of differences vis-à-vis the reference example of the comparative test (see decision T 1323/17 cited in Case Law of the Boards of Appeal, 10th edition 2022, I.D.4.3.2).

2.12 In the case at issue, the appellant correctly observed that the comparative binder chosen by the respondent (Polyvidon™ VA 64) is not mentioned in the closest prior art, document D13. In the absence of any arguments from the respondent's side as to why the selected comparative examples nevertheless reflect the closest prior art, the board, agreeing with the appellant, finds that the respondent's data do not show a technical effect linked to the cellulosic binder over document D13.

2.13 As a consequence, the alleged improvement of stability brought about by the cellulosic binder cannot be taken into consideration when formulating the objective technical problem.

Conclusion on distinguishing features (a) and (b)

2.14 It follows that no technical effect has been shown for distinguishing features (a) and (b) vis-à-vis the closest prior art, document D13.

2.15 The objective technical problem must therefore be formulated as the provision of a further hormone replacement therapy (HRT) formulation comprising estradiol and NETA.

2.16 As a solution to this problem, the claimed invention proposes a pharmaceutical formulation in accordance with claim 1.

Obviousness of the proposed solution

2.17 The proposed solution would have been obvious, starting from document D13 and in view of the common general knowledge.

2.17.1 As explained in point 2.2 above, document D13 already proposes unit dosages of between 0.5 and 2 mg/day for estradiol and 0.1 and 1 mg/day for NETA. As a consequence, the board concurs with the appellant that the amounts of estradiol and NETA recited in claim 1 constitute an obvious implementation of the teaching of document D13. This was not contested by the respondent.

2.17.2 Likewise, the use of a cellulosic binder would have been an obvious choice for the skilled person to solve the objective technical problem posed. As correctly observed by the appellant, cellulosic binders form part of the common general knowledge, as evidenced by document D39, which is an excerpt from a handbook of pharmaceutical excipients. This document reports the use of hydroxypropyl cellulose as a tablet binder (see page 223, right-hand column, table).

Overall conclusion on the main request

2.18 In light of the above considerations, the board concludes that the appellant's objection of lack of inventive step succeeds, and the main request is thus not allowable under Article 56 EPC.

3. Admittance of auxiliary requests 1 to 6 into the proceedings (Article 12(4) RPBA 2007)
 - 3.1 The appellant submits that the auxiliary requests were not sufficiently substantiated within the meaning of Article 12(2) RPBA 2007 and therefore should not be admitted into the appeal proceedings under Article 12(4) RPBA 2007. However, irrespective of this issue, the board takes these requests into account pursuant to Article 12(4) RPBA 2007 (applicable pursuant to Article 24 and Article 25(1) and (2) RPBA 2020) for reasons of procedural economy, in order to decide upon them on their merits. This is not to the appellant's detriment, since these auxiliary requests are not allowable.

4. Auxiliary requests 1 to 6 - claim 1 - inventive step (Article 56 EPC)
 - 4.1 The amendments made to claim 1 of each of auxiliary requests 1 to 6 (see point VII. above) further distinguish the claimed formulations from the closest prior art, document D13.
 - 4.2 The respondent did not invoke any technical effect linked to any of these additional distinguishing features. The objective technical problem thus remains the same as for claim 1 of the main request (see point 2.15 above).
 - 4.3 The board sees no reason to disagree with the appellant's submissions that the additional features of claim 1 of each of auxiliary requests 1 to 6 form part of the common general knowledge (see point XIV. above), considering also that in its submissions to the board

the respondent did not contest that this was common general knowledge.

- 4.4 The board therefore concludes that the solution proposed in claim 1 of each of auxiliary requests 1 to 6 would have been an obvious choice for the skilled person when solving the technical problem posed.

Overall conclusion on auxiliary requests 1 to 6

- 4.5 It follows that the subject-matter of claim 1 of each of auxiliary requests 1 to 6 does not involve an inventive step within the meaning of Article 56 EPC.

Overall conclusion

5. Since none of the claim requests is allowable, the patent has to be revoked.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chair:



I. Aperribay

M. Pregetter

Decision electronically authenticated