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Datasheet for the decision of 18 October 2013

Case Number: T 1060/09 - 3.3.02

Application Number: 01918326.8

Publication Number: 1267852

IPC: A61K31/00

Language of the proceedings: EN

Title of invention:
PHARMACEUTICAL COMPOSITIONS OF CONJUGATED ESTROGENS AND METHODS OF ANALYZING MIXTURES CONTAINING ESTROGENIC COMPOUNDS

Applicant:
Duramed Pharmaceuticals, Inc.

Headword:
Conjugated Estrogens/DURAMED

Relevant legal provisions:
RPBA Art. 15(3), 12(4)
EPC Art. 54(2)
EPC R. 137(3), 100(1)

Keyword:
Oral proceedings - held in absence of appellant
Novelty - main request (no)
Auxiliary requests submitted with grounds of appeal - not admitted: not justified as means of redressing decision under appeal

Decisions cited:
G 0004/92, G 0010/93

Catchword:

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Beschwerdekammern
Boards of Appeal
Chambres de recours

European Patent Office
D-80298 MUNICH
GERMANY
Tel. +49 (0) 89 2399-0
Fax +49 (0) 89 2399-4465

Case Number: T 1060/09 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 18 October 2013

Appellant: (Applicant)	Duramed Pharmaceuticals, Inc. 5040 Duramed Drive Cincinnati, OH 45213-2520 (US)
Representative:	Chalk, Anthony John Harrison Goddard Foote LLP Saviour House 9 St Saviourgate York YO1 8NQ (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 16 December 2008 refusing European patent application No. 01918326.8 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman: M. C. Ortega Plaza
Members: M. T. Sommerfeld
R. Cramer

Summary of Facts and Submissions

I. The present appeal lies from a decision of the examining division, posted on 16 December 2008, refusing European patent application No. 01918326.8, filed as the international application published as WO 01/68074.

II. The documents cited in the examination and appeal proceedings include the following:

D3 US 5,908,638
TAB A: Copy of a letter of 8 March 2000 from Ms Yana Ruth Mille, Department of Health & Human Services of the US FDA, to Mr Valentino of the US Pharmacopeia Convention (USPC)
TAB B: Copy of US Pharmacopeia (USP) 23, pages 627-629
TAB E: Declaration of Mr Swarbrick dated 23 April 2009
TAB F: Curriculum vitae of Mr Swarbrick

III. The decision of the examining division is based on the sets of claims of the main request which was filed with letter of 12 February 2008, and was filed again with letter of 17 October 2008, and auxiliary requests 1 to 7 filed on 17 October 2008.

The set of claims according to the main request comprised 28 claims, of which claim 1 read as follows:

"1. A composition of matter comprising:
a mixture of estrogenic compounds, wherein said mixture of estrogenic compounds comprises salts of conjugated estrone, conjugated equilin, conjugated $\Delta^{8,9}$-dehydroestrone, conjugated 17α-estradiol, conjugated 17α-dihydroequilin, conjugated 17β-dihydroequilin, conjugated 17β-estradiol, conjugated equilenin,

conjugated 17α-dihydroequilenin, and conjugated 17β-dihydroequilenin, wherein said mixture is present in chemically pure form, and wherein said mixture comprises the same essential estrogenic compounds present in naturally derived equine conjugated estrogens."

Claim 1 was left unchanged in auxiliary requests 1, 2, 4, 5 and 6.

Claim 1 of auxiliary requests 3 and 7 differed from claim 1 of the main request in that the expression "present in chemically pure form" was replaced by "substantially devoid of impurities present in naturally derived equine conjugated estrogen products".

IV. The examining division considered that there was a lack of unity of invention for the claim set of the main request (Article 82 EPC). The two separate groups of inventions corresponded to the subject-matter of claims 1 to 14, directed to compositions of estrogenic compounds, and to the subject-matter of claims 15 to 28, directed to analytical methods.

The examining division found that the subject-matter claimed in claims 1 to 6 and 9 to 14 of the main request lacked novelty vis-à-vis document D3. It further considered that some of the features on which the applicant relied to support the novelty of the claims lacked clarity (Articles 52(1), 54(2) and 84 EPC). Additionally, according to the examining division, the subject-matter claimed in claims 7 and 8 did not involve an inventive step (Article 56 EPC). The examining division further considered that the subject-matter of claims 15 to 28 of the main request lacked an inventive step (Article 56 EPC).

As regards auxiliary requests 1 and 2, the examining division was of the opinion that they failed for reasons analogous to those given for the main request in relation to novelty, clarity and inventive step (Articles 52(1), 54(2), 84 and 56 EPC).

In relation to auxiliary request 3, the examining division was of the opinion that the introduced feature did not restore novelty over the prior art and that the claims lacked clarity (Articles 52(1), 54(2) and 84 EPC). Moreover, the examining division stated that the subject-matter claimed did not involve an inventive step (Article 56 EPC).

As regards auxiliary requests 4 to 7, the examining division considered that the objections raised under Articles 52(1), 54(2), 56 and 84 EPC for the previous requests applied *mutatis mutandis*. In addition, the objection of lack of unity of invention raised for the main request also applied to auxiliary request 4 (Article 82 EPC).

V. The applicant (appellant) lodged an appeal against said decision and filed grounds of appeal. It also filed a new main request, auxiliary requests 1 to 8, and documents which were designated TAB A through TAB F.

The **main request** comprises 14 claims, which are identical to claims 1 through 14 of the main request which served as the basis for the decision of the examining division, claims 15 through 28 (which were directed to analytical methods) having been deleted. Therefore, claim 1 of the main request filed with the grounds of appeal is identical to claim 1 of the main

request before the examining division (see supra, section III).

Auxiliary request 1 comprises 16 claims, and differs from the main request in the wording of claims 1 and 2 and in that new dependent claims 4 and 5 have been added (amendments shown for claim 1 and new claims 4 and 5: additions underlined, deletions struck through):

"1. A composition of matter comprising:

a mixture of estrogenic compounds, wherein said mixture of estrogenic compounds ~~comprises~~ consists essentially of salts of conjugated estrone, conjugated equilin, conjugated $\Delta^{8,9}$-dehydroestrone, conjugated 17α-estradiol, conjugated 17α-dihydroequilin, conjugated 17β-dihydroequilin, conjugated 17β-estradiol, conjugated equilenin, conjugated 17α-dihydroequilenin, and conjugated 17β-dihydroequilenin, wherein said mixture is present in chemically pure form, and wherein said mixture comprises the same essential estrogenic compounds present in naturally derived equine conjugated estrogens."

"4. The composition of matter according to any of Claims 1 to 3, wherein said mixture of estrogenic compounds is substantially devoid of impurities present in naturally derived equine conjugated estrogens."

"5. The composition of matter according to any of Claims 1 to 4, wherein said mixture of estrogenic compounds is substantially devoid of indican, sulphated benzyl alcohol, hippuric acid, benzoic acid and creatinine."

Auxiliary request 2 differs from auxiliary request 1 in that claim 2 has been amended.

Auxiliary request 3 differs from auxiliary request 1 in that claim 2 has been deleted and claim 1 has been amended by addition of features at its end:

"1. A composition of matter comprising:
a mixture of estrogenic compounds, ..., and
wherein said estrogenic compounds are derived from sources other than naturally derived conjugated estrogens."

Auxiliary request 4 differs from auxiliary request 2 in that claim 1 has been amended by addition of the following expression at the end:

"1. (...)
wherein said estrogenic compounds are derived from other than natural sources."

Auxiliary requests 5, 6, 7 and 8 essentially differ from auxiliary requests 1, 2, 3 and 4, respectively, in that the expression "consists essentially" has been replaced by the expression "consists" in each claim 1.

VI. As an annex to the summons to oral proceedings, the board issued a communication pursuant to Article 15(1) RPBA.

In said communication the board summarized the situation and expressed a detailed negative opinion on the set of claims corresponding to the main request, which included observations in relation to lack of novelty and clarity (Articles 52(1), 54(2) and 84 EPC). In addition, the board indicated that auxiliary requests 1 through 8 were considered not to be admissible (Article 12 RPBA and Rule 137 EPC), since

they introduced new dependent claims without any justification. The board also pointed out that, since the main request did not contain the claims directed to analytical methods, Article 82 EPC was no longer an issue.

VII. The appellant did not file any substantive reply to the board's communication but instead informed the board, by letter dated 27 August 2013, that it would not attend the oral proceedings.

VIII. On 2 September 2013 the board sent a brief communication informing the appellant that the oral proceedings were maintained.

IX. Oral proceedings took place on 18 October 2013 as scheduled and in the absence of the appellant.

X. The appellant's arguments, in so far as relevant to the present decision, can be summarized as follows:

The essential estrogenic compounds present in naturally derived equine conjugated estrogens of the prior art (such as Premarin®, Conjugated Estrogens USP) were not known at the priority date of the application, as evidenced by TAB A, TAB B and TAB E. As such it was not possible prior to the invention to formulate a chemically pure and/or synthetic mixture of estrogenic compounds which comprised the same essential natural estrogenic compounds.

TAB A consisted of a letter from the Food and Drug Administration (FDA) to the United States Pharmacopeial Convention (USPC), containing a proposal for "revisions to the current USP 24 monograph for Conjugated Estrogens" (first sentence); the letter commented that

"many of the compounds included in the specific "fingerprint" peaks have not been identified yet, and may include non-steroidal as well as steroidal compounds" (last paragraph of the first page of TAB A).

TAB B consisted of the USP 23 monograph (referred to in D3, legend to Table 1) containing the description of conjugated estrogens available in the USP. This description did not include all estrogenic compounds listed in claim 1, and, for this reason, was "deficient when considered in the context of claim 1".

TAB E consisted of a declaration by a technical expert in the field, James Swarbrick D. Sc., Ph. D., whose curriculum vitae was provided in the document submitted as TAB F. According to this declaration, it was not possible prior to the invention to formulate a chemically pure and/or synthetic mixture of estrogenic compounds which comprised the same essential natural estrogenic compounds present in naturally derived equine conjugated estrogens, i.e those present in Premarin® (Conjugated Estrogens, USP), because it was not known that the ten estrogens set forth in claim 1 were the only essential estrogenic compounds present in Premarin® (TAB E, paragraph 5.).

Contrary to the compositions of the prior art, the composition of the invention was in a chemically pure form, which meant that impurities that arose from fecal contamination due to isolation from mare's urine were eliminated.

XI. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request filed with the grounds of appeal,

or alternatively, on the basis of one of the auxiliary requests 1 to 8 also filed with the grounds of appeal.

Reasons for the Decision

1. The oral proceedings before the board took place in the absence of the appellant, who was duly summoned but decided not to attend.
The present decision is based on facts and evidence put forward during the written proceedings and on which the appellant has had an opportunity to comment.
Therefore the conditions set forth in Enlarged Board of Appeal opinion G 4/92, OJ EPO 1994, 149, are met.

Moreover, as stipulated by Article 15(3) RPBA, the board shall not be obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned who may then be treated as relying only on its written case.

2. The appeal is admissible.

3. Main request - Novelty

3.1 Document D3 specifically discloses in Table 1, at column 9, a conjugated estrogen composition which comprises sodium estrone sulfate, sodium equilin sulfate, sodium 17-alpha-estradiol sulfate, sodium 17-alpha-dihydroequilin sulfate, sodium 17-beta-dihydroequilin sulfate, sodium 17-beta-estradiol sulfate, sodium 17-alpha-dihydroequilenin sulfate, sodium 17-beta-dihydroequilenin sulfate, sodium

equilenin sulfate, and $\Delta^{8,9}$-dehydroestrone sulfate. These are the same conjugated estrogens as in the composition claimed in claim 1, which includes salts thereof (such as sodium sulfate). Moreover, sodium sulfate salts are specifically indicated as embodiments of the invention in the application, e.g. page 2, last two lines to page 3, line 12.

3.2 The feature "said mixture is present in chemically pure form" does not render the composition of claim 1 novel over the composition known from document D3, as correctly appreciated by the examining division. This expression is ambiguous, as it is not apparent what is meant by "chemically pure form" in the context of the mixture claimed in claim 1, since the exact and complete definition of the claimed composition is not specified (i.e. no complete list of specific components and their percentages is provided). In the application, this expression is defined as meaning "substantially devoid of impurities present in naturally derived equine conjugated estrogen products" (page 4, lines 28 to 31); however this definition is itself unclear as it is not possible to establish precisely what falls within its scope: in particular, the expression does not allow to distinguish from the prior art, in which there is no reference to any "impurities".

3.3 Additionally, the present situation is different from a situation in which a certain chemical product, present in nature, is separated and chemically identified for the first time and said product is therefore not disclosed at all in the prior art. In the present case all the estrogen compounds forming the claimed mixture were products known *per se* (and they were commercially available, as acknowledged in the application as filed - see page 6, lines 14 to 16 - and in D3 - paragraph

bridging columns 8 and 9, just before Table 1), and the claimed mixture is specifically disclosed in document D3 (together with its medical purposes).

3.4 Furthermore, the disclosure in document D3 of the product constituted by the mixture of estrogen components in Table 1 cannot be restricted on the basis of a particular origin or manner of its preparation. The fact that the composition containing the known compounds listed in Table 1 of document D3 is made by mixing does not make the product claimed novel over document D3.

3.5 Finally, the feature "wherein said mixture comprises the same essential estrogenic compounds present in naturally derived equine conjugated estrogens" is not suitable either to establish novelty over the composition disclosed in the prior art D3. This feature is either redundant in the context of claim 1, which already specifies which estrogenic compounds are to be present in the mixture, or else unclear, in that it is not apparent what these "essential estrogenic compounds" should be if they are different from the ones listed. According to the application (page 4, line 32 to page 5, line 12), the essential estrogenic compounds present in naturally derived equine conjugated estrogens are those listed in claim 1, and even more preferably the sodium sulfate salts thereof; these are also the compounds present in the composition of document D3, which thus, by definition, also comprises "the same essential estrogenic compounds present in naturally equine conjugated estrogens".

3.6 Accordingly, document D3 anticipates the subject-matter of claim 1.

3.7 As regards the appellant's arguments that it would not have been possible before the invention to prepare a chemically pure composition according to claim 1, document D3, and in particular its Table 1, is in itself a completely enabling disclosure for a composition of matter comprising a mixture of estrogenic compounds as listed in claim 1. Table 1 discloses a "conjugated estrogen composition" (title of Table 1), and even provides the concentration range for each of the ten listed estrogens. The reference in D3 (legend to Table 1) to USP 23, Second Suppl., May 15, 1995, is solely in relation to the assay performed for the calculation of the percentages in the estrogen composition; it does not imply that the composition as disclosed in D3 is the same as that disclosed in the USP 23 monograph (corresponding to TAB B). It is, thus, immaterial for the assessment of the disclosure in document D3 whether the exact composition appearing in Table 1 of said document is also reflected in the USP 23 monograph for conjugated estrogens (TAB B). Moreover, the copy of the letter submitted by the appellant as document TAB A, which concerns some recommendations in relation to a revision of the USP 24 monograph for conjugated estrogens, does not affect the disclosure of D3, which is per se clear and complete.

3.8 According to TAB E, the presence of contaminants stems from the fact that the compounds in the prior art are isolated from mare urine. Apart from the fact that claim 1 of the main request does not exclude mare urine as a source of the estrogenic compounds, the claimed composition is known from D3 and this fact cannot be changed by introducing artificial requirements to the claim's wording.

3.9 It is further noted that purified mixtures of conjugated estrogens containing the essential estrogenic compounds present in naturally derived equine conjugated estrogens have been commonly used for medical purposes for many years. The fact that some estrogen preparations of the prior art may contain further components apart from the ten essential components named in claim 1 does not mean that the known medicaments approved and sold under the names Premarin®, Prempo® or Premphase® (all cited in the description of the present application: page 7, lines 10 to 18) show fecal contamination from the mare's urine as has been argued in the grounds of appeal. It cannot be seen from the data in the application as filed that this particular aspect was proven by the applicant.

3.10 Therefore, claim 1 of the main request lacks novelty over document D3, and thus the main request is not allowable (Articles 52(1) and 54(2) EPC).

4. Auxiliary requests - Admissibility

4.1 According to Article 12(1) RPBA, ex parte appeal proceedings shall be based inter alia on the notice of appeal and statement of grounds of appeal, Article 12(1)(a) RPBA. Moreover, Article 12(2) RPBA stipulates that the statement of the grounds of appeal shall set out clearly and concisely the reasons why it is requested that the decision under appeal be reversed, amended or upheld.

4.2 Additionally, as stated in Enlarged Board of Appeal decision G 10/93 (OJ EPO 1995, 172), "proceedings before the boards of appeal in ex parte cases are

primarily concerned with examining the contested decision", and thus, the appeal proceedings are intended to review the correctness of the decision of the first instance rather than to continue examination by other means.

4.3 In the present case, however, the statement of the grounds of appeal does not contain any justification for the introduction of new dependent claims in the auxiliary requests, nor does it mention why the introduction of new dependent claims should be considered as a valid attempt to overcome the negative findings in relation to independent claim 1 of the main request in the first-instance decision.

4.4 All auxiliary requests introduced two new dependent claims, which are not justified as means of redressing the first instance decision. In the absence of any substantive reply to the objections on admissibility raised by the board in its communication sent as annex to the summons, the board concludes that auxiliary requests 1 through 8 are not admissible (Rule 137(3) EPC in conjunction with Rule 100(1) EPC, and Article 12 RPBA).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

N. Maslin M. C. Ortega Plaza

Decision electronically authenticated