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Datasheet for the decision of 23 September 2025

Case Number: T 1936/23 - 3.3.07

Application Number: 20162018.4

Publication Number: 3811927

IPC: A61K9/00, A61K9/08, A61K38/09, A61K47/12, A61P15/00

Language of the proceedings: EN

Title of invention:
A STABLE PARENTERAL DOSAGE FORM OF CETRORELIX ACETATE

Patent Proprietor:
Sun Pharmaceutical Industries Ltd

Opponent:
Weickmann & Weickmann Patent- und Rechtsanwälte PartmbB

Headword:
Cextrorelix/SUN

Relevant legal provisions:
EPC Art. 99(1), 107, 108, 123(2), 123(3), 84, 56
RPBA 2020 Art. 13(1)

Keyword:

Admissibility of opposition and appeal (Yes)
Main request - Clarity and extension over the scope of the claims as granted (No)
Auxiliary request 8 - Admissibility (Yes)
Auxiliary request 8 - Clarity and amendments (Yes)
Auxiliary request 8 - Inventive step (Yes)

Decisions cited:

G 0009/92, G 0004/93, G 0001/12, G 0002/10, T 1320/13, T 2203/14

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Boards of Appeal

Chambres de recours

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

Case Number: T 1936/23 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 23 September 2025

Appellant: (Opponent)	Weickmann & Weickmann Patent- und Rechtsanwälte PartmbB Richard-Strauss-Straße 80 81679 Munich (DE)
Respondent: (Patent Proprietor)	Sun Pharmaceutical Industries Ltd Sun House, Plot N°. 201 B/1 Western Express Highway Goregoan (E) 400063 Mumbai, Maharashtra (IN)
Representative:	Harrison IP Limited Mereside, Alderley Park Congleton Road Nether Alderley Macclesfield, Cheshire SK10 4TG (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 9 November 2023 concerning maintenance of the European Patent No. 3811927 in amended form.**

Composition of the Board:

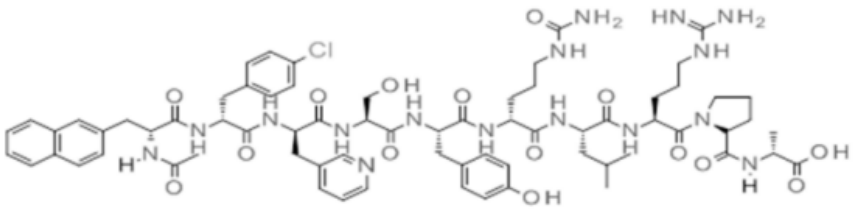
Chairman A. Usuelli
Members: D. Boulois
S. Ruhwinkel

Summary of Facts and Submissions

I. European patent 3 811 927 B1 was granted on the basis of a set of 12 claims.

Independent claim 1 as granted read as follows:

"1. A parenteral dosage form comprising:
a ready-to-inject sterile, stable aqueous solution comprising:
(i) Cetrorelix, or a pharmaceutically acceptable salt thereof, in an amount of 0.25mg/ml,
(ii) lactic acid to adjust the pH in the range of 3 to 5,
(iii) Impurity A, a decapeptide of formula I in an amount less than 1% w/v of Cetrorelix base,



Formula I,

(iv) an osmotic agent, and
(v) water for injection."

II. An opposition was filed under Article 100 (a), (b) and (c) EPC on the grounds that its subject-matter lacked inventive step, was not sufficiently disclosed, and extended beyond the content of the application as filed.

III. The appeal lies from the decision of the opposition division that the patent in amended form met the requirements of the EPC. The decision was based on the main request filed with letter of 10 January 2023.

Claim 1 of the main request differed form claim 1 as granted in the reformulation of feature (i) and in the specification of feature (ii), namely:

"(i) Cetrorelix in an amount of 0.25mg/ml, or a pharmaceutically acceptable salt thereof,
(ii) lactic acid in a concentration sufficient to adjust the pH in the range of 4.00 to 5.00".

IV. The documents cited during the opposition proceedings included the following:

D1: US 2013/0303464 A1
D2: US 7,214,662 B2
D3: WO 03/045419 A1
D4: US 7,718,599 B2
D5: WO 01/87265 A2
D6: US 2018/0325993 A1
D7: EP 2 662 073 A1
D8: WO 2015/004125 A1
D9: US 2013/0288968 A1
D10: US 2003/0216302 A1
D11: submission of the Patent Proprietor during the examination proceedings of the patent dated 01 April 2021
D12: WO 2021/079339 A1, a family member of the patent in dispute claiming the same priority of 24 October 2019 (IN 201921043355)

D13: Wikipedia article "Cetrorelix" dated 18 April 2019
D14a: Cetrotide® product information (updated version of 3 October 2019)
D14b: Screenshot of the European Medicines Agency webpage concerning Cetrotide® of 15 October 2019 (proving the publication of D14a)

V. According to the decision under appeal, claims 1 and 12 of the main request met the requirements of Articles 123(2) and 123(3) EPC.

The examination of clarity was not permissible, and in any case the amendments made in the claims of the main request met the requirements of Article 84 EPC

The claims of the main request met the requirements of Article 83 EPC.

With regard to inventive step, D1-D3 were equally suitable starting points for the assessment of inventive step. Since both parties used D1 at the oral proceedings as the closest prior art, this approach was followed in the decision. The features which distinguished the formulation defined in claim 1 of the main request were:
(1) the presence of lactic acid in a concentration sufficient to adjust the pH;
(2) the pH of the aqueous solution being in the range of 4.00 to 5.00.
The technical problem to be solved was seen as the provision of a further stable cetrorelix parenteral dosage form. The claimed solution was not obvious in starting from D1 in combination with any of documents D4-D10.

VI. The opponent (hereinafter the appellant) filed an appeal against said decision.

VII. With its reply to the statement of grounds of appeal dated 12 June 2024, the patent proprietor (hereinafter the respondent) filed auxiliary requests 1-7 and submitted the following evidence:

D15: German Company Register Extract

VIII. With a letter dated 17 October 2024, the appellant submitted the following evidence:

D16: Confirmation letter to Association No. 589

IX. With a letter dated 7 March 2025, the respondent filed auxiliary requests 8 and 9.

Claim 1 of auxiliary request 8 differed in the formulation of feature (i):
"(i) Cetrorelix, or a pharmaceutically acceptable salt thereof, in an amount of 0.25mg/ml".

X. A communication from the Board, dated 2 May 2025, was sent to the parties.

XI. Oral proceedings took place on 23 September 2025. During oral proceedings, after the decision that the main request did not comply with the requirements of Articles 123(3) and 84 EPC, the respondent stated that it wanted to proceed with the auxiliary requests in the following order: auxiliary request 8, auxiliary request 4, auxiliary requests 1 to 3, auxiliary request 5, 6, 7, 9.

XII. The arguments of the appellant, as far as relevant to the present decision may be summarised as follows:

Admissibility of the opposition and appeal

The opposition and appeal were admissible. The legal entity "Weickmann & Weickmann Patent- und Rechtsanwälte PartmbB" indeed validly filed the present opposition/ appeal; the designation “Weickmann & Weickmann PartmbB” was an obvious abbreviation of the registered name and likewise pointed to the legal entity. It was therefore requested that the designation of the opponent/ appellant be corrected to “Weickmann & Weickmann Patent- und Rechtsanwälte PartmbB” based on Rule 139, first sentence, EPC.

Main request - Amendments

Section (i) of claim 1 of the main request stated "Cetrorelix in amount of 0.25 mg/ml, or a pharmaceutically acceptable salt thereof". This language was different from claim 2 as filed and from claim 1 as granted. The amendment introduced in feature (i) of claim 1 led to a violation of the requirements of Article 123(2) EPC and Article 123(3) EPC.

There was also an ambiguity regarding the meaning of section (i), which constituted a violation of Article 84 EPC.

Admission of auxiliary request 8 into the appeal proceedings

This request was late filed and no reason were provided for this late-filing. All objections were already present on file since the opposition proceedings. The

respondent could not improve its position, in view of the prohibition of *reformatio in peius*. The opponent was the sole appellant against an interlocutory decision by an opposition division maintaining the patent in amended form, and the patentee was primarily restricted in the appeal proceedings to defending the patent as thus maintained. This new request was a return to claim 1 as granted, which constituted an abuse of procedure and should not be allowed.

Moreover, the subject-matter of this request was not convergent with the previous request.

Auxiliary request 8 - Amendments

Feature (i) of claim 1 was not supported by the application as filed and there was no basis for feature (ii). The pH range of 4.00-5.00 did in particular not find a basis in the application as originally filed. Particularly, the list of single pH values of page 9 of the patent application could not serve as a basis for construing a pH range according to feature (ii) whereas the ranges given on the same page were not disclosed with the same level of accuracy.

Claim 12 did neither meet the requirements of Article 123(2) EPC. It was based on original claim 13 combined with original claim 2, for which there was no reference in claim 13.

Auxiliary request 8 - Article 84 EPC

Feature (ii) was unclear, since the skilled person would not know which pH value was to be adjusted. The formulation might furthermore encompass embodiments

which did not comprise lactic acid. Moreover, there was no lower limit of lactic acid in claim 1.

Auxiliary request 8 - Inventive step

Claim 1 differed from D1 in the presence of lactic acid; the presence of lactic acid instead of acetic acid was not associated with a technical effect.

The upper endpoint of the pH range of 2.5 to 5.0 disclosed in D1 overlapped with the upper endpoint of the pH range 4.00 to 5.00 as defined in claim 1. Thus, the range in claim 1 could not be considered as a novel range in view of D1. Working in a range known from the prior art could not provide a technical effect.

The preferred pH range of D1 was from pH 2.8-3.5. According to Table 4 on page 13 of the opposed patent, a formulation at pH 3.5 had a content of 0.40% Impurity A after storage for six months at 25°C/60% RH and thus complied with the stability requirement of the patent, and even with the most stringent stability requirement of claim 9, i.e., stability for at least 6 months at a temperature of 25°C and 60%. Thus, even according to the opposed patent itself, there was no technical effect between pH 3.5 and pH 4.00. There could not be any technical effect in view of D1 over the whole claimed pH range.

The technical problem underlying the opposed patent was the provision of a further stable Cetrorelix parenteral dosage form.

The solution was obvious in view of D1 or D4-D10.

XIII. The arguments of the respondent, as far as relevant to the present decision, may be summarised as follows:

Admissibility of the opposition and appeal

The appellant was not an existing natural or legal person, there was no such legal entity with the name “Weickmann & Weickmann PartmbB”, as required by Articles 99(1) EPC and 107 EPC. According to an extract from a search of the German company register (D15) conducted for any company having the name "Weickmann & Weickmann", the only search result was the entry "Weickmann & Weickmann Patent- und Rechtsanwälte PartmbB". The appellant did not seek to correct this issue when explicitly invited to do so by the Opposition Division during the Opposition. The respondent was entitled to legal certainty regarding the party opposing or appealing the validity of their patent. The requirements for a correction under Rule 139 EPC were not met.

Main request - Amendments

The original language of claim 2 as filed encompassed a cetrorelix salt where the quantity of cetrorelix base present was 0.25mg/ml. This understanding was set out in detail in the explanation clearly given on page 8, final paragraph of the application as filed.

Additionally, it was abundantly clear that within the art, the active ingredient was referenced by the concentration of the active ingredient, cetrorelix base, even when the active ingredient is present as a salt, such as in D14a.

Admission of auxiliary request 8 into the appeal proceedings

Auxiliary Request 8 corresponded to the current main request, except that the wording in section (i) of the claim reverted to the original wording set out in claim 1 as granted.

Auxiliary request 8 - Amendments

The basis for feature (i) was original claim 2, while feature (ii) found a basis on page 9 of the application as filed.

Auxiliary request 8 - Article 84 EPC

Claim 1 was clear to the skilled person.

Auxiliary request 8 - Inventive step

D1 was the closest prior art and the example of the patent showed a significant reduction in a single and total impurity level relative to the level of impurity noted in D1. The problem was the provision of a cetrorelix composition with improved stability and the claimed solution was not obvious in view of any of the cited documents.

XIV. Requests

The appellant requested that the decision under appeal be set aside and the patent be revoked. Further, it requested not to admit auxiliary requests 8 and 9 into the proceedings.

The appellant also requested that its designation was corrected to “Weickmann & Weickmann Patent- und Rechtsanwälte PartmbB”.

The respondent requested that the appeal be dismissed, alternatively that the decision under appeal be set aside and the patent be maintained according to one of auxiliary request 8, auxiliary request 4, auxiliary requests 1 to 3 or auxiliary requests 5,6,7 or 9. Wherein auxiliary requests 1 to 7 were filed with the reply to the grounds of appeal and auxiliary requests 8 and 9 were filed with letter of 7 March 2025, .

The respondent further requested that the appeal be dismissed on the basis that "Weickmann & Weickmann PartmbB" was not a legal person and therefore could not file an opposition or an appeal.

Reasons for the Decision

1. Admissibility of the opposition and the appeal

The opponent and appellant had identified itself as "Weickmann & Weickmann PartmbB".

The respondent considers that “Weickmann & Weickmann PartmbB” is not an existing legal person and therefore cannot file an opposition or an appeal.

1.1 It is established case law of the Boards of Appeal that, even if a party's indication differs from the registered name, this will not lead to inadmissibility of the opposition or appeal (Article 99 EPC and Rules 76(2)(a), 41(2)(c) EPC/Articles 107, 108 EPC and Rules

99(1)(a), 41(2)(c) EPC), provided that the opponent/ appellant was identifiable by the end of the opposition/appeal period, so that the incorrect designation may be rectified in accordance with Rule 101(2) EPC and this correction only expresses what was intended when the opposition/appeal was filed (Case Law of the Boards of Appeal, 11th edition/July 2025, IV.C. 2.2.4a; V.A.2.5.2a; G 1/12, reasons points 26-30).

1.2 In the present case, the excerpt from the German company register submitted by the respondent (see D15) demonstrates that "Weickmann & Weickmann Patent- und Rechtsanwälte PartmbB" was the only result for the search term "Weickmann & Weickmann".

The Board observes that there is no reasonable doubt that the registered "Weickmann & Weickmann Patent- und Rechtsanwälte PartmbB" is the opponent/appellant.

There is in particular no indication for the coexistence of two legal entities (PartmbBs). Moreover, the addition "Patent- und Rechtsanwälte" is merely a descriptive reference to the activity of the legal entity. Therefore, it appears obvious that the designation "Weickmann & Weickmann PartmbB" is merely an abbreviation of the registered name and refers to the identical legal entity.

Thus, it is established beyond doubt that both the opposition and the appeal were filed by this legal entity within the time limits laid down in Articles 99(1) and 108 EPC.

1.3 By letter of 07 March 2025, the respondent also argues with regard to the appellant's reference to the registered association of representatives before the

EPO under No. 589 "Weickmann & Weickmann PartmbB" (see D16, filed by the appellant with letter of 17 October 2024) that the names of the natural persons opposing their patent and filing the appeal are not recognisable, since the composition of the association can be changed at any time.

However, the opposition and the appeal were filed by a legal entity in its own right (Partnerschaftsgesellschaft mit beschränkter Berufshaftung, PartmbB, see § 8(4) Partnerschaftsgesellschaftsgesetz). This legal entity is the party to the proceedings, regardless of the natural persons who are its members.

1.4 In view of this, the appellant's request for correction of its designation to “Weickmann & Weickmann Patent- und Rechtsanwälte PartmbB” was allowable. The designation of the appellant is correctable under Rule 139, first sentence, EPC, since the correction introduces what was originally intended (see G 1/12, reasons 37; Case Law of the Boards of Appeal, loc. cit., V.A.2.5.2a), namely, as pointed out above, the filing of the opposition and the appeal on behalf of the appellant as a legal entity with the registered name "Weickmann & Weickmann Patent- und Rechtsanwälte PartmbB". The Board also considers that the request for correction was filed without delay (see G 1/12, reasons 37; Case Law of the Boards of Appeal, loc. cit., V.A. 2.5.2a). The opposition division did not object to the identity of the appellant and considered the opposition admissible (see decision under appeal, page 1 point II and page 3 point II). The respondent objected for the first time in its reply to the grounds of appeal that the appellant was not an existing natural or legal person and therefore could not file an opposition or an

appeal. In its communication of 2 May 2025 (see point 11), the Board indicated that it considered the opposition and the appeal to be admissible and invited the appellant to correct its designation. In direct response to this, the appellant filed a request for correction of its designation with letter of 23 July 2025. The Board considers this to be sufficient, as the appellant had no reason to submit such a request previously, and this request was filed two months before the oral proceedings.

1.5 Consequently, the opposition and the appeal are admissible and the appellant's request for correction of its designation is allowed.

2. Main request - Amendments

2.1 Feature (i) of claim 1 has been amended during the opposition proceedings. In claim 1 of the main request, feature (i) reads now: ”**Cetrorelix in an amount of 0.25 mg/ml, or a pharmaceutically acceptable salt thereof**”.

The subject-matter of claim 1 as granted reads:
"(i) Cetrorelix, or a pharmaceutically acceptable salt thereof, in an amount of 0.25mg/ml".

Claim 2 as originally filed reads:
"the amount of Cetrorelix or a pharmaceutically acceptable salt thereof is 0.25 mg/ml".

2.2 Feature (i) as present in granted claim 1 or in claim 2 as originally filed indicates that cetrorelix and its salts are present **at the same concentration, namely 0.25 mg/ ml.**

The wording of claim 1 of the main request presents a different meaning and an ambiguity with regard to the amount of the salt of cetrorelix which can be present in the dosage form. Feature (i) has indeed been interpreted in several manners:

(a) As mentioned by the opposition division in its decision, the proprietor explicitly explained during the oral proceedings before the opposition division that **feature (i) of claim 1 of the main request defines both the free base and any salt in terms of absolute amounts, and this amount is 0.25 mg/ml** (see point 1.6.2 of the decision of the opposition division).

(b) During the appeal proceedings, the respondent contested both the decision of the opposition division and its own interpretation, and argued that the quantity of cetrorelix is given **by reference to cetrorelix base**, ignoring the anion component of a cetrorelix salt. According to the respondent, this understanding is set out in detail in the explanation clearly given on page 8, final paragraph of the application as filed and abundantly clear from the art, where the active ingredient is referenced by the concentration of the active ingredient, namely cetrorelix base, even when the active ingredient is present as a salt (see, for example, D14a).

(c) The appellant interpreted furthermore feature (i) such that **the amount of salt is not specified at all**, and that the amount of salt is totally open.

2.3 In the Board's view, all three interpretations (a)-(c) are plausible and none of them can be ruled out as

technically absurd. Thus, claim 1 contains an ambiguity as to the amount of the salt of cetrorelix in the dosage form: this could be 0.25 mg/ml, or 0.25 mg/ml based on the free base, or even any amount. It follows that the subject-matter of claim 1 lacks clarity.

Accordingly, the main request does not meet the requirements of Article 84 EPC.

2.4 Moreover, the meaning of feature (i) as granted is that cetrorelix or a salt therefore are present **at the same claimed concentration of 0.25 mg/ml.**

Interpretations (b) and (c) lead to potential amounts of the salt different from 0.25 mg/ml, which goes beyond the scope of the subject-matter as granted.

Consequently, the main request does not meet the requirements of Article 123(3) EPC.

3. Admissibility of auxiliary request 8

3.1 Auxiliary request 8 was filed with the letter dated 7 March 2025, i.e. after the respondent's reply to the statement of grounds. During oral proceedings, this request was promoted to first auxiliary request.

Feature (i) of claim 1 of this request has been amended as follows:
"(i) Cetrorelix, or a pharmaceutically acceptable salt thereof, in an amount of 0.25mg/ml".

This wording corresponds to the wording of feature (i) in claim 1 as granted.

3.2 The provisions of Article 13(1) RPBA are the ones applicable to the assessment of the admittance of auxiliary request 8 into the appeal proceedings. According to Article 13(1) RPBA, any amendment to a party's appeal case after it has filed its grounds of appeal or reply is subject to the party's justification for its amendment and may be admitted only at the discretion of the Board. Article 12, paragraphs 4 to 6, RPBA shall apply *mutatis mutandis*. The Board shall exercise its discretion in view of, i*nter alia*, the complexity of the amendment, the suitability of the amendment to overcome prima facie the issues raised by the other party or by the Board, and the need for procedural economy.

In the Board's view, this request constitutes a clear attempt to overcome the objections raised under Articles 123(2), 123(3) and 84 EPC, and does not present any complexity. It appears also *prima facie* relevant to overcome the objections raised under Articles 123(2), 123(3) and 84 EPC.

Accordingly, auxiliary request 8 is admitted into the appeal proceedings.

3.3 The Board could not follow the appellant's arguments regarding the prohibition of *reformatio in peius* and that the subject-matter of this request does not present a convergence with the previous request.

Since the opponent is the sole appellant in the present case, the patentee is primarily restricted in the appeal proceedings to defending the patent as maintained (see G 9/92 and G 4/93; Case Law of the Boards of Appeal, 11th edition 2025, V.A.3.1 and V.A. 3.1.5). The wording of feature (i) of claim 1 expresses

now clearly that cetrorelix or its salt are present in the precise amount of 0.25 mg/ml. This wording corresponds to the wording of claim 1 as granted and constitutes in particular **a restriction over the formulation of the main request maintained by the opposition**. Accordingly, the principle prohibiting *reformatio in peius* is respected.

As regards the issue of lack of convergence, the Board considers that, in cases involving multiple objections under Article 123(2) EPC, the patent proprietor may legitimately submit several auxiliary requests each addressing a specific objection of added subject-matter. In such situations, strict convergence of the subject-matter across the auxiliary requests may not always be achievable. In the present case, this argument is furthermore irrelevant since auxiliary request 8 is the first request on file to be discussed after the main request.

4. Auxiliary request 8 - Article 123(2) EPC

4.1 Features (i) and (ii) of claim 1 were objected to by the appellant. Said features read:

"(i) Cetrorelix, or a pharmaceutically acceptable salt thereof, in an amount of 0.25mg/ml,
(ii) lactic acid in a concentration sufficient to adjust the pH in the range of 4.00 to 5.00".

The subject-matter of claim 12 was also objected to by the appellant. Said claim reads:

"12. A parenteral dosage form according to claim 1, for use in inhibiting premature luteinizing hormone surges in women undergoing controlled ovarian stimulation".

4.2 According to the "gold standard", any amendment can only be made within the limits of what a skilled person would derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing, from the whole of the documents as filed, here the patent application (G 2/10, OJ 2012, 376).

4.3 Feature of section (i)

Dependent claim 2 of the original application reads: "a parenteral dosage form according to claim 1, wherein the amount of Cetrorelix or a pharmaceutically acceptable salt thereof is 0.25 mg/ml".

Contrary to the appellant's position, the Board considers that the presence of two commas in the wording of claim 1 of auxiliary request 8 does not alter the meaning of this feature compared to original claim 2. Accordingly, feature (i) finds a direct basis in dependent claim 2 of the application as filed.

4.4 Feature (ii)

A basis for the feature "lactic acid in a concentration sufficient to adjust the pH in the range of 4.00 to 5.00" can be found in the first paragraph of page 9 of the application as filed. This passage discloses that "the ready-to-inject sterile, stable aqueous solution of Cetrorelix according to the present invention comprises an organic acid as a pH adjusting agent at a concentration sufficient to adjust the pH in the range of 3 to 5, more preferably in the range of 4 to 4.5.".

The pH range is derivable from the combination of the upper limit of the pH range of "3 to **5**" with the lower limit of the range "**4** to 4.5".

With regard to the different degree of accuracy between the now claimed pH range of "4.00 to 5.00" in comparison to the original pH ranges of "3 to 5" and "4 to 4.5" disclosed in the first paragraph of page 9, the Board agrees with the appellant that values characterized by different degrees of accuracy may not have the same meaning (cf cited decision T 2203/14).

The Board considers however that in the present case the pH range of "4.00 to 5.00", expressed with two digits after the decimal point, is derivable directly and unambiguously from the ranges disclosed in the first paragraph of page 9 together with the further specific values discloses in the same paragraph.

The next sentence of this paragraph discloses indeed that "the pH of the ready-to-inject sterile, stable aqueous solution according to the present invention may be for example, 3, 3.05, 3.10, 3.15, 3.20, 3.25, 3.30, 3.35, 3.40, 3.45, 3.5, 3.55, 3.60, 3.65, 3.70, 3.75, 3.80, 3.85, 3.90, 3.95, 4.00, 4.05, 4.10, 4.15, 4.20, 4.25, 4.30, 4.35, 4.40, 4.45, 4.50, 4.55, 4.60, 4.65, 4.70, 4.75, 4.80, 4.85, 4.90, 4.95, 5.00, 5.05, 5.10, 5.15, 5.20, 5.25, 5.30, 5.35, 5.40, 5.45, 5.50, 5.55 and 6 or intermediate ranges thereof".

Even if this enumeration of individual values cannot form the basis of the claimed range of "4.00 to 5.00" (cf cited decision T 1320/13), the skilled person would make a link between the preferred ranges and the individualized values, and consider that the range

limits can be expressed with two digits after the decimal point.

In the Board's view, the skilled person reading the description, in particular page 9, will realise that the application discloses pH values using varying number of decimal places: in some instances no decimal digit is provided, in other one or two decimal digits are used. Different number of digits are also used within the definition of a range (e.g 4 to 4.5) or in a sequence of individual values of pH 3, 3.05, 3.10...6. Entire values are sometimes written as "N" sometimes as "N,00" (e.g. 4 (line 7) or 4,00 (line 9)). In view of the above, the Board considers that the range 4.00 to 5.00 defined in claim 1 does not add any information vis-á-vis the original disclosure.

The claimed range of "4.00 to 5.00" is therefore derivable directly and unambiguously from the disclosure of page 9, fist paragraph.

The same paragraph discloses furthermore lactic acid as the preferred organic acid used as pH adjusting agent.

Consequently, feature (ii) is derivable in its entirety directly and unambiguously from the disclosure of page 9, fist paragraph.

4.5 The subject-matter of claim 12

4.5.1 Claim 12 of auxiliary request 8 reads:

"12. A parenteral dosage form according to claim 1, for use in inhibiting premature luteinizing hormone surges in women undergoing controlled ovarian stimulation".

The subject-matter of this claim is based on independent claim 13 as filed which reads:

"13. Use of a parenteral dosage form comprising: a ready-to-inject sterile, stable aqueous solution comprising:
(i) Cetrorelix or a pharmaceutically acceptable salt thereof,
(ii) an organic acid to adjust the pH in the range of 3 to 5,
(iii) Impurity A, a decapeptide of formula I in an amount less than 1% w/v of Cetrorelix base,
(iv) an osmotic agent, and
(v) water for injection, for inhibiting premature luteinizing hormone surges in women undergoing controlled ovarian stimulation."

4.5.2 In view of the reference to claim 1, the dosage form of claim 12 is characterized by a pH of 4.00 to 5.00 and by a concentration of 0.25 mg/ml of active ingredient. In contrast, original claim 13 indicates a pH of 3 to 5 and does not indicate the concentration of the active ingredient.

However, the skilled person would understand from the entire original application (see for instance the first paragraph of page 1) that the specific medical use defined in claim 12 is not linked to the pH of the composition or to the concentration of cetrorelix.

Accordingly, claim 12 of auxiliary request 8 is derivable directly and unambiguously from the application as filed.

4.6 Consequently, auxiliary request 8 meets the requirements of Article 123(2) EPC.

5. Auxiliary request 8 - Article 84 EPC

5.1 The subject-matter of claim 1, is considered to comply with the requirements of clarity.

5.2 Feature (i) is identical to feature (i) of claim 1 as granted and therefore it cannot be challenged for lack of clarity.

5.3 The wording of feature (ii) which reads "(ii) lactic acid in a concentration sufficient to adjust the pH in the range of 4.00 to 5.00", appears also self-explanatory and clear.

The Board could in particular not follow the appellant's arguments that:
- claim 1 does not define which pH is to be adjusted, i.e. the pH of the aqueous solution or the pH of the parenteral dosage form;
- it is unclear whether lactic acid is present in the composition, in the absence of any claimed amount of lactic acid in claim 1, and since compositions having the claimed pH may be obtained in the absence of lactic acid.

Feature (ii) defines the properties of the aqueous solution and it expresses clearly that the pH value of 4.00 to 5.00 relates to this solution. This interpretation is in line with page 9, line 7 of the original description which refers to the "pH of the ready-to-inject sterile, stable aqueous solution...". The language "the parenteral dosage form comprising... the aqueous solution", does not imply the presence of a second solution, comprising the aqueous solution, and having a different pH. Such an interpretation is not

supported by the description and does not appear realistic from a technical point of view.

Feature (ii) also expresses clearly that lactic acid must be present in the composition. The fact that it would be possible to reach the claimed pH value in the absence of lactic acid is irrelevant in this regard. The examples of the patent comprise lactic acid to adjust the pH and prove in a credible way the effectiveness of lactic acid as pH-adjusting agent.

6. Auxiliary request 8 - Inventive step

6.1 The claimed invention relates to a stable parenteral dosage form of cetrorelix. The dosage form is physically stable in terms of control on aggregation or turbidity development but also chemically stable such that impurities remain low while the parenteral dosage form is stored on the shelf and until it is injected into the patient.

6.2 The opposition division considered that D1-D3 were equally suitable starting points for the evaluation of inventive step and based its decision essentially with D1 as the closest prior art.

The appellant agrees with the choice of D1 and submitted in its statement of grounds of appeal that the arguments presented with regard to D1 as closest prior art also apply when starting from D2 and D3.

6.3 D1 relates to a stable ready-to-use aqueous pharmaceutical preparation of cetrorelix for parenteral administration, comprising cetrorelix or its pharmaceutically acceptable salt in an amount of 0.025% w/v or more, i.e. 0.25 mg/ml or more, glacial acetic

acid, a tonicity adjusting agent and optionally other pharmaceutically acceptable excipients, dissolved in water (see for instance claim 1). The pH may be 2.5-5 (see par. [0022], [0025], [0026] [0032] or claim 5) but is preferably in the range of **2.8 to 3.5** (see par. [0036]).

Example 1 discloses a sterile solution containing 0.25 mg cetrorelix acetate, mannitol (i.e., an osmotic agent), **acetic acid** and water for injection (see paragraphs [0052]-[0055]). The pH of the filtered solution was **3.05** and the osmolarity was 317 mOsm/kg (see the Table in paragraph [0057]).

The stability of the solution was assessed at 2-8°C and 25°C/60% RH for up to 6 months, no aggregation was observed and the solution remained colourless (paragraphs [0056] and [0057]). The Table in paragraph [0057] shows furthermore a level of single max. impurity and total impurity after 6 months at 60% RH of respectively 1.00% and 1.59%, which amounts correspond to the stability requirements according to the contested patent in paragraph [0018]. The Board notes in particular that it can be deduced from the data of paragraph [0057] that the level of impurity A is as low as in the claimed dosage form, i.e. less than 1.0%.

D1 does not disclose the presence of lactic acid and a pH range of the aqueous solution between 4.00 to 5.00. The appellant pointed out that according to claim 5 of D1 the pH of the composition is comprised between 2.5 and 5. In its view the pH range of 4 to 5 would not be novel over the pH of D1 in view of the disclosure in D1 of the pH value of 5. However, as discussed above, the composition of example 1 of D1 has a pH of 3.05. As to claim 5 of D1, the Board notes that this claim refers

back to claim 1 which may contain higher amounts of cetrorelix than those claimed in claim 1 of auxiliary request 8 and does not define the amount of impurities.

Thus, the range of pH of 4.00 to 5.00 represents a distinguishing feature over D1.

According to an additional line of argument, the appellant contended that the dosage form of claim 1 was not limited by the pH range of 4.00 to 5.00, since this range referred only to the aqueous solution contained within the dosage form. However, for the reasons set out in point 5.3 above, the Board considers that the wording of claim 1 does not imply the existence of a second solution that contains the aqueous solution and has a different pH. This argument is therefore not persuasive.

6.4 The opposition division defined the problem as the provision of a further stable cetrorelix parenteral dosage form.

The appellant defined the problem as the provision of an alternative parenteral composition of cetrorelix.

The respondent defines the problem as the provision of a cetrorelix composition with improved stability.

6.5 The respondent relies *inter alia* on the examples and Table 4 of the patent in support of a technical effect over the compositions of D1.

All this evidence relates to the effect of the pH on the composition comprising cetrorelix. There is no evidence on file that the presence of lactic acid

provides an advantage over the pH adjusting agent acetic acid used in D1.

6.5.1 Examples 1-9 of the patent relate to compositions comprising *inter alia* cetrorelix acetate and lactic acid with a pH between 3 and 5; the compositions of examples 7, 8 and 9 have a pH of respectively 4, 4.5 and 5.

Table 4 of the patent summarizes the different amounts of impurities formed upon storage at 25°C/60%RH for the compositions tested, after respectively 1, 3 and 6 months.

Table 4

	Observation at different time points upon storage at (25°C/60%RH)															
pH	Impurity A (%)				Impurity B (%)				Single maximum unknown impurity (%)				Total impurity (%)			
	Time points (months)															
	0	1	3	6	0	1	3	6	0	1	3	6	0	1	3	6
3	BQL	0.20	0.54	1.0	0.055	ND	ND	BQL	0.113	0.123	0.112	0.431	0.363	0.398	0.748	1.829
3.5	BQL	0.07	0.23	0.40	0.068	ND	BQL	BQL	0.105	0.148	0.189	0.392	0.335	0.292	0.623	1.059
4	BQL	BQL	0.09	0.15	0.039	ND	ND	ND	0.095	0.162	0.196	0.388	0.308	0.302	0.496	0.792
4.5	ND	BQL	BQL	0.04	0.058	ND	ND	ND	BQL	0.159	0.204	0.331	0.308	0.237	0.331	0.563
5	BQL	BQL	-	-	ND	BQL	-	-	0.119	0.125			0.205	0.208	-	-
ND: Not Detected; RH - Relative Humidity; BQL: Below Quantifiable limit																

Table 4 shows that the compositions of examples 7-8 of the patent, i.e. compositions with respectively a pH value of 4 and 4.5 in Table 4, show a content of impurity A after storage for six months at 25°C/60%RH of **0.15%** and **0.04%**, whereas the composition at pH 3.5 presents a level of impurity A of **0.4%**.

A comparison of the amounts of total impurities after 6 months gives a result of **0.792%** and **0.563%** at pH 4 and 4.5, instead of **1.059%** at pH 3.5.

These results provide a first evidence of the existence of a technical effect on stability linked with the pH of the composition.

Table 5 of the contested patent provides further results in support of the presence of an improved effect linked with the pH range of 4.0-5.0, with regard to impurity A(%) and the total impurity (%).

6.5.2 D1 provides aggregation-stability data in paragraph [0057], indicating the impurities formed after six months of storage at 25 °C/60% RH.

			1 M	2 M	3 M	6 M	
	Initial		25° C./	25° C./	25° C./	25° C./	
Parameters	Unfiltered	Filtered	60% RH	60% RH	60% RH	60% RH	2-8° C.
Description	CCS	CCS	CCS	CCS	CCS	CCS	CCS
pH	3.09	3.05	3.01	3.03	3.05	3.06	3.07
Assay of Cetrorelix	98.9	98.7	98.0	98.0	97.2	95.7	96.6
			Related substances				
Single max. impurity	0.235	0.23	0.24	0.25	0.52	1.00	0.16
Total impurity	0.286	0.284	0.50	0.55	0.93	1.59	0.27
Osmolality	317 mOsm/kg						

CCS—Clear colorless solution
NA—Not Analyzed

The stability data of D1 show that the initial maximum impurity amount was 0.23% and even after a storage time of 6 months at 25°C and 60% RH the maximum single impurity amount was **1.00%** and the total impurity amount was **1.59%**. The data confirm indirectly that the composition of D1 at pH of around 3 complies with the stability requirements of the patent (see par. [0018] of the contested patent).

The data provided in the Table of paragraph [0057] of D1 are obtained under the same conditions of storage of the data of the examples of the contested patent and

allow therefore an indirect comparison. This comparison confirms an effect on stability linked with the pH of the compositions of claim 1.

Indeed, the result shown for the composition of example 7 comprising lactic acid at a pH of 4.0 amounts to **0.388%** for the maximum single impurity, whereas the compositions of D1 show an amount of **1.00%** for the maximum single impurity. Thus, example 7 and Table 4 of the patent show for the claimed compositions a significant reduction in a single impurity level relative to the level of impurity noted in D1.

D1 gives also a figure for the Total Impurity of **1.59%** after 6 months at 25°C and 60% RH, which also contrasts markedly to the figure obtained for Total Impurity in Example 7 and Table 4 of the patent, namely **0.792%**.

Consequently, Table 4 shows an improvement in stability over D1 with regard to the presence of impurity A and of the total impurities after 6 months at 15°C/60 %RH when the pH is 4.0 or higher.

6.5.3 Accordingly, the problem over D1 is as defined by the respondent, namely the provision of a cetrorelix composition with improved stability.

6.5.4 The Board cannot follow the appellant's arguments with regard to the analysis of the data on file and the consequent definition of the problem.

The appellant considers indeed that there is no effect shown between pH 3.5, i.e. the upper endpoint of the preferred range of D1 and the claimed range of pH 4.00 to 5.00. In this regards it observes that according to Table 4 on page 13 of the opposed patent, a formulation

at pH 3.5 has a content of 0.40% Impurity A after storage for six months at 25°C/60% RH and thus complies with the stability requirement of the patent, and even with the most stringent stability requirement of claim 9, i.e., stability for at least 6 months at a temperature of 25°C and 60%. Thus, even according to the opposed patent itself, there is no technical effect between pH 3.5 and pH 4.00

The appellant considers furthermore that example 7 is directed to a composition having a pH of 4, which is not at the same accuracy level as in present claim 1, namely 4.00. It is therefore unclear whether example 7 falls in the claimed scope or is a comparative example.

In the Board's view, Table 4 demonstrates a significant improvement in stability with regard to the presence of impurity A and of the total impurities after 6 months at 15°C/60%RH when the pH is 4 or higher. The fact that a composition at pH 3.5, corresponding to the composition disclosed in D1, fulfils the stability criteria after storage for 6 months is irrelevant for a comparison between the compositions of D1 and of the claimed invention. **The definition of the problem over the prior art depends on the effect achieved by the claimed invention over the prior art.**

Moreover, the accuracy level of the pH values shown in Table 4 appears secondary and irrelevant in the present case. Table 4 indicates a clear tendency toward a decrease in impurities for pH values comprised between 4 and 5.

6.6 With regard to obviousness, documents D1, D4, D5 and D6-D10 were cited by the appellant.

6.6.1 Among these documents, only D1, D4 and D5 relate to compositions comprising cetrorelix, but none of these documents suggests to adjust the pH to the claimed value for improving the stability.

D1 discloses that the pH of the cetrorelix composition might be comprised between 2.5 and 5, which overlaps with the claimed range. The preferred pH range is 2.8 to 3.5 (see par. [0036]). There is nothing in D1 which would suggest that the shown improvement in stability noted in the patent in suit, as referenced by the lack of impurities, could be achieved at a pH of 4.00 to 5.00.

D4 mentions that the stability of various cetrorelix salts can be improved by addition of an acid, such as *inter alia* gluconic acid or lactic acid (see D4, col. 2, lines 57-60). Table 1 shows that a concentration of 2.5 mg/ml cetrorelix with no gluconic acid and a pH of 3.7 or higher at best lasts only 2 days before showing aggregation. The same formulation with a pH of 3.1 had an improved stability of 12 days prior to aggregation. Table 2 shows that a 2.5mg/ml concentration of cetrorelix at pH 3.0 can last more than 30 days without aggregation. The results of Tables 1 and 2 clearly demonstrate that stability of cetrorelix acetate is improved by dropping the pH, with a pH of 3.7 or lower being required to improve shelf-life, with increased stability with decreased pH. Consequently, D4 teaches away the claimed solution.

D5 is the corresponding PCT publication of D4.

6.6.2 The other cited documents do not relate to cetrorelix, and their teaching cannot be extrapolated to the

claimed composition. They are irrelevant for this reason.

D6 discloses aqueous parenteral solutions of octreotide acetate having a pH of 3.9-4.5; example 1 shows a composition with lactic acid and at pH of 4.2. Such composition shows an improved chemical stability of the active agent (cf. par. [0059]). D6 is however not concerned with a formulation relating to cetrorelix. Octreotide is a cyclic peptide and the skilled person would have no reason to combine the teachings of D6 and D1.

The same conclusion applies to D7-D10:
- D7 discloses a parenteral composition of octreotide acetate with lactic acid at pH 4.2 with a good chemical stability (see examples 1 and 2);
- D8 relates to compositions comprising lanreotide as active ingredient at pH from 4.0 to 7.5;
- D9 relates to an aqueous parenteral solution of leuprolide acetate having a pH of 4.5-6.5 (paragraph [0019]). According to examples 3 and 4, a composition having a pH of 4.86 has high chemical and physical stability (Tables 3 and 5);
- D10 relates to stable aqueous compositions of desmopressin.

Accordingly, the claimed solution is not obvious in view of the cited prior art for this reason.

6.7 D2 or D3 as closest prior art

D2 discloses in example 1 a composition comprising cetrorelix, tween 80, delta lactone of gluconic acid, mannitol and water at a pH of 3.12.

D2 discloses that the former aqueous solution has a good shelf life (column 2, lines 19-21, 23-29). The disclosure of D3 is very similar to the disclosure of D2 and the composition of example 1 is the same as in D2.

The distinguishing features between the claimed subject-matter and the disclosure of D2/D3 is the same as for D1. Accordingly, the conclusions presented in relation to the assessment starting from D1 apply *mutatis mutandis* also when starting from these documents.

6.8 Consequently, auxiliary request 8 meets the requirements of Article 56 PC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent on the basis of auxiliary request 8 filed on 7 March 2025 and the description to be adapted thereto if necessary.

The Registrar: The Chairman:

A. Vottner A. Usuelli

Decision electronically authenticated