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Datasheet for the decision of 17 May 2018

Case Number: T 2132/15 - 3.3.07

Application Number: 04766052.7

Publication Number: 1638595

IPC: A61K38/24, A61K47/26, A61K9/19

Language of the proceedings: EN

Title of invention:
FREEZE-DRIED FSH / LH FORMULATIONS

Patent Proprietor:
ARES TRADING S.A.

Opponent:
Ferring B.V.

Headword:
FREEZE-DRIED FSH / LH FORMULATIONS/ARES TRADING S.A.

Relevant legal provisions:
EPC Art. 111(1), 56
RPBA Art. 13(1), 12(4)

Keyword:
Remittal to the opposition division (no)
Main request - Inventive step (no)
Admission into the proceedings - Auxiliary requests 1-3 (yes)
Auxiliary requests 1-3 - Inventive step (no)
Admission into the proceedings - Auxiliary request 4 (no)

Decisions cited:

Catchword:

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Beschwerdekammern

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Case Number: T 2132/15 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 17 May 2018

Appellant: (Opponent)	Ferring B.V. Polaris Ave 144 2132JX Hoofddorp (NL)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Respondent: (Patent Proprietor)	ARES TRADING S.A. Zone Industrielle de l'Ouriettaz 1170 Aubonne (CH)
Representative:	Weickmann & Weickmann PartmbB Postfach 860 820 81635 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 29 October 2015 rejecting the opposition filed against European patent No. 1638595 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairwoman	Y. Podbielski
Members:	D. Boulois
	S. Albrecht

Summary of Facts and Submissions

I. European patent No. 1 638 595 was granted on the basis of a set of 21 claims.

Independent claim 1 as granted read as follows:
"1. A freeze-dried formulation consisting of follicle-stimulating hormone (FSH) or a variant thereof as well as luteinising hormone (LH) or a variant thereof, a surfactant selected from a polysorbat including Tween 20 (polyoxyethylene (20) sorbitan monolaurate), Tween 40 (polyoxyethylene (20) sorbitan monopalmitate), Tween 80 (polyoxyethylene (20) sorbitan monooleate), an antioxidant which is methionine, a phosphate buffer and a stabilizer and tonicity agent selected from the group consisting of monosaccharides, disaccharides and sugar alcohols."

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 by the opponent (hereinafter the appellant) lies from the decision of the opposition division to reject the opposition. The decision was based on the claims as granted.

IV. The documents cited during the opposition proceedings included the following:
D1: US 5 384 132
D2: EP 0 853 945 A1
D3: EP 1 176 976 B1
D11a: SPC Gonal F

D12: SPC Luveris
D17: Repronex package insert (2002)
D19: Humegon from epgonline.org (2001)
D22: Burgues et al (2001)

V. According to the decision under appeal, the requirements of Article 123(2) EPC were met. The opposition division also considered that the claimed invention was sufficiently disclosed, since the claimed products could be made without undue burden.

D22 was not seen as prima facie novelty-destroying and was not admitted into the opposition proceedings. Novelty, which had not been substantiated in the notice of opposition, was not further considered as a ground of opposition.

As regards inventive step, the opposition division considered D2 as the closest prior art, since it related to a freeze-dried composition of FSH and LH, further comprising Tween 20/80, methionine and sucrose. Claim 1 differed by the presence of a phosphate buffer and was limited by the term "consisting of". The problem was seen as the provision of a further freeze-dried formulation of FSH and LH. The solution was a formulation including a phosphate buffer but excluding the presence of a polycarboxylic acid. There was no teaching in D2 for removing the polycarboxylic acid, which was the stabilising compound of the composition. Claim 1 was thus inventive over D2.

The same conclusions also applied when D1, D3, D11a or D12 were considered as closest prior art. D11a and D12 disclosed freeze-dried compositions comprising either only FSH in the case of D11a or only LH in the case of D12, but comprising all other claimed components. Said

compositions of D11a and D12 were combined before administration, and both documents emphasized the need to tailor the patient's treatment to the individual response, wherein the dose of FSH would have been adapted. A lyophilised composition comprising both FSH and LH would never have arisen from these documents; claim 1 was inventive over D11a and D12.

VI. With the statement setting out the grounds of appeal the appellant requested that the decision under appeal be set aside and the patent be revoked. It also submitted inter alia following new documents:
D23: Fass 2003, published April 29, 2003, pages 1-3, 723-725, 932, 933
D23a: English translation of D23.

VII. With a letter dated 1 July 2016, the proprietor (hereinafter the respondent) requested that the appeal be dismissed and, as an auxiliary measure, filed auxiliary requests 1 to 3.

The subject-matter of the independent claim 1 of auxiliary requests 1-3 read as follows, difference(s) compared with claim 1 of the main request shown in bold:

Auxiliary request 1

"1. A freeze-dried formulation consisting of follicle-stimulating hormone (FSH) or a variant thereof as well as luteinising hormone (LH) or a variant thereof, a surfactant selected from a polysorbat including Tween 20 (polyoxyethylene (20) sorbitan monolaurate), Tween 40 (polyoxyethylene (20) sorbitan monopalmitate), Tween 80 (polyoxyethylene (20) sorbitan monooleate), an antioxidant which is methionine, a phosphate buffer and

~~**a stabilizer and tonicity agent selected from the group consisting of monosaccharides, disaccharides and sugar alcohols**~~ **sucrose**."

Auxiliary request 2

"1. A freeze-dried formulation consisting of **human** follicle-stimulating hormone (FSH) ~~**or a variant thereof**~~ as well as **human** luteinising hormone (LH) ~~**or a variant thereof**~~, a surfactant selected from a polysorbat including Tween 20 (polyoxyethylene (20) sorbitan monolaurate), Tween 40 (polyoxyethylene (20) sorbitan monopalmitate), Tween 80 (polyoxyethylene (20) sorbitan monooleate), an antioxidant which is methionine, a phosphate buffer and a stabilizer and tonicity agent selected from the group consisting of monosaccharides, disaccharides and sugar alcohols."

Auxiliary request 3

"1. A freeze-dried formulation consisting of **human** follicle-stimulating hormone (FSH) ~~**or a variant thereof**~~ as well as **human** luteinising hormone (LH) ~~**or a variant thereof**~~, a surfactant selected from a polysorbat including Tween 20 (polyoxyethylene (20) sorbitan monolaurate), Tween 40 (polyoxyethylene (20) sorbitan monopalmitate), Tween 80 (polyoxyethylene (20) sorbitan monooleate), an antioxidant which is methionine, a phosphate buffer and ~~**a stabilizer and tonicity agent selected from the group consisting of monosaccharides, disaccharides and sugar alcohols**~~ **sucrose**."

VIII. A communication from the Board, dated 3 April 2018, was sent to the parties. In this it was considered in particular that the invention claimed in all requests

was not inventive when D11a or D12 were taken as closest prior art.

IX. With a letter dated 16 April 2018, the respondent submitted a new auxiliary request 4. It also requested that the case be remitted to the department of first instance in case the Board considered documents D11a and D12 as closest prior art.

The subject-matter of the independent claim 1 of auxiliary request 4 read as follows, difference(s) compared with claim 1 of the main request shown in bold:

"1. A freeze-dried formulation consisting of **recombinant human** follicle-stimulating hormone (FSH) as well as **recombinant human** luteinising hormone (LH), a surfactant selected from a polysorbat including Tween 20 (polyoxyethylene (20) sorbitan monolaurate), Tween 40 (polyoxyethylene (20) sorbitan monopalmitate), Tween 80 (polyoxyethylene (20) sorbitan monooleate), an antioxidant which is methionine, a phosphate buffer ~~**and a stabilizer and tonicity agent selected from the group consisting of monosaccharides, disaccharides and sugar alcohols**~~ **and sucrose wherein the ratio of FSH to LH is 2:1.**"

X. With a letter dated 14 May 2018, the appellant requested the Board not to admit auxiliary requests 1-4 into the proceedings and that, in the case auxiliary request 4 is admitted into the proceedings, the proceedings be adjourned and the respondent made to bear the full costs of this adjournment.

XI. With a letter dated 14 May 2018, the respondent filed a corrected version of auxiliary requests 1-4. The

corrections concerned the dependent claims of said requests.

XII. Oral proceedings took place on 17 May 2018.

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

Remittal to the opposition division

A remittal to the opposition division in the case D12 or D11a are taken as closest prior art for assessing inventive step could not be justified. Documents Dlla and D12 were already cited in the opposition proceedings as relevant prior art for the claims as granted.

The question of whether or not Dlla and D12 were actually published before the priority date of the opposed patent was raised only at the oral proceedings by the opposition division ex officio. Clearly, the opponent actually had no possibility to address this issue at any earlier time.

It was also not true that, during the first instance proceedings, documents Dlla and D12 had not been considered as relevant by the opposition division since they do not relate to the same purpose as the present invention. Indeed, in the summons to oral proceedings of the opposition division, during the oral proceedings before the opposition division, and in its decision, the opposition division discussed D11a and D12 as such, even if it considered them as more distant documents than D2 as regards the assessment of inventive step.

Main request - Inventive step

D12 should be seen as the closest prior art, since this document presented the smallest number of features differing from the claimed subject-matter, namely only the presence of further FSH. Claim 1 of the main request did not relate to any treatment protocol or stability level.

The problem was seen as the provision of an alternative formulation. The solution was proposed in D12 which suggested the association with a freeze-dried composition of FSH and found in document D11a which discloses the same composition but comprising FSH. Several documents, such as D17 or D19, disclosed a combination of LH and FSH which was already on the market as a commercial product. The claimed subject-matter was not inventive.

Both documents D12 and D11a were publicly available at the priority date of the contested patent, as demonstrated by the documents presented on the Internet site of the European Commission for the registration of medicaments (http://ec.europa.eu/health/documents/community-register/html/h155.htm), under Luveris® and Gonal®. It was inter alia confirmed by the Swedish "Fass 2003" book (D23 and D23a) which showed the same monographs and compositions of Luveris® and Gonal®.

Auxiliary requests 1-3 - Admission into the proceedings

Auxiliary requests 1-3 were late filed; they all addressed issues which could have been addressed during first instance proceedings as the respective issues were raised with the original notice of opposition.

All requests comprised further amendments which were not occasioned by the grounds of appeal. Thus, they contravened also Rule 80 EPC.

Auxiliary requests 1-3 Inventive step

All amendments to these requests were already known from D12, these requests could therefore not be inventive over D12.

Auxiliary request 4 - Admission into the proceedings

Auxiliary request 4 had been late filed and should not be admitted into the proceedings.

During first instance proceedings, the patent proprietor chose to not file any auxiliary requests at all but only defended the patent as granted.

Documents Dlla and D12 were cited already in the original opposition as relevant prior art for the claims as granted and could not constitute a surprise and a reason to file new requests; additionally, reference was made to the publication dates of these documents as well as to the availability of the respective compositions which were on the market before the priority date of the opposed patent. The important question was not the interpretation of Dlla and D12 and their relevance by the opposition division in first instance proceedings. The correct question was whether they were introduced as potentially relevant to the opposition. These documents were very explicitly cited as closest prior art documents by the opponent in the original opposition, and have been discussed as such throughout the first and second instance proceedings.

Moreover, auxiliary request 4 is not prima facie allowable, since the amendments made thereto violated Article 123(2) EPC and raised a new problem of sufficiency of disclosure. The claimed subject-matter could also not be inventive over D12, which disclosed a FSH:LH ratio of 2:1 in combination with the composition of D11a. Moreover, there was a lack of clarity in view of the dependent claim 10, which related to a composition excluding a FSH:LH ratio of 2:1.

Finally, it was impossible in such a short period of time to react in any substantive manner to the allegation that it was the claimed particular ratio which provided the claims with an inventive activity over the art.

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

Remittal to the opposition division

Remittal of the case to the department of first instance was requested in case the Board considers documents D11a and D12 as closest prior art for the assessment of inventive step, as argued in the Board's communication of 3 April 2018. With this communication, the proprietor was for the first time confronted with D11a or D12 as closest prior art for the assessment of inventive step. There existed doubt as regards the validity of the publication date of D11a and D12, necessitating a new discussion and a remittal should thus be ordered.

During the first instance proceedings, documents D11a and D12 had not been considered as relevant by the opposition division since they did not relate to the

same purpose as the present invention. Further, during the first instance proceedings the opponent had not provided any evidence of the public availability of documents D11a and D12. The opponent addressed this issue with the grounds of appeal for the first time. Thus, during the whole first instance proceedings, these documents had not been considered as relevant prior art by the opposition division. The proprietor should have the right to have the case decided by two instances based on D11a or D12 as closest prior art.

Main request - Inventive step

D12 was not seen as the closest prior art, which was rather D2. D12 concerned the medical use, dosing, administration and side-effects of a LH-containing pharmaceutical composition, but did not relate to the preparation of a pharmaceutical composition. It did in particular not address the problem of stability and related to a single composition that the skilled person would have never considered. On the other hand, D2, D3 and D22 were suitable starting points, since they related to compositions comprising both FSH and LH. Similarly, D1 could be chosen as a suitable starting point as it showed a lyophilized composition comprising both FSH and LH in example VIII.

The treatment protocol disclosed in D12 foresaw a flexible dose ratio by combining the LH composition with a second FSH composition, such as shown in D11a. There was a clear pointer in D12 not to consider to replace both formulations of D12 and D11a by a single formulation. The skilled person would not have considered a stable composition comprising both FSH and LH in a fixed dose ratio. The composition as claimed presented the advantage of a better handling and a

simpler and easier way to use. Performing a treatment protocol with a single formulation comprising a particular ratio of the hormones FSH and LH eased the (self)-administration of the patient compared to D12 which required mixing of the respective hormone amounts prior to each administration. Accordingly, the objective technical problem was the provision of a formulation for an improved treatment protocol comprising administration of FSH and LH.

The solution to this problem was not obvious in view of the prior art, since D12 taught away from it. A combination with the disclosure of D17 was also not possible, since the compositions disclosed therein contained also at least traces of other actives, such as HCG, and comprised other excipients.

Admission of auxiliary requests 1-3 into the proceedings

Said requests were a response to the statement of grounds of appeal and had to be admitted.

Auxiliary requests 1-3 -Inventive step

As regards the issue of how auxiliary requests 1-3 overcame the lack of inventive step objections which applied to the subject-matter of claim 1 of the patent, all newly introduced constituents were also known from D12.

Auxiliary request 4 - Admission into the proceedings

This request was a response to the Board's communication which selected for the first time D12 and D11 a closest prior art. This constituted a surprise,

since it deviated from the decision of the opposition division.

The claimed subject-matter was clearly inventive over D12, in view of the claimed FSH:LH ratio of 2:1, since neither D12, nor D17 envisaged such protocol of treatment.

XV. Requests

The appellant (opponent) requested that:
- the decision under appeal be set aside and the patent be revoked;
- auxiliary requests 1-4 not be admitted into the proceedings and that - in the case auxiliary request 4 is admitted into the proceedings - the proceedings be adjourned and the respondent made to bear the full costs for this adjournment.

The respondent (patent proprietor) requested that:
- the appeal be dismissed;
- alternatively, that the decision under appeal be set aside and the patent be maintained according to one of the sets of claims filed as auxiliary requests 1-4 with letter of 14 May 2018;
- the case be remitted to the first instance in case the Board considered documents D11a and D12 as closest prior art.

Reasons for the Decision

1. Remittal to the opposition division

1.1 The respondent requested a remittal to the opposition division in case the Board considers documents D11a and

D12 as closest prior art for the assessment of inventive step.

1.2 The Board cannot follow the respondent's request for the following reasons.

1.2.1 D11a and D12 were already cited during the opposition proceedings. The opponent's notice of opposition mentioned *inter alia* a combination of the teaching of D11a with the teaching of D12, with the opponent's final statement that "on the basis of this combination, the subject-matter of all claims is not inventive". Besides, in its response to the notice of opposition, the proprietor provided *inter alia* arguments as regards inventive step against said combination of D11a with D12.

As highlighted by the minutes of the oral proceedings before the opposition division, the relevance of both documents D12 and D11a was discussed in the context of inventive step during the oral proceedings. The point regarding the validity of the date of publication of both D11a and D12 was raised for the first time during said oral proceedings.

Finally, in its decision, the opposition division considered that document D2 was a more relevant closest prior art than D1, D3 and either D12 or D11a. It however also assessed specifically inventive step as regards these documents, in particular over D11a and D12 (cf. point 15.7 of the decision).

Hence, the history of the proceedings before the opposition division shows not only that D11a and D12 were known from the beginning of the opposition proceedings, but also that their relevance for

inventive step had been debated in writing and orally during the opposition proceedings, and that the decision under appeal included an assessment of whether the subject-matter of claim 1 of the patent as granted involved an inventive step starting from D11a or D12.

Consequently, their citation in the appeal proceedings does not constitute a surprise for the respondent.

In addition, the respondent had considerable time to consider and respond to the appellant's inventive step attack starting from D11a and D12 as repeated in the statement of grounds of appeal.

1.2.2 The fact that the opposition division considered D2 as the closest prior art instead of D11a or D12 in its decision, can also not constitute an argument or a reason to remit the case to the opposition division for reconsidering the relevance of these documents as regards inventive step. These documents have indeed already been discussed in the context of inventive step. Moreover, as regards the choice of the closest prior art, the Board is of the view that if there are several possible different prior art documents, each of which might plausibly be taken as a starting point for the assessment of inventive step, it is established case law that inventive step may be assessed relative to all these pieces of prior art before any decision confirming inventive step is taken. A shift to D11a or D12 as closest prior art in the appeal proceedings therefore cannot constitute a surprise or a ground for remitting the case to the opposition division.

1.2.3 As regards the validity of the publication date of documents D11a and D12, this point was raised for the first time during the oral proceedings before the

opposition division. The appellant responded to this point in its notice of appeal, by providing several different pieces of evidence for the public availability of documents D11a and D12 before the priority date of the contested patent. The respondent has not provided any substantive arguments in reply thereto. There is no need to remit the case to the opposition division for discussing this point either.

1.3 Accordingly, D12 and D11a were on file since the beginning of the opposition proceedings as regards inventive step, and, for this reason can be regarded as suitable starting points for the assessment of inventive step.

The Board decides not to remit the case to the opposition division for consideration of inventive step starting from D12 or D11a.

2. Main request - Inventive step

2.1 The invention relates to the field of freeze-dried formulations of follicle-stimulating hormone (FSH) and luteinising hormone (LH).

2.2 The opposition division considered D2 as closest prior art, which was also the choice of the respondent. The appellant chose D12 or D11A as preferred closest prior art, and mentions also D2, D3 and D22.

2.2.1 D2 relates to liquid compositions comprising a gonadotropin, with stabilising amounts of a polycarboxylic acid, such as sodium citrate, and a thioether, such as methionine. The examples show liquid compositions of FSH with sucrose, sodium citrate, polysorbate 20 and methionine. D2 envisages on page 5,

line 21 that the liquid formulations of its invention could be freeze-dried, without an explicit example thereof. D2 even appears to teach away from freeze-drying, which is seen as a costly and time-consuming process step (see D2, page 2, l. 51-page 3, l. 5). This document does thus neither disclose a composition comprising both FSH and LH, nor a freeze dried composition. It also emphasizes the necessity to use a polycarboxylic acid as stabilising agent for the liquid compositions.

2.2.2 D12 relates to the medicament Luveris®, which is a freeze dried composition of 75 IU of human recombinant LH, with polysorbate 20, a phosphate buffer, sucrose and methionine (see pages 2 and 6). Said excipient content of Luveris® is identical to the formulation of the claims and example of the contested patent. Said composition has a shelf life of 24 months, which shows its stability (see point 6.3).

The composition disclosed in D12 does in particular not comprise FSH, but D12 mentions that one vial of Luveris® (75 IU of LH) can be reconstituted with one or two ampoules of FSH, namely 37.5 IU, 75 IU or 150 IU of FSH in 1 ml of solvent (see point 6.6), and that the usual starting regimen commences at 75 IU of LH with 75-150 IU of FSH (see page 2).

2.2.3 D11a relates to the medicament Gonal®, which is a freeze-dried composition of human recombinant FSH with polysorbate 20, a phosphate buffer, sucrose and methionine having a shelf life of two years (see page 27, points 6.1 and 6.3). Said composition comprises the same excipients as claimed by claim 1 of the main request and the same stability requirements, but does not comprise any LH. D11a mentions that it can be

combined with a composition of FSH as a single injection (see point 6.6).

2.2.4 D3 discloses freeze dried compositions of LH, sucrose, phosphate buffer and tween 20 (see [0033]), which corresponds to the disclosure of D12, and freeze dried composition of FSH with methionine and phosphate buffer (see [0047]). It also suggests that FSH and LH may be formulated together (see [0025]).

2.2.5 Consequently, documents D12 or D11a have the most features in common with the composition of claim 1 of the main request.

The Board is not convinced by the respondent's argument that D12 or D11a should not be regarded as closest prior art, as the documents address a different problem. When considering a pharmaceutical composition, the skilled person would also consider documents in the medical field which contain the same or similar compositions as the one claimed. There is no reason to assume that the skilled person would be limited to prior art documents concerning solely the problem of stability. Moreover, D12 and D11a deal implicitly with the problem of stability, since they both mention a shelf-life of 24 months (see D12 and D11a, par. 6.3).

The public availability of D12 and D11a at the priority date of the present patent has been convincingly demonstrated by the appellant. The Internet registration site of the European Commission gives a publication date of 15 May 2002 for the monograph document D12 of Luveris®, and of 7 June 2002 for the monography document D11a of the medicament Gonal®. The public availability of said monographs was also confirmed by the content of the Fass Book 2003 (D23 and

D23a), the Swedish version of the "Rote Liste" giving all available information on medical products for public review, published in January 2003 and received on 29 April 2003 by the library "Det Farmaceutiske Fakultetsbibliotek, Kobenhavns Universitetsbibliotek" (The pharmaceutical Faculty Library, Copenhagen University Library).

Thus, the Board considers D11a or D12 as the closest state of the art. Given that D12 mentions explicitly the dosage ratio of FSH and LH to be administered, the Board will use it as the starting point for the assessment of inventive step.

2.3 According to the respondent, the problem is the provision of a formulation for an improved treatment protocol comprising the simultaneous administration of FSH and LH, especially in view of a better handling and an easier and simpler way to use the formulation. The respondent argued that performing a treatment protocol with a single formulation comprising a particular ratio of FSH and LH would ease the (self-)administration of the patient compared to D12 which requires mixing of the respective hormone amounts prior to each administration.

2.4 The solution is a freeze-dried formulation comprising both FSH and LH.

2.5 It has to be investigated whether the alleged effect is real, namely whether a formulation presenting a fixed ratio of FSH:LH provides indeed a simpler and easier handling and use than two formulations comprising either FSH or LH alone and mixed before use.

It is known that the usual protocol and posology of the combined treatment with FSH and LH demands a constant adaptation of the dose, in particular of FSH, according to the ovarian response to the treatment. This is explicitly disclosed in document D12 (see point 4.4), which states that a recommended regimen commences at 75 IU of LH with 75-150 IU of FSH, and dose adaptation should preferably be after 7-14 days by increments of 37.5-75 IU of FSH (see point 4.2). Such constant dose adaptation or treatment by cycles is also disclosed and confirmed by documents D11a (see page 22), and in D15 which is a monograph of the medicament corresponding to the claimed subject-matter published after the priority date of the contested patent (see page 2).

It is therefore immediately apparent that a formulation with a fixed LH:FSH ratio does not present a better handling and an easier and simpler way to use the formulation, since it necessitates an adaptation of the FSH dose with a further FSH formulation; a formulation as claimed would allow a simplified handling only in specific and restricted parts of the protocol and only if the specific chosen ratio corresponds to the treatment protocol. It is therefore not possible to see in the claimed formulation comprising a combination of FSH:LH an improvement over the existing formulations comprising LH alone or FSH alone and the problem must be reformulated as the provision of an alternative formulation, as was argued by the appellant.

2.6 Since the problem consists in the provision of an alternative formulation, it belongs to the normal activity of the skilled person to accomplish routine modifications, such as choosing a known alternative formulation comprising both FSH and LH and to adapt it to the compositions disclosed in D12.

It is known from D11a that a formulation of FSH in a composition comprising sucrose, methionine, polysorbate 20 and a phosphate buffer presents the necessary stability property for a product to be put on the market.

The combination of FSH and LH in a same lyophilized composition was known from example VIII of D1, disclosing a composition of 75 IU of rFSH, 75 IU rLH, sucrose, polysorbate 20 and sodium citrate.

Another lyophilised composition of 75 IU or 150 IU of FSH and LH with lactose and phosphate buffer was known from D17. The fact that this composition might contain impurities due to the urine extraction of FSH and LH, as argued by the respondent, has no incidence on the relevance of this document.

A further composition comprising FSH and LH in a lyophilized state is mentioned in D19 which discloses the commercial product Humegon®, comprising 75 IU of FSH and LH, mannitol and a phosphate buffer.

Consequently, the skilled person, starting from the disclosure of D12, would arrive at the subject-matter of claim 1 of the main request in an obvious manner in order to solve the problem posed.

2.6.1 It should be noted that, if the problem to be solved had been as defined by the respondent, namely the provision of a formulation for an improved treatment protocol comprising the simultaneous administration of FSH and LH, especially in view of a better handling and an easier and simpler way to use the formulation, the

conclusions as regards obviousness of the solution would have been the same.

A treatment protocol combining both LH and FSH is indeed explicitly disclosed in D12. In view of the problem posed, the skilled person would inevitably have combined this teaching with the already existing teaching of lyophilized compositions comprising both FSH and LH together, as disclosed in D1, D17 or D19, and thus solving said problem.

2.6.2 It follows that the main request does not involve an inventive step.

3. Admission of auxiliary requests 1-3 into the proceedings

These requests have been filed in response to the statement of grounds of appeal, thus at the earliest stage of the appeal proceedings.

The restriction of the subject-matter of claim 1 of each of these requests constitutes a direct response to the appellant's statement of grounds of appeal. The Board is not convinced that the respondent should have filed these requests already before the opposition division.

The Board thus sees no reason not to admit them into the proceedings (Article 12(4) RPBA and Rule 80 EPC).

4. Auxiliary request 1 - Inventive step

The subject-matter of claim 1 of this request has been restricted to "sucrose" as stability and tonicity agent. Since sucrose is also present in the

compositions disclosed in D12, the conclusion drawn above for the main request apply *mutatis mutandis* to this request.

Thus, the subject-matter of claim 1 of auxiliary request 1 is obvious vis-à-vis document D12 and auxiliary request 1 does not meet the requirements of Article 56 EPC.

5. Auxiliary request 2 - Inventive step

Claim 1 of auxiliary request 2 has been restricted to "human" FSH and "human" LH. Documents D12 and D11a also relate respectively to human LH and human FSH. The amended feature does thus not provide a further difference with regard to the teaching of these documents and therefore cannot affect the reasoning and conclusions on inventive step raised above for the main request.

Auxiliary request 2 does not meet the requirements of Article 56 EPC.

6. Auxiliary request 3 - Inventive step

Claim 1 of auxiliary request 3 has been restricted to "sucrose" as stability and tonicity agent and to "human" FSH and "human" LH, thus the corresponding respective amendments to claim 1 of auxiliary requests 1 and 2. As for these requests, and since D12 and D11a also disclose compositions comprising sucrose and human LH and FSH, the amendments do not provide a further difference with regard to the teaching of these documents and therefore cannot affect the reasoning and conclusions on inventive step raised above for the main request.

Auxiliary request 3 does not meet the requirements of Article 56 EPC.

7. Auxiliary request 4 - Admission into the proceedings

7.1 This request has been filed after the issue of the Board's communication. The subject-matter of claim 1 of auxiliary request 4 has been amended by the specification of "recombinant human follicle stimulating hormone (FSH)" and "recombinant human luteinising hormone (LH)", and by the feature "wherein the ratio of FSH to LH is 2:1".

7.2 According to the respondent, the submission of this request was a response to the Board's communication which raised for the first time an objection as regards inventive step based on D12 and D11a. This request was also clearly inventive over D12 in combination with D17.

7.3 Under Article 13(1) RPBA, "Any amendment to a party's case after it has filed its grounds of appeal or reply may be admitted and considered at the Board's discretion. The discretion shall be exercised in view of inter alia the complexity of the new subject matter submitted, the current state of the proceedings and the need for procedural economy". It is generally accepted practice that the subject-matter of late filed requests should be such that it can be easily understood and regarded as allowable. A new request may be considered admissible, if the claims it encompasses solve all previous issues raised by the Board or in the impugned decision and do not give rise to any new objection (cf. Case law of the Boards of appeal of the EPO, 8th.

edition, section IV.E.4.4.2, first paragraph). This is not the case.

7.4 In the present case, the Board finds it appropriate to exercise its discretion by not admitting auxiliary request 4 into the proceedings for the following reasons (Article 13(1) RPBA).

7.4.1 This request has been filed late in the proceedings after the Board's communication which did not raise any new point as regards inventive step which was already present on file before.

As explained above under point 1.2, the consideration of D12 as closest prior art cannot constitute a surprise for the respondent. The history of the proceedings before the opposition division shows that D12 was known from the beginning of the opposition proceedings, and was cited again in the statement of grounds of appeal as closest prior art by the appellant.

The same conclusion applies to the combination of D12 with documents such as D17 or D19 which was present in the statement of grounds of appeal of the appellant.

Accordingly, the argument as to a surprise or to a new line of objection does not hold.

7.4.2 The amendment brought to claim 1 of this request does also not seem likely to prima facie overcome the lack of inventive step observed for the main request and auxiliary requests 1-3.

D12 relates specifically to human recombinant LH, and mentions explicitly a treatment protocol with a

starting combination of FSH and LH at a ratio of 1:1 or 2:1 (see point 4.2). A restriction to the recombinant form of FSH and LH and to the specific ratio of 2:1 does therefore not have any effect on the discussion of inventive step and appears to prima facie not overcome the lack of inventive step observed for the subject-matter of the previous requests.

7.5 Accordingly, auxiliary request 4 is not admitted into the proceedings (Article 13(1) RPBA).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

S. Fabiani Y. Podbielski

Decision electronically authenticated