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# Datasheet for the decision of 9 August 2007

**Case Number:** T 1074/06 - 3.3.04

**Application Number:** 01900491.0

**Publication Number:** 1250148

**IPC:** A61K 38/24

**Language of the proceedings:** EN

**Title of invention:**
Use of FSH for treating infertility

**Patentee:**
Applied Research Systems ARS Holding N.V.

**Opponent:**
Akzo Nobel N.V.

**Headword:**
Infertility/ARS

**Relevant legal provisions:**
EPC Art. 52(4), 56, 83, 114(2), 123(2)(3)

**Keyword:**
"Main request - sufficiency of disclosure - (no)"
"First auxiliary request - added subject-matter - (no), admissibility, patentable subject-matter, inventive step, sufficiency of disclosure - (yes)"

**Decisions cited:**
T 0019/90, T 0633/97, T 1020/03

**Catchword:**
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Beschwerdekammern | Boards of Appeal | Chambres de recours

**Case Number:** T 1074/06 **-** 3.3.04

# D E C I S I O N
**of the Technical Board of Appeal 3.3.04**
**of 9 August 2007**

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**Decision under appeal:** **Interlocutory decision of the Opposition Division of the European Patent Office posted 12 May 2006 concerning maintenance of the European No. 1250148 in amended form.**

**Composition of the Board:**

**Chairman:** U. Kinkeldey
**Members:** M. Wieser
D. Rogers

## Summary of Facts and Submissions

I. The Patent Proprietor (Appellant I) and the Opponent (Appellant II) lodged appeals against the interlocutory decision of the Opposition Division, whereby the European patent No. 1 179 012 was maintained in amended form pursuant to Article 102(3) EPC.

II. The Opposition Division decided that the claims set out in Patent Proprietor's main request before them, claims 1 to 19 as granted, did not involve an inventive step (Article 56 EPC). In an obiter dictum the Opposition Division expressed their view that the claims of the main request also did not meet the requirements of Article 83 EPC.

In addition the Opposition Division decided that the claims of the first and second auxiliary request before them contained added subject-matter contrary to the requirements of Article 123(2) EPC and that claims 1 to 18 of the third auxiliary request did not involve an inventive step.

However, the Opposition Division decided that claims 1 to 19 of the fourth auxiliary request met all requirements of the EPC.

III. The Board expressed its preliminary opinion in a communication dated 5 February 2007.

Oral proceedings were held on 9 August 2007.

IV. Appellant I requested that the decision under appeal be set aside and the patent be maintained on the basis of

claims 1 - 17 of the main request filed on 5 April 2007; or claims 1 - 15 of the first auxiliary request filed at the oral proceedings on 9 August 2007.

Appellant II requested that the decision under appeal be set aside and the patent be revoked.

V. Claims 1 and 6 of Appellant I's main request read as follows:

"1. The use of FSH and/or a biologically active analogue thereof in the production of a medicament for the stimulation of multiple follicular development in the treatment of infertility in women, wherein the medicament is for administration at a dose in the range of from **300 to 600 IU** on every third day of the first six days of the stimulation phase. (Emphasis added by the Board)

6. The use of FSH and/or a biologically active analogue thereof in the production of a medicament for promoting monofollicular development and reducing multifollicular development in the treatment of infertility in women, wherein the medicament is for administration at an initial dose in the range of from **100 to 500 IU** and wherein the second dose is for administration between three and six days after the initial dose in the stimulation phase." (Emphasis added by the Board)

VI. Claims 1 and 6 of Appellant I's auxiliary request I read as follows:

"1. The use of FSH and/or a biologically active analogue thereof in the production of a medicament for

the stimulation of multiple follicular development in the treatment of infertility in women, wherein the medicament is for administration at a dose in the range of from **400 to 600 IU** on every third day of the first six days of the stimulation phase. (Emphasis added by the Board)

6. The use of FSH and/or a biologically active analogue thereof in the production of a medicament for promoting monofollicular development and reducing multifollicular development in the treatment of infertility in women, wherein the medicament is for administration at an initial dose in the range of from **100 to 350 IU**, and wherein the second dose is for administration between three and six days after the initial dose in the stimulation phase, **and wherein the second dose is in the range of from 50 to 200 IU**." (Emphasis added by the Board)

Dependent claims 2 to 5, 14 and 15 referred to preferred embodiments of the use of claim 1, claims 7 to 15 referred to preferred embodiments of the use of claim 6.

VII. The following documents are referred to in this decision:

(5) Proc. Natl. Acad. Sci. USA, vol.89, 1992, pages 4304 to 4308

(6) TFO Tijdschr. Fertiliteitsonderz., vol.63, 1995, pages 46 to 54

(7) Fertility and Sterility, vol.63, 1995, pages 1272 to 1277

(8) Endocrinology, vol.131, no.6, 1992, pages 2514 to 2520

(9) Abstracts of the 12th annual meeting of the EHSRE, Maastricht 1996, abstract P076, pages 130 to 131

(10) Human Reproduction, vol.2, no.7, 1987, pages 553 to 556

(16) Endocrinology, vol.53, 1953, pages 604 to 616

(19) Endocrine Reviews, vol.21, no.1, February 2000, pages 5 to 22

VIII. The submissions made by Appellant I, as far as they are relevant for the present decision, may be summarised as follows:

The therapeutic effect of the medicaments produced according to claims 1 and 6 of the main request, namely stimulation of multiple follicular development on one side and promotion of monofollicular development on the other side, was designated in said claims and allowed a skilled practitioner to carry out the invention. In detail he/she could chose the amount of FSH to be administered with the second dose according to the method of claim 6, although it was not explicitly defined in the claim. Therefore, the invention according to claims 1 and 6 of the main request was disclosed in a manner sufficiently clear and complete

for it to be carried out by a person skilled in the art (Article 83 EPC).

The claims of the first auxiliary request have been amended with regard to the main request by introducing features from dependent claims into the independent claims 1 and 6. This had been done in a straightforward way to respond to an objection under Article 83 EPC and did not cause any additional difficulties with regard to other provisions of the EPC. Thus, although filed at a late stage the request should be allowed into the proceedings.

The subject-matter of claims 1 to 15 of the first auxiliary request, which was based on the application as originally filed, could not be derived in an obvious way from the disclosure in the closest prior art document (10), either if taken alone or in combination with any other prior art document on file. The embodiment of the invention referring to the use of FSH analogues referred only to biologically active analogues whose activity could be indicated in International Units (IU) determined by a standard method well known in the art and described in document (16). Thus, a skilled person could put into practice the claimed invention over the whole breadth of the claims without exercising undue burden.

IX. The submissions made by Appellant II, as far as they are relevant for the present decision, may be summarised as follows:

Claims 1 and 6 of the main request referred to the preparation of a medicament for different therapeutic

purposes wherein the medicament was to be administered at a specific dosage regimen. The regimens according to claims 1 to 6 were overlapping. Contrary to the requirements of Article 83 EPC, the patent did not disclose the invention according to the embodiment wherein the regimen were overlapping in a manner sufficiently clear and complete for it to be carried out by a skilled person.

The application as originally filed did not contain a definite connection between the specific therapeutic purpose indicated in claims 1 and 6, stimulation of multiple follicular development, respectively promotion of monofollicular development, and the specific dosage regimen indicated in the claims.

Document (10), representing the closest state of the art, was concerned with the possibility of reducing the number of FSH injections to be administered to patients in need thereof. When considering the disclosure in document (10) and in related prior art documents (5) to (9), the skilled person trying
to solve the problem underlying the invention and to provide a more user-friendly regimen while maintaining good follicle growth, would consider to modify the prior art regimen of administration on alternate days and would arrive at the regimen disclosed in claims 1 and 6 in an obvious way.
Moreover, it was highly unlikely that the posed problem was indeed solved by all substances falling within the broad term "biologically-active analogue".

The patent contained in paragraph [0025] a non limiting list of possible FSH analogues. It was highly unlikely

that all compounds belonging to one of the different groups of substances indicated in this passage had a biological activity allowing their use for the purpose of claims 1 and 6. It was the duty of the Patent Proprietor to prove that the problem underlying the patent in suit could in fact be solved by all these substances in order to fulfil the requirements of Article 56 EPC.

The patent in suit did not contain any example referring to the production of a medicament containing an FSH analogue. Moreover, the use of such medicament for either stimulating multiple follicular development or promoting monofollicular development was not described in any of the examples. The test for determining the biological activity of FSH according to document (16) was not applicable to different kinds of FSH analogues. Therefore, to put into practice this embodiment of the claimed invention amounted to an undue burden and contravened the requirements of Article 83 EPC.

## Reasons for the decision

*Main Request*

*Sufficiency of disclosure - Article 83 EPC*

1. Claim 1 refers to the use of FSH and/or a biologically active analogue in the preparation of a medicament for the **simulation of multiple follicular development** in the treatment of infertility in woman.

Claim 6 refers to the use of the same substances in the preparation of a medicament for **promoting monofollicular and reducing multifollicular development** in the treatment of infertility in woman.

2. Thus, although aiming at the same general result, namely to treat infertility in woman, the medicaments produced according to claims 1 and 6 have different objectives. While the medicament according to claim 1 is intended to be used by women undergoing a treatment of infertility by assisted reproduction technologies (ART) requiring ovarian stimulation to increase the number of female gametes and thus the chance of a successful treatment outcome, the medicament according to claim 6 is intended to be used by infertile anovulatory patients diagnosed as having polycystic ovary syndrome (PCOS) who are very sensitive to gonadotropin stimulation and for whom ovarian hyperstimulation is a major risk factor (see patent, paragraph [0003]).

3. The medicament of claim 1 is characterised as being "... for administration at a dose in the range of from 300 to 600 IU on every third day of the first 6 days of the stimulation phase." This is further defined in dependent claim 5, disclosing that the administration is on days 1 and 4, days 2 and 5 or days 3 and 6 of the stimulation phase.

The medicament of claim 6 is characterised as being "... for administration at an initial dose in the range of from 100 to 500 IU and wherein the second dose is for administration between three and six days after the initial dose in the stimulation phase."

4. Thus, both claims encompass the use of FSH and/or a biologically active analogue for the manufacture of a medicament, wherein the medicament, in both cases, is for administration in the overlapping range from 300 to 500 IU on every third day within the first six days of the stimulation phase. However, in one case this administration of the medicament is said to effect the stimulation of multiple follicular development (claim 1), in another case promotion of monofollicular development and reduction of multifollicular development (claim 6).

5. The patent contains two examples.

Example 1, starting on page 5, was designed to assess multiple follicular development and describes the treatment of 35 patients with two doses of 450 IU FSH on every third day of the first six days of the stimulation phase. A control group of 33 patients was treated with 150 IU FSH once daily during the first six days of the stimulation phase. The statistical summary in tables 1 to 7 of the patent shows that the injection of 450 IU FSH every third day resulted in higher quality, more viable oocytes leading to a higher pregnancy rate when compared with the control group.

Example 2 compares ovarian performance and hormonal levels after ovarian stimulation in patients with PCOS using recombinant FSH. Patients received 300 IU r-FSH on cycle day three. No treatment was given on the following two days and the therapy was reinitiated three days later by administering 75 IU FSH. A control group was treated by a "low dose step-up protocol" well

known and widely used in the art (see prior art documents cited in paragraph [0006] of the patent). As summarised in paragraph [0078] the step-down approach according to the patent in suit is considered to be more appropriate for ovulation induction in PCOS patients in order to achieve monofollicular cycles then the step-up approach.

6. Both examples disclose treatment regimens lying respectively outside of the overlap jointly encompassed by claims 1 and 6, as defined in point (4) above.

Appellant I has argued that the claims 1 and 6 refer to medicaments for different patient groups and that a skilled person knowing the effect to be achieved by the respective treatment would be in a position to choose the correct regimen.

It is not called into question, that a skilled practitioner in the field of gonadotrophin treatment of subfertile or unfertile women in a real life situation is able to distinguish between the therapeutic target to be achieved when treating a woman undergoing a treatment by assisted reproduction technology or when treating a woman having PCOS.

However, here, in the situation of patent law, the wording of patent claims is decisive and the Board has to judge whether the skilled practitioner would, when reading the claims, get the technical information required to achieve said targets, namely **simulation of multiple follicular development** in case of the woman undergoing a treatment by assisted reproduction technology, and **promotion of monofollicular and**

**reduction of multifollicular development** in case of the woman having PCOS.

The Board is convinced that this is not so, because the claims encompass a treatment regimen which is broadly overlapping, both, with regard to the quantity of the active ingredient to be administered and the time intervals between the individual doses (see point (4) above). As claim 6 does not specify the amount of FSH to be administered with the second dose the claim encompasses the administration of two identical doses, for instance two times 300 to 500 IU.

7. The patent does not contain information enabling a skilled person to put into practice the claimed invention according to an embodiment which is within the subject-matter of both claims 1 and 6, and which in one case effects the stimulation of multiple follicular development and in another case promotion of monofolicullar development and reduction of multifollicular development.

Therefore the invention is not disclosed in a manner sufficiently clear and complete for it to be carried out requirements of Article 83 EPC.

*First Auxiliary Request*

*Admissibility*

8. Appellant I filed claims 1 to 15 at the oral proceedings, after having been informed by the Board that the claims of the main request contravened the

requirements of Article 83 EPC (see points (1) to (7) above).

9. With regard to the main request the claims of the first auxiliary request contain the following amendments:

The lower limit of the range indicating IU of FSH to be administered in claim 1 has been changed from 300 IU to 400 IU. This lower limit was disclosed in claim 2 of the main request.

Similarly, the upper limit of the range disclosed in claim 6 has been changed to 350 IU, which was disclosed in claim 8 of the main request. Additionally the subject-matter of claim 11 of the main request has been introduced into claim 6 of the first auxiliary request and claims 7 and 11 of the main request have been deleted. Finally the back references in the dependent claims have been adapted.

Thus, the only amendments carried out consist of the introduction of features from dependent claims of the main request into independent claims 1 and 6 of the first auxiliary request.

10. In general, to expedite the proceedings, parties are supposed to submit all facts, evidence and requests at the outset, or - if this is not possible - as soon as they can. They should not be filed piecemeal, this principle being enshrined in Articles 10a and 10b of the Rules of Procedure of the Boards of Appeal.

Appellant II argued that the first auxiliary request filed at the oral proceedings could in fact have been

filed by Appellant I at an earlier stage as the objection under Article 83 EPC with regard to his main request has been known to him before the oral proceedings.

11. According to Article 114(2) EPC the European Patent Office may disregard facts or evidence which are not submitted in due time by the parties concerned. Thus, the Board may exercise its discretion when deciding on the admittance of late submissions.

Among others, the decision to admit a new request into the procedure should be governed by a general interest in the appeal proceedings being conducted in an effective manner, i.e. dealing with as many of the issues raised by the parties as possible, while still being brought to a close within a reasonable time (cf decision T 633/97 of 19 July 2000, point (2) of the reasons for the decision)
The Board takes the view that a new auxiliary request filed by the Appellant/Patent Proprietor at oral proceedings in response to an objection under Article 83 EPC with regard to his main request, which auxiliary request is distinguished from the main request only in so far as features from dependent claims have been introduced into the independent claims, does not raise additional technical or legal issues that neither the Board nor the other party could have expected to deal with.

Therefore, in order to conduct the appeal proceedings in an effective manner, the Board exercises its discretion and admits Appellant I's first auxiliary request into the proceedings.

*Amendments - Article 123(2) and (3) EPC*

12. Appellant II argued that claims 1 and 6 of the first auxiliary request do not have a basis in the application as originally filed (published as WO 01/54715). Although the specific dosage regimens contained in said claims can be found on page 7, second paragraph and on page 8, first and second paragraph, there is no direct link between these regimens and the therapeutic effects to be achieved according to the claims, namely stimulation of multiple follicular development in claim 1 and promotion of monofollicular development and reduction of multifollicular development in claim 6.

13. Page 7, second paragraph of the application as published discloses that, according to one embodiment of the invention, FSH is for administration at a dose in the range of from 300 to 600 IU FSH, preferably 400 to 500 IU, on every third day of the stimulation phase. It is further said that this embodiment provides results which in terms of follicular development are at least the same as the results obtained with the conventional administration of 150 IU/day and indeed results in a higher pregnancy rate. A comparison between the conventional administration of 150 IU/day and 450 IU FSH on every third day of the stimulation phase is carried out in example 1. This example shows exactly the results disclosed on page 7, second paragraph and is designed to assess multiple follicular development (page 12, line 3 of the application as published).

Page 8 of the application as published refers to another embodiment of the invention, wherein an initial dose of 100 to 500 IU FSH, more preferably 250 to 350 IU is administered to a patient, followed by a second dose administered between three and six days later. The second dose may be in the range of from 50 to 200 IU. This embodiment is said to be particularly effective at promoting monofollicular development and reducing multifollicular development (page 8, lines 7 to 9).

14. Considering this disclosure in the application as published, Appellant II's argument must fail. The Board is convinced that claims 1 to 15 of the first auxiliary request do not contain subject-matter extending beyond the content of the application as published.

15. The patent has been granted with 19 claims. Claim 1 thereof, the only independent claim, referred to the use of FSH and/or a biologically active analogue for the preparation of a medicament to treat infertility in woman. The medicament was for administration at an initial dose in the range from 100 to 600 IU followed by a second dose at least three days later in the stimulation phase.

Compared with claim 1 as granted, claims 1 and 6 of the first auxiliary request contain additional features which result in a restriction of the scope of protection.

16. Claims 1 to 15 meet the requirements of Article 123(2) and (3) EPC.

*Patentable Inventions - Article 52(4) EPC*

17. In the notice of opposition, dated 25 February 2005, Appellant II has argued that the claims, which referred to the use of a compound in the production of a medicament for the treatment of infertility characterized by a specific regimen, were directed to a method of treatment of the human body, which was not considered to be a patentable invention within the meaning of Article 52(4) EPC.

The Opposition Division, by referring to decision T 1020/03 (OJ EPO 2007, 204), decided in point (3) of the decision under appeal that Appellant II's argument was without merit and that the claims were not in conflict with the requirements of Article 52(4) EPC. Appellant II, at the oral proceedings before the Board of Appeal, stated that he does not maintain the objection under Article 52(4) EPC.

The Board, having no reason to deviate from the findings of the Opposition Division, will not, therefore, consider the objection under Article 52(4) EPC any further.

*Inventive step - Article 56 EPC*

18. In accordance with the problem and solution approach, the Boards of Appeal in their case law have developed certain criteria for identifying the closest prior art providing the best starting point for assessing inventive step. It has been repeatedly pointed out that this should be a prior art document disclosing subject-matter conceived for the same purpose or aiming at the

same objective as the claimed invention and having the most relevant technical features in common, i.e. requiring the minimum of structural modifications (cf Case Law of the Boards of Appeal of the European Patent Office, 5th Edition 2006, chapter I.D.3.1).

19. Upon consideration of the subject-matter of claims 1 and 6 (see section (VI) above) and of the criteria elaborated by the Boards of Appeal, the present Board, in agreement with both parties concludes that document (10) represents the closest state of the art.

The document is concerned with a comparison of treatments with exogenous FSH to promote folliculogenesis in patients with quiescent ovaries. Three different regimens are tested with the aim to provide the optimum treatment regimen for each approach in terms of clinical efficiency and cost effectiveness (page 553, right column, first full paragraph). Group I women obtained daily injection containing 150 IU FSH for eight days. Group II received 300 IU FSH on alternate days for four injections and group III 150 IU FSH for four injection. The results are discussed on page 555, right column. It is concluded that the evidence from the study strongly suggests that the intramuscular administration of 300 IU FSH at 48-h intervals is likely to elicit a greater biological response than the daily administration of 150 IU and that oocytes recovered after such treatment have a satisfactory potential for development.

20. The problem to be solved by the patent in suit in the light of the disclosure in document (10) was the

provision of a more user-friendly regimen while maintaining good follicle growth.

21. The following questions have to be answered by the Board:

Has the above problem been solved by the patent in suit over the entire scope of the claims?

Do the cited prior art documents contain information that would encourage a skilled person, trying to solve the problem, to modify the disclosure in the closest prior art and to arrive at the claimed subject-matter in an obvious way?

22. With regard to the first question Appellant II argues that the term "biologically-active analogue" according to paragraph [0025] of the patent in suit includes a vast number of substances including muteins, peptidic analogues, non-peptidic analogues and chimeras. It is considered to be highly unlikely that all substances belonging to one of these classes would indeed be able to solve the problem underlying the present invention.

Many of these analogues would have a different pharmacological action profile, such as prolonged in-vivo half-life or a different receptor binding profile when compared with wild-type FSH. Some of the analogues may even be toxic when administered in vivo.

23. Contrary to this, Appellant I argued that the subject-matter of claims 1 and 6 was restricted to such analogues only which had the biological activity of FSH wherein said activity could be expressed in

International Units (IU). The standard method for quantitatively assay FSH activity and to determine the FSH potency of a substance was disclosed in document (16).

The accuracy and reliability of the test disclosed in document (16) for the measurement of the activity of all kinds of FSH analogues was questioned by Appellant II who referred in this context to document (19).

24. Document (19) is a review article published February 2000 and is concerned with the definition and measurement of FSH. Chapter (VI) thereof, starting on page 11, refers to assay systems used for measurement of FSH. Page 11, left column, lines 32 to 38 read:

"The assay developed in 1953 by Steelman and Pohley (139) based on the stimulation of ovarian weight in gonadotropin (LH)-treated immature rats, has proved to be a robust specific ***in vivo*** bioassay for FSH activity. This assay remains the basis of pharmacopeial monographs for the statutory determination of the FSH potency of therapeutic preparations (EP)."

Reference (139) is document (16) in the present procedure.

Document (19) continues that certain FSH isoforms exert no biological action in the Steelman-Pohley assay, and that the test **may** be differently affected by forms of FSH produced by genetic engineering techniques which have extended or shortened biological half-lives. It is summarised that **it might** be necessary to redesign ***in vivo*** bioassays to accommodate differences in activity

of different molecular forms of FSH as novel use of existing units, which **may** not reflect different aspects of the activity of some preparations, will need to be defined clearly to avoid confusion in their clinical usage (page 11, right column).

25. Claims 1 and 6 refer to the use of FSH and/or a biologically-active analogue in the production of a medicament for the achievement of a specific therapeutic effect.

It can be taken from examples 1 and 2, (see especially tables 1 to 7, I and II) and has not been disputed by Appellant II, that a medicament containing wild-type FSH causes the desired therapeutic effect and thus solves the problem underlying the present invention. According to the wording of the claims the use of FSH, biologically-active FSH analogues as well as wild-type FSH, in the production of a medicament is further defined by indicating that the medicament is for administration at a dose having a specific potency of the active ingredient expressed in International Units.

26. The method for measuring the FSH potency of a therapeutic preparation has been developed in 1953 (see document (16)) and was, 47 years later, in 2000 still considered to be a robust and specific in vivo bioassay for FSH activity (see document (19)).

The doubts expressed by the authors of document (19), that this test **may** not give reliable results when applied for specific forms of FSH produced by genetic engineering techniques having extended or shortened biological half-lives, are not substantiated by

verifiable facts such as experimental data. These vague and imprecise remarks cannot be interpreted such, that a person skilled in the art is not able to determine the FSH potency of a biologically-active FSH analogue by using the assay described in document (16).

Accordingly, there is no basis for putting into question that a medicament containing an FSH analogue having the biological activity of FSH, which medicament is administered to a patient in the form as determined in claims 1 and 6, namely in the potency and within the time intervals described, will indeed solve the problem underlying the patent in suit.

27. Document (10), representing the closest state of the art, and disclosing the administration of FSH on alternate days (in 48-hours interval), does not itself contain a hint to further space the time interval between consecutive doses.

Documents (5) and (8) disclose a recombinant FSH-analogue, wherein the carboxyl-terminal peptide (CTP) of hCG β-subunit has been fused to the carboxyl-terminus of the FSH β-subunit. The analogue has identical in vitro receptor-binding and biological activity as wild-type FSH, but an increased circulating half-life. It is concluded that the analogues "...could be effective long-acting agonists for therapeutic use." (see document (5), page 4307, and right column). Animal tests (rats) were carried out in order to investigate whether alternative models of administration resulting in a reduced frequency of hormone administration influenced the relative in vivo bioactivities of wild-type FSH and analogues. However, the longest time gap

between two doses described is 52 hours (see document (8) abstract and the passage bridging left and right columns on page 2515).

Document (6) which is concerned with the development of new regimens for treating infertile women with recombinant gonadotrophins having higher biological half-lives and different iso-hormone profiles, does not mention any precise regimen data.
Document (7), investigating the FSH threshold level for follicle maturation in superovulated cycles, discloses the administration of a single IM injection containing 450 IU on cycle day 2 and the additional administration of 75 IU daily from day 4 onwards in subsequent cycles.

Document (9) describes an alternate day step-down regimen. Stimulation with FSH commenced at a starting dose of 450 IU on day 1 and 3, with a step- down on day 5 to 300 IU, which was continued on alternate days until three or more follicles of 17 mm mean diameter were monitored (page 131, left column, first full paragraph).

28. The Opposition Division has decided that "... the subject-matter relating to the use of a biologically active analogue of FSH..." did not involve an inventive step in view of the disclosure in documents (5) and (8). Since the purpose of the FSH analogues disclosed in said documents was to provide FSH forms with increased circulating half-lives which enabled a reduction of the frequency of administration of the therapeutic agent, it was obvious for the skilled person to increase the gap between consecutive doses from two days to as many days as possible.

29. The Board does not agree with this finding. As described above, neither document (10) itself, representing the closest state of the art, nor any other prior art document on file, including documents (5) and (8), discloses or even suggests to modify the different treatment regimens compared in document (10) with three groups of patients with quiescent ovaries, by further spacing the time interval between two consecutive doses of FSH or a biologically-active analogue, and to apply the treatment regimen according to present claims 1 and 6.

Consequently, the subject-matter of claims 1 to 15 of the first auxiliary request involves an inventive step and meets the requirements of Article 56 EPC.

*Sufficiency of disclosure - Article 83 EPC*

30. Appellant II has argued, that the patent did not disclose the embodiment of the invention referring to the use of biologically active FSH analogues in a manner sufficiently clear and complete for it to be carried out by a skilled person.

As such analogues could be expected to have a pharmacological action profile differing from the one of wild-type FSH with respect to in vivo half-life or receptor binding profile, it was considered to amount to undue burden, to find analogues which could be used for the purpose of claim 1. This is all the more so as the classical test to determine the FSH potency of therapeutic preparations seemed not to be applicable

for new forms of FSH produced by genetic engineering techniques.

31. The doubts expressed in document (19) concerning the accuracy and reliability of the standard test to determine the FSH potency of a therapeutic preparation, which has been developed by Steelman and Pohley in 1953 (see document (16)), are vague and imprecise and not substantiated by experimental data (see also point (25) above).

32. The Opposition, in an obiter dictum on page 5 of the decision under appeal, has stated, that "...the skilled person is left completely unguided as to how to put into practice the claimed invention, as far as it relates to analogues." The Opposition Division continued that "... it cannot be accepted that an FSH analogue exhibiting a substantially different pharmacological profile of action could be considered to be a fair and sufficiently disclosed extrapolation of the effects demonstrated for wild-type FSH."

33. The Board does not agree that the skilled person is "left completely unguided" with regard to the use of FSH analogues. He is told to use an analogue having the biological activity of FSH defined in a range of International Units which are determined by using an assay which, in the here relevant technical field, is considered to be the basis in pharmacopeial monographs for the determination of FSH potency of therapeutic preparations. The argument that FSH analogues per definition exhibit a pharmacological profile which differs from the one of wild-type FSH, which makes it unacceptable to extrapolate results obtained with wild-

type FSH to FSH analogues, is not substantiated by experimental data and remains an allegation.

34. A patent may only be objected to for lack of sufficient disclosure if there are serious doubts, substantiated by verifiable facts. The mere fact that a claim is broad is not in itself a ground for considering the patent as not complying with the requirements of sufficient disclosure under Article 83 EPC (cf decision T 19/90, OJ EPO 1990, 476).

35. The Board arrives at the decision that the patent discloses the invention according to claims 1 to 15 of the first auxiliary request in a manner sufficiently clear and complete for it to be carried by a person skilled in the art. The requirements of Article 83 EPC are met.

## Order

## For these reasons it is decided:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent as amended in the following version:

   Claims 1 to 15 of the first auxiliary request received during oral proceedings of 9 August 2007.

   Description: pages 1, 2, 5 to 15 of the patent specification and pages 3, 3a, 4 and 16 received during oral proceedings of 9 August 2007.

Registrar: Chair:

P. Cremona U. Kinkeldey