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**Datasheet for the decision  
of 23 October 2012**

**Case Number:** T 0209/10 - 3.3.02

**Application Number:** 04101615.5

**Publication Number:** 1438957

**IPC:** A61K 31/4535, A61P 19/10,  
A61P 5/24

**Language of the proceedings:** EN

**Title of invention:**  
Raloxifene in the treatment of postmenopausal osteoporosis

**Patentee:**  
ELI LILLY AND COMPANY

**Opponents:**  
Teva Pharmaceuticals Industries Ltd.  
TECNIMEDE SOCIEDADE TECNICO-MEDICINAL S.A.  
Hammer, Jens

**Headword:**  
Use of raloxifene in the treatment of postmenopausal  
osteoporosis/ELI LILLY

**Relevant legal provisions:**  
EPC Art. 100(c)  
RPBA Art. 13

**Keyword:**  
"Main request: added matter (yes)"

**Decisions cited:**  
-

**Catchword:**  
-



Case Number: T 0209/10 - 3.3.02

**D E C I S I O N**  
**of the Technical Board of Appeal 3.3.02**  
**of 23 October 2012**

**Appellant:** ELI LILLY AND COMPANY  
(Patent Proprietor) Lilly Corporate Center  
Indianapolis, IN 46285 (US)

**Representative:** Graf von Stosch, Andreas  
Graf von Stosch  
Patentanwalts-gesellschaft mbH  
Prinzregentenstrasse 22  
D-80538 München (DE)

**Respondent I:** Teva Pharmaceutical Industries Ltd.  
(Opponent 1) 5 Basel Street  
IL-49131 Petah Tiqva (IL)

**Representative:** Pohlman, Sandra M.  
df-mp  
Fünf Höfe  
Theatinerstrasse 16  
D-80333 München (DE)

**Respondent II:** TECNIMEDE SOCIEDADE TECNICO-MEDICINAL S.A.  
(Opponent 2) R. Prof. Henrique de Barros,  
Edificio Sagres 3.A  
PT-2685-338 Prior Velho (PT)

**Representative:** HOFFMANN EITLE  
Patent- und Rechtsanwälte  
Arabellastraße 4  
D-81925 München (DE)

**Respondent III:** Hammer, Jens  
(Opponent 3) Leopoldstrasse 4  
D-80802 München (DE)

**Decision under appeal:** **Decision of the Opposition Division of the  
European Patent Office posted 22 December 2009  
revoking European patent No. 1438957 pursuant  
to Article 101(3) (b) EPC.**

**Composition of the Board:**

**Chairman:** U. Oswald  
**Members:** M. C. Ortega Plaza  
L. Bühler

## Summary of Facts and Submissions

- I. European patent No. 1 438 957, based on European patent application No. 04101615.5 which was filed as a divisional application of application No. 97200262.0 (parent application), which was filed as divisional application of application No. 93305860.4 (root application), was granted with nine claims.

Claim 1 as granted reads as follows:

"1. The use of raloxifene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for preventing or treating postmenopausal osteoporosis in a postmenopausal woman wherein said medicament is in the form of a tablet or capsule".

- II. Oppositions were filed and revocation of the patent in its entirety was requested pursuant to Article 100(c) (the subject-matter of the patent extends beyond the content of the application as filed), 100(b) (lack of sufficiency of disclosure) and 100(a) EPC (lack of novelty and lack of inventive step).

- III. The following documents were cited *inter alia* in the opposition and appeal proceedings:

D1 Jordan et al., Breast Cancer Research and Treatment 10: 31-35 (1987)

D3 US 4859585

D22 Lindgren and Jordan, Acta Orthopædica Scandinava 61(1) Suppl. 235, page 55 (1990)

P26 Lindstrom's memorandum dated 14 September 1987

P28 declaration of Mr Sawchuk dated 19 August 2012

P29 chapter 2 of Handbook Estrogen/Antiestrogen Action and Breast Cancer Therapy, 1986, Publisher: Madison, Wis., University of Wisconsin Press

D40 C Dwivedi, FASEB J. 1:303-307, 1987

D41 declaration of Mr Jordan dated 19 September 2012

D42 declaration of Mr Ringe dated 20 September 2012

D43 Chemical Abstracts entries 10540-29-1 (Tamoxifen) and 84449-90-1 (Raloxifene).

IV. The present appeal lies from the decision of the opposition division revoking the patent (Article 101(3) (b) EPC).

V. The opposition division's decision is based on the main (and sole) request, which is the set of claims filed with the letter of 8 October 2009. Claim 1 of the main request is identical to claim 1 as granted.

The opposition division considered that the grounds of opposition under Article 100(c) EPC (Articles 123(2) and 76(1) EPC) did not prejudice the maintenance of a patent.

The opposition division further considered that the specification of the dosage form as a tablet or capsule

conferred novelty on the use claimed in claim 1 vis-à-vis the content of document D1, and that an analogous analysis applied in relation to document D22. Additionally, in the opposition division's view, document D3 did not disclose the treatment of osteoporosis.

As regards inventive step, the opposition division considered document D1 as the closest prior art, since it disclosed the use of raloxifene for the treatment of osteoporosis. Moreover, the opposition division was of the opinion that D1 disclosed that raloxifene showed stabilisation of bone loss in ovariectomized rats and that this was an "accepted model for postmenopausal women". According to the opposition division's findings, the disclosure in document D1 was enabling for the treatment of osteoporosis in postmenopausal women. The opposition division defined the problem to be solved as "to provide a real dosage unit for the treatment of postmenopausal osteoporosis". The solution related to the choice of a tablet or a capsule. The opposition division considered that the solution was obvious for the skilled person.

Since the main request failed for lack of inventive step, the opposition division's decision does not contain an assessment of the grounds of opposition under Article 100(b) EPC.

VI. The patent proprietor (appellant) filed an appeal against said decision and requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request before the opposition division. The appellant filed with its

grounds of appeal further documents (documents P25 to P27).

- VII. Respondent I (opponent O1) filed a response to the appellant's grounds of appeal. It requested that the appeal be dismissed ("to uphold the decision of the opposition division to revoke the patent in suit") and gave reasons. Furthermore, respondent I maintained its objections in relation to the grounds of appeal under Article 100(b) and (c) EPC and questioned the right to the priority date for the subject-matter claimed in the main request. Additionally, it filed further documents (documents D39 and D40).
- VIII. Respondent III (opponent O3) filed a response to the grounds of appeal. It requested that the appeal be dismissed and gave reasons. It also clarified that it maintained the objections in relation to the ground of opposition under Article 100(b) EPC.
- IX. A board's communication pursuant to Article 15(1) RPBA was sent to the parties as an annex to the summons to oral proceedings. In said communication the board expressed the preliminary opinion that the assessment of the grounds of opposition under Article 100(b) and (c) EPC were within the framework of the present appeal.

Moreover, the board expressed a preliminary opinion in relation to Article 100(c) EPC for claim 1 of the set of claims of the main request filed with the letter of 8 October 2009 and in relation to its entitlement to the priority date. Additionally, the board expressed a preliminary opinion in relation to document D1. In said

communication the parties were reminded that the admissibility of any requests and submissions filed thereafter would have to be considered at the oral proceedings, in particular under Article 13 RPBA.

- X. The appellant filed with a letter dated 23 August 2012 a reply to the board's communication which was sent as an annex to the summons to oral proceedings. It filed as an annex thereto a declaration of Mr Sawchuk (P28) and a copy of a handbook (P29).
- XI. Respondent I filed with a letter dated 20 September 2012 a response to the board's communication and to the appellant's reply dated 23 August 2012. It filed as an annex thereto a declaration of Mr Jordan (D41), a declaration of Mr Ringe (D42), and Chemical Abstracts entries (D43).
- XII. Oral proceedings took place on 23 October 2012 in the absence of respondents II and III.
- XIII. The appellant's arguments, as far as relevant for the present decision, may be summarised as follows.

Documents D41, D42 and D43 had been filed by respondent I with its letter of 20 September 2012, i.e. after the time limit for response to a communication. The admissibility of the declarations D41 and D42, as well as respondent I's request for hearing of experts in the present oral proceedings, should be refused since they should have been filed earlier. Bioavailability had long been the subject of discussion and thus respondent I could not have been taken by surprise by the appellant's last submissions. Oral

bioavailability was essential for the assessment of the "invention". There were fundamental questions in relation to bioavailability which had not been presented by respondent I in accordance with the technical knowledge in the field. This was the reason for filing the declaration of a technical expert P28, as well as P29. Although the board's communication sent as an annex to the summons to oral proceedings did not set any time limit for reply, two months before the oral proceedings should suffice.

The criterion of a literal disclosure was not appropriate when assessing the ground of opposition pursuant to Articles 100(c) and 123(2) EPC. The skilled person would consider the whole application in the light of his general knowledge. It was only natural that applications as originally filed concerned a broader disclosure than the claims as granted. Postmenopausal osteoporosis was referred to for instance on page 2 of the application as originally filed, in the paragraph starting on line 4. Said paragraph defined postmenopausal osteoporosis as a result of low estrogen levels. In the state of the art postmenopausal osteoporosis had been treated by means of estrogen replacement therapy. However, long-term estrogen therapy had been implicated in a variety of disorders. Thus, there was a need to develop an alternative therapy for bone loss within the framework of postmenopausal osteoporosis. This was achieved by the present "invention" (page 3, lines 13-16 of the application as originally filed). The treatment of postmenopausal osteoporosis in postmenopausal women was also disclosed on page 5, lines 23-25 as the treatment after cessation of menstruation. Furthermore, on page 8,



lines 21-24, it was disclosed that the treatment disclosed included both medical therapeutic and/or prophylactic treatment. Example 1 concerned a model for the treatment of postmenopausal osteoporosis and the further examples illustrated modes of performing the "invention". Example 5 related to clinical studies concerning postmenopausal women. The subject-matter claimed in claim 1 did not derive from the selection from several lists in the application as originally filed. The medical indication claimed was the preferred medical indication to be treated, and raloxifene was the most preferred compound (page 11, lines 11-13). As regards the choice of tablets and capsules, these dosage forms were disclosed on page 14, lines 17-20. Mention of tablets and capsules was also made in claims 4 and 5 of the application given rise to the patent in suit. Moreover, almost all of the formulations exemplified in the application as originally filed, starting on page 17, related to tablets and capsules, with the exception of formulation 8, which was a suspension. Moreover, raloxifene was the most preferred compound. Thus, claim 1 did not concern an unallowable selection; it concerned the merely deletion of some option(s) from one list. The last paragraph on page 15 was a standard passage commonly present in applications in the pharmaceutical field.

Asked by the board what technical information was encompassed by claim 1 and whether it was directly and unambiguously derivable from the application as originally filed, the appellant answered that claim 1 specifically related to the medical use, expressed in a Swiss-type form, of raloxifene or a pharmaceutically acceptable salt thereof for the prevention or treatment

of postmenopausal osteoporosis in postmenopausal women. This use took place by means of a medicament in the form of a tablet or capsule. The application as originally filed concerned the compounds of formula I, which in fact represented a generalisation of raloxifene and were structurally very close to it. Raloxifene was a particular compound which was disclosed as mostly preferred (see page 11, line 2, page 4, lines 7-10, and page 12, line 11 of the application as originally filed) and it was used in the formulations illustrated by many of the examples. Additionally, page 2, starting on line 4, disclosed the medical indication for which raloxifene was to be used, namely postmenopausal osteoporosis. The indication relating to the treatment of postmenopausal osteoporosis was essential (see pages 2, 3 and 5, lines 19-25 of the application as originally filed). Postmenopausal osteoporosis was the osteoporosis which originated from estrogen deficiency (see page 2 of application as originally filed). Postmenopausal women where subject to postmenopausal osteoporosis caused by estrogen deficiency (see page 2 of the application as originally filed) and page 8, lines 19-21 disclosed that the indication could also be for preventive use. The present "method" contemplated the inhibition of bone loss in postmenopausal osteoporosis in postmenopausal women. The prevention of bone loss was disclosed on page 1, lines 4-6 and page 3 of the application as originally filed. Page 3, lines 13-16 of the application as originally filed disclosed bone loss in connection with the treatment of osteoporosis. Moreover, the skilled person reading the application in its entirety would immediately understand that tablets and capsules could be used for the said indication. The

skilled person would not be faced with any new subject-matter. The subject-matter claimed was disclosed in the application as originally filed. The skilled person was not presented with any new technical information in claim 1.

The appellant also mentioned example 5 of the application as originally filed which, in its opinion, disclosed the treatment of postmenopausal women with raloxifene. The illustrative examples mostly referred to tablets or capsules.

The appellant further submitted that estrogen deficiency could cause different diseases but the disclosure on page 2 of the application as originally filed gave the context for the specification of postmenopausal osteoporosis in postmenopausal women. As regards the technical link between the claim's features, the appellant submitted the following. The treatment with raloxifene was linked to estrogen deficiency, since raloxifene was an estrogen agonist. The treatment of postmenopausal osteoporosis in postmenopausal women was due to estrogen deficiency. Although example 5 did not display any results it was in line with the disclosure on page 3, line 13 and following of the application as originally filed. The bone loss was a consequence of osteoporosis, example 1 concerned a model of postmenopausal osteoporosis and in example 5 postmenopausal women were treated with raloxifene administered in capsules. The subject-matter claimed in claim 1 did not arise from "cherry-picking" from the application as originally filed; it was directly derivable therefrom.

XIV. Respondent I's arguments, as far as relevant for the present decision, may be summarised as follows.

Documents P28 and P29 which had been filed with the appellant's letter of 23 August 2012, i.e. outside the opposition and appeal period, dealt with issues known to everybody long in advance, and thus there was no justification for admitting them. Moreover, if these documents were to be admitted, then the documents filed with respondent I's letter of 20 September 2012 should also be admitted as a direct response thereto. As regards the respondent I's request for oral submissions by the technical experts, it had been made one month before the date of the oral proceedings, in line with the Enlarged Board of appeal decision G 4/95, OJ EPO, 412, 1996.

Furthermore, the board's communication had been sent without a deadline for reply, but it explicitly referred to Article 13 RPBA in relation to the admissibility of further submissions. The issue of bioavailability had been already discussed during the first-instance proceedings and was mentioned in the opposition division's decision. Therefore, there was no objective reason for not complying with the requirements of Article 13 RPBA.

The preliminary opinion expressed by the board in the communication sent as an annex was positive in relation to Article 100(c) EPC. However, the terms postmenopausal osteoporosis in a postmenopausal woman appeared nowhere in the application as originally filed. The specific treatment claimed had no basis in the application as originally filed in connection with a

tablet (or with a capsule). Selection in three or four directions had to be performed from the content of the application as originally filed in order to arrive at the subject-matter claimed. The following selections had taken place: selection of raloxifene as a compound of formula I, selection of postmenopausal osteoporosis (from *inter alia* bone loss, osteoporosis, menopausal syndrome, osteoporosis in men, osteoporosis in women not due to menopause), and selection of tablets or capsules from other formulations (twofold selection, first oral administration and then tablets and capsules). The subject-matter claimed related to selections from two or more lists in a manner which was not directly and unambiguously derivable from the application as originally filed. In this context, respondent I cited the board of appeal decisions T 727/07 of 22 June 2001, T 631/06 of 19 November 2008, T 602/05 of 28 June 2007. Moreover, the application as originally filed did not disclose in an individualised form the medical indication now singled out in the claim. Respondent I cited board of appeal decision T 1374/07 of 13 January 2009, from the same board 3302 in another composition.

Claim 1 addressed a medical use claim in which the selection of the disease to be treated together with the selection of the dosage form amounted to an individualisation or singling out which was not directly and unambiguously derivable from the application as originally filed. When the application as originally filed referred to the "invention" it referred to the prevention or treatment of bone loss (page 4, lines 10-13, page 5, line 12). Under the umbrella of bone loss were numerous conditions. On

page 1, lines 19-24 of the application as originally filed it was stated that bone loss occurred in a wide range of subjects, including post-menopausal women among many others. The prevention of bone loss was disclosed in connection with estrogen-deficient animals (page 6, lines 14-15 of the application as originally filed) but the ability of the compounds of formula I to address estrogen deficiency was also disclosed in connection with the treatment of menopausal syndrome (page 6, line 17 of the application as originally filed) and not necessarily with postmenopausal bone loss. The animal model in example 1 not only served as a model for postmenopausal osteoporosis, but also for bone loss more generally, and osteoporosis more generally. Thus, it could not serve as a valid basis for the medical indications singled out in the claim. There had been a selection of the dosage form from several options such as tablets, capsules, suspensions, powders, etc. (page 14, lines 13 to 20 of the application as originally filed) and elixirs, solutions for oral administration, and solutions for parenteral administration (intramuscular, subcutaneous, intravenous routes (page 15, lines 9-13 of the application as originally filed). The disclosure on page 15, lines 20-24 made it clear that the selection of the route of administration depended on the disease to be treated, thus there were two lists in relation to the medicament: first, selection of the route of administration as oral and second, selection of tablets and capsules. In the application as originally filed there was no preference either for the oral administration or the choice of tablets and capsules. Additionally, the examples in the application as

originally filed illustrated specific formulations and did not allow an intermediate generalisation.

One of the essential problems under Article 100(c) EPC was that the specific use claimed was not disclosed together with the selection of the active substance and pharmaceutical form of the medicament. Even assuming in favour of the appellant that the claimed subject-matter claimed was conceptually encompassed by the application as originally filed, the appellant had undertaken a singling out which was not directly and unambiguously disclosed in the application as originally filed. The application as originally filed concerned a broad compound class, a broadly defined medical condition, namely "bone loss", and a pool of very different diseases. In the application as originally filed there was not stated which diseases were preferentially to be treated or which were the preferred forms for the medicament to be used. There was no disclosure in the application as originally filed about the specific prevention or the treatment of postmenopausal osteoporosis in postmenopausal women. The application as originally filed did not focus on oral administration or on tablets or capsules. The claim established a technical link between the choice of the specific indication and the form of the medicament which could not be derived from the application as originally filed. The application as originally filed did not disclose any technical link between the selection of the tablet or capsule and the specification of the medical indication in the claim. Example 5 referred to clinical studies without yet knowing their outcome, so they could not serve as an allowable basis within the meaning of Article 123(2)

EPC. The application as originally filed concerned therapy of bone loss and did not singularise the treatment of postmenopausal osteoporosis in postmenopausal women.

Furthermore, respondent I disagreed with the appellant's statement that the treatment of osteoporosis mentioned on page 3 could only concern postmenopausal osteoporosis in postmenopausal women. It submitted that osteoporosis had multifactor causes, such as for instance, long treatment with corticosteroids. According to page 3 of the application as filed, women suffering from osteoporosis should not be subjected to the adverse stress associated with estrogen therapy; nothing else could be extracted from the disclosure there.

- XV. The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request filed with the letter of 8 October 2009.

The respondent I (opponent O1) requested that the appeal be dismissed. The respondent II (opponent O2) requested in writing that the appeal be dismissed.



## Reasons for the Decision

### 1. *Admissibility*

1.1 The appeal is admissible.

1.2 *Admissibility of the documents P28, P29, D41, D42, D43*

Article 13(1) RPBA provides that 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. Article 13(3) RPBA provides that amendments sought to be made after oral proceedings have been arranged shall not be admitted if they raise issues which the Board or the other party or parties cannot reasonably be expected to deal with without adjournment of the oral proceedings.

The question of bioavailability was dealt with in point 4.5 of the opposition division's decision. In its grounds of appeal (see page 10 and following) the appellant submitted its arguments in relation to bioavailability, analysed the documents on file and filed further documents (*inter alia* document P26). Respondent I filed with its letter dated **9 September 2010** a response to the grounds of appeal. In point IX, 3.3.1 it replied to the appellant's arguments concerning bioavailability. It also commented on document P26, and filed a further document (D40).

Respondent's III reply to the grounds of appeal was filed with the letter dated 13 September 2010.

The board sent on 24 May 2012 a communication pursuant to Article 15(1) RPBA as an annex to the summons to oral proceedings. With said communication the board reminded the parties that the admissibility of any requests and submissions filed thereafter would have to be considered at the oral proceedings, in particular under Article 13 RPBA.

The justification given by the appellant in favour of the admission of documents P28 and P29 was that they represented a reply to respondent I's arguments on bioavailability. However, respondent I had commented on bioavailability with its letter dated 9 September 2010 and the appellant waited until 23 August 2012 (i.e. almost two years after respondent I's submissions) to give a reply with counter-arguments and to file additional documents, namely a declaration of an expert (P28) and some copies from a book (P29). Thus, the board is of the opinion that documents P28 and P29 could have been filed earlier.

Additionally, their filing is not justified as a direct reply to the board's communication sent as an annex to the summons to oral proceedings, which merely concerned a preliminary opinion expressed as the facts on file stood, but neither raised any new issues nor invited the parties to file any further evidence in relation to bioavailability.

Therefore, documents P28 and P29 are not admitted into the proceedings.

Documents D41, D42 and D43, which were filed with the respondent I's letter dated 20 September 2012 in reply to the appellant's submissions in its letter of 23 August 2012 and the documents filed therewith (P28 and P29), are also not admitted into the proceedings.

2. *Main (sole) request*

2.1 Claim 1 of the main request is identical to claim 1 as granted. The assessment of the ground of opposition under Article 100(c) EPC is within the framework of the present appeal. In particular, the decision of the opposition division has to be reviewed also in relation to Article 100(c) EPC, and respondent I already submitted arguments pursuant to Article 100(c) EPC with its response to the grounds of appeal (see point VI of respondent I's letter dated 9 September 2010).

2.2 The patent in suit derives from European patent application 04101615.5, which was filed as a divisional application of European patent application 97200262.0 (parent application), published as EP-A-0781555. The parent application was filed as a divisional application of European patent application 93305860.4 (root application), published as EP-A-0594952. The documents concerning the description and examples as originally filed are identical for the three applications: root (GA), parent (PA) and its divisional (OA) (i.e. the application from which the patent in suit derives). However, the claims as originally filed in the root application (GA) are different from the claims as originally filed in the parent (which are the same as in its divisional application).

It is an undisputable fact that the set of claims of the application as originally filed (OA) does not contain any claim or combination of claims which corresponds to the use in claim 1 of the main request. As a matter of fact claims 1 to 8 of the application as originally filed (OA) related to a pharmaceutical unit dosage form comprising **an amount of from 50 to 200 mg** of a compound of formula I (generic compound class defined by means of a Markush formula). Moreover, none of the claims of the application as originally filed (OA) specified any medical indication. Thus, the claims of the application as originally filed do not provide any allowable basis under Article 123(2) EPC for claim 1 as granted.

Therefore, it has to be investigated whether the description and examples of the application as filed provide a basis for the subject-matter claimed in claim 1 of the main request. Such an investigation corresponds identically to the investigation of the basis in the root (GA) and parent (PA) applications, in view of the identical text of the description and examples.

- 2.3 Claim 1 of the main request is a medical use claim in the Swiss-type form, which relates to the use of a single drug, namely raloxifene, which may also be in the form of a pharmaceutically acceptable salt. The particular use to which the drug has to be functionally linked concerns the specific medical indication of the prevention or treatment of postmenopausal osteoporosis, and the particular subgroup of patients is identified as "a postmenopausal woman". As regards the form in

which the medicament is to be administered, it is specified as a tablet or capsule. A body of jurisprudence of the technical boards of appeal identifies the technical elements which have been specified in claim 1 (e.g. identity of the drug, form of the medicament and/or mode of administration, medical indication concerning a disease or ailment, group of patients) as technical features which may confer novelty and/or inventive step on the subject-matter of a medical use claim in the Swiss-type form.

Therefore, it has to be assessed whether the application as originally filed singles out the "invention" specified in claim 1, and whether the claim includes technical information not directly and unambiguously derivable from the application documents as originally filed.

- 2.4 The application as originally filed discloses a group of 2-phenyl-3-arylbenzothiophenes **in the prevention of bone loss** (page 1, lines 5 and 6). However, the prevention of bone loss is not a synonym for the prevention of postmenopausal osteoporosis in a postmenopausal woman. As stated on page 1, lines 7-11 of the application as originally filed: "The mechanism of bone loss is not well understood, but in practical effect, the disorder arises from an imbalance in the formation of new healthy bone and the resorption of old bone, skewed toward a net loss of bone tissue". Claim 1 of the main request does not explicitly reflect the technical effect of "prevention of bone loss".

Moreover, as stated in the paragraph bridging pages 1 and 2 of the application as originally filed,

"Unchecked, bone loss can lead to osteoporosis, a major debilitating disease **whose prominent feature** is the loss of bone mass (decreased density and enlargement of bone spaces) without reduction in bone volume, producing porosity and fragility" (emphasis added). In other words, bone loss is not the only feature of osteoporosis, and thus the prevention of bone loss does not equate to the prevention of osteoporosis.

Further, on page 8, lines 21-24 of the application as originally filed it is stated that: "The **inhibition of bone loss** contemplated by the present method includes both medical therapeutic and/or prophylactic treatment" (emphasis added). Therefore, this passage does not disclose the preventive treatment of postmenopausal osteoporosis in a postmenopausal woman (which may *inter alia* address secondary prevention of osteoporosis in an earlier stage of post-menopause, as well as tertiary prevention in a post-menopausal woman already suffering from advanced post-menopausal osteoporosis); it simply discloses the prophylactic treatment which is exclusively linked to the technical effect (not mentioned in claim 1) of inhibition of bone loss.

This understanding of the content of page 8 is in line with the following passage on page 6, lines 21-26 of the application as originally filed: "Thus, the current invention provides a method of **inhibiting bone loss** comprising administering to a human in need of treatment an amount of a compound of formula I that **inhibits bone loss** but does not significantly affect the primary sex target tissues" (emphasis added).

Moreover, as stated on page 2, lines 6-9, "A **significant feature** of post-menopausal osteoporosis is the **large and rapid loss of bone mass** due to the cessation of estrogen production by the ovaries" (emphasis added). On the one hand there is a specific form of bone loss encountered in post-menopausal osteoporosis, which is not shared by each patient suffering from bone loss, and on the other hand bone loss is not the only feature of post-menopausal osteoporosis.

2.5 Therefore, the application as originally filed discloses the technical effect of prevention of bone loss, which is not identical to the prevention of post-menopausal osteoporosis in a post-menopausal woman, as can be inferred from the following passage: "The benzothiophenes of formula I are able to antagonize classical estrogenic responses in primary sex target tissues **without significantly reducing bone density** when given **to intact or estrogen treated animals**, and they **prevent bone loss in estrogen deficient animals**. This dichotomy indicates selective agonist/antagonist actions on specific target cells which would appear to be highly desirable **in treatment of menopausal syndrome**" (page 6, lines 9-17) (emphasis added).

2.6 In view of the analysis above, the application as originally filed does not specifically disclose the prevention of post-menopausal osteoporosis in a postmenopausal woman.

2.7 Additionally, if taken in general terms, "Bone loss occurs in a **wide range of subjects**, including post-menopausal women, patients who have undergone

hysterectomy, patients who are undergoing or have undergone long-term administration of corticosteroids, patients suffering from Cushing's syndrome, and patients having gonadal dysgenesis" (page 1, lines 19-24) (emphasis added). Therefore, post-menopausal women are selected from a list of several possible options for the patients to be treated.

Even considering that raloxifene is disclosed as the most preferred compound of formula I (page 11, lines 10-13), apart from the selection and individualisation of the disease to be treated and the subgroup of patients, a further selection has also taken place in claim 1 of the main request, namely that concerning the form of the medicament as a tablet or capsule. The application as originally filed discloses that the compounds of formula I can be formulated with common excipients, diluents or carriers, "and formed into tablets, capsules, suspensions, powders and the like" (page 14, lines 17-20 of the application as originally filed. "The compounds can also be formulated as elixirs or solutions for convenient oral administration or as solutions appropriate for parenteral administration, for instance by intramuscular, subcutaneous or intravenous routes" (page 15, lines 9-13).

Further, on page 15, lines 20-24 it is stated: "The particular dosage of a compound of formula I required to treat or inhibit bone loss according to this invention will depend upon the severity of the disease, its route of administration, and related factors that will be decided by the attending physician". The application as originally filed does not single out



tablets and capsules in connection with the prevention and treatment of post-menopausal osteoporosis in a post-menopausal woman. On page 16, lines 9-13 it is stated that "It is also advantageous to administer such a compound by **the oral route to an aging human** (e.g. a post-menopausal female or a male showing evidence of bone loss by X-ray analysis)" (emphasis added). First of all, the oral route does not equate with the selection of tablets and capsules since other forms such as solutions and suspensions may also be possible. Moreover, the patient is identified as an aging human and there is no preference for post-menopausal women to be linked to a particular dosage form. The previously cited passage on page 16 of the application as originally filed ends with the following statement (lines 12-14): "For such purposes the following oral dosage forms are available". This is followed by a new section with the title "Formulations", in which several specific examples are disclosed with the proviso that "in the formulations which follow, "Active ingredient" means a compound of formula I" (page 16, lines 18-19 of the application as originally filed). Formulations 2, 3 4 and 5 relate to specific "Raloxifene capsules" in which the raloxifene is in the form of **raloxifene hydrochloride**. The tablets of formulations 6 and 7 relate to "an active ingredient", and table 1 on pages 21-22 lists **raloxifene as free base** and as **hydrochloride salt** (compounds 20 and 21). The capsules and tablets exemplified are not representative of any possible tablet or capsule containing raloxifene or a pharmaceutically acceptable salt thereof, but illustrate particular tablets and capsules. Additionally, suspensions are also exemplified (see end of page 19 and formulation 8 of the application as

originally filed). In the ovariectomized rat model for post-menopausal osteoporosis illustrated in example 1 of the application as originally filed, the rats are treated with raloxifene, **administered as the hydrochloride** (page 18, lines 6-7). Even if in example 3 of the application as originally filed it is stated (see page 41, line 5) that raloxifene was administered orally to the ovariectomized rats, there is no basis in examples 1 or 3 for the choice of the form of the medicament as tablet or capsule. As regards example 5, raloxifene was administered as the **hydrochloride** (page 45, lines 11-12) to a particular **subgroup of post-menopausal women**, namely those aged 45-60, receiving **oral capsule formulations** (page 46, lines 23-24).

Summarising, the examples concerning formulations illustrate specific formulations where the drug is present as hydrochloride salt, or as free base, but do not allow a generalisation to any tablet or any capsule. As regards the examples which concern the animal model for the treatment of post-menopausal osteoporosis, they do not provide any basis for the choice of tablets and capsules as the preferred form of the medicament. Finally, example 5 exclusively concerns the administration of the hydrochloride salt in the form of capsules.

- 2.8 Therefore, claim 1 includes technical information which is not directly and unambiguously derivable from the application as originally filed and singles out subject-matter which was not disclosed in an individualised manner in the application as originally

filed (this analysis applies *mutatis mutandis* to the PA and the GA).

Consequently, the main request fails on grounds pursuant to Article 100(c) EPC since claim 1 extends beyond the content of the application as originally filed and the parent and root applications as originally filed.

**Order**

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar:

The Chairman:

N. Maslin

U. Oswald