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**Datasheet for the decision  
of 22 July 2016**

**Case Number:** T 2547/12 - 3.3.04

**Application Number:** 10180447.4

**Publication Number:** 2266598

**IPC:** A61K38/29, A61P19/08

**Language of the proceedings:** EN

**Title of invention:**

Method of increasing bone toughness and stiffness and reducing fractures

**Applicant:**

Eli Lilly and Company

**Headword:**

Reducing bone fracture /ELI LILLY

**Relevant legal provisions:**

EPC Art. 54, 56, 76(1), 83, 84, 123(2)

**Keyword:**

Sole request: requirements of EPC met (yes)

**Decisions cited:**

**Catchword:**

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**Boards of Appeal**  
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Case Number: T 2547/12 - 3.3.04

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.04**  
**of 22 July 2016**

**Appellant:** Eli Lilly and Company  
(Applicant) Lilly Corporate Center  
Indianapolis, IN 46285 (US)

**Representative:** Marshall, Cameron John  
Carpmaels & Ransford LLP  
One Southampton Row  
London WC1B 5HA (GB)

**Decision under appeal:** **Decision of the Examining Division of the European Patent Office posted on 25 July 2012 refusing European patent application No. 10180447.4 pursuant to Article 97(2) EPC.**

**Composition of the Board:**

**Chairwoman** G. Alt  
**Members:** B. Claes  
M. Blasi

## Summary of Facts and Submissions

- I. The appeal lies from the decision of the examining division to refuse European patent application No. 10180447.4, published as EP-A-2 266 598, having the title "*Method of increasing bone toughness and stiffness and reducing fractures*".
- II. The application is a divisional application of 06027055.0 (published as EP-A-1 769 804), which in turn is a divisional application of 02079227.1 (published as EP-A-1 295 605), which in turn is a divisional application of 99942350.2 (EP-A-1 059 933, filed as international application published as WO 00/10596). The description and drawings of all four applications are identical.
- III. In the decision under appeal the examining division considered a main request and six auxiliary requests and ruled that the claims of all requests lacked compliance with the requirements of novelty (Article 54 EPC), inventive step (Article 56 EPC), clarity (Article 84 EPC) and/or that their subject-matter extended beyond the content of the earlier application and/or the application as filed (Article 76(1) and/or Article 123(2) EPC). The examining division held in particular that claim 1 of auxiliary request 6 did not comply with the requirements of Article 76(1) EPC. It held that the dose of 20 µg/day could not be taken out of the context of example 3 of the application without adding matter.

Claim 1 of auxiliary request 6 read:

"1. Human PTH(1-34) for use in preventing or reducing the incidence of vertebral and/or non-vertebral

fracture in a human with or at risk of progressing to osteoporosis, wherein the PTH(1-34) is administered by subcutaneous injection at a dose of 20 µg/day."

- IV. With the statement of grounds of appeal the applicant (appellant) re-submitted the six auxiliary requests considered by the examining division in the decision under appeal as main request and auxiliary requests 1 to 5 and filed new auxiliary requests 6 to 8.
- V. Observations under Article 115 EPC dated 7 April 2014 were received stating that none of the requests pending before the board complied with the requirements of Articles 76(1) and 123(2) EPC as well as those of Articles 83 and 84 EPC. The appellant replied to the observations under Article 115 EPC with a letter dated 26 August 2014.
- VI. In a communication pursuant to Article 15(1) RPBA, annexed to the summons to oral proceedings, the board expressed its preliminary view that claim 1 of all pending requests failed to comply with the requirements of Article 123(2) EPC. The same finding applied *mutatis mutandis* to certain further independent claims of the requests. The board furthermore raised concerns on the clarity of the certain claims (Article 84 EPC).
- VII. The appellant made further written submissions in response to the communication of the board and filed seven further auxiliary requests.
- VIII. During the oral proceedings, which took place on 22 July 2016, the appellant withdrew all pending claim requests and submitted a new sole request, *i.e.* fifteen replacement pages of the description as filed and four claims. The claims read:

"1. Human PTH(1-34) for use in preventing or reducing the incidence of vertebral and non-vertebral fracture in a human with or at risk of progressing to osteoporosis, wherein the PTH(1-34) is administered by subcutaneous injection at a dose of 20 µg/day, wherein the human also receives effective doses of calcium and vitamin D.

2. Human PTH(1-34) for use according to claim 1, wherein the human is a woman.

3. Human PTH(1-34) for use according to claim 2, wherein the woman is a postmenopausal woman.

4. Human PTH(1-34) for use according to any preceding claim, wherein the PTH(1-34) is administered as a stabilized solution including a stabilizing agent, a buffering agent and a preservative."

At the end of the oral proceedings the chairwoman announced the decision.

IX. The appellant requested that the decision under appeal be set aside and that the case be remitted to the examining division with the order that a patent be granted on the basis of the set of claims filed at the oral proceedings, and the amended description.

## **Reasons for the Decision**

1. The appeal is admissible.

*Added subject-matter (Articles 76(1) and 123(2) EPC)*

2. Example 3 of the application as filed relates to a clinical study in which recombinant human parathyroid hormone (PTH) (1-34) was administered subcutaneously at a dose of *inter alia* 20 µg/day to postmenopausal women and wherein the treatment was supplemented with vitamin D and calcium. The results of the study are displayed in Tables 15 to 19 demonstrating the effect of the PTH(1-34) treatment on the number and severity of vertebral and non-vertebral fractures, bone mineral content and density as well as bone area. Reference is made in particular to the title of the example on page 46 and parts of the "Discussion" section of the example on page 51, lines 20 to 21; page 52, lines 16 to 18, lines 22 to 26 and line 30 to page 53, line 4, which frame the results of the experiment in a general context in relation to human patients, as opposed to female patients of a particular age, and independent of the duration of the treatment.
3. In view of the above considerations, the board is satisfied that the features of claims 1 to 4 are disclosed in this example and the subject-matter does not constitute an intermediate generalisation of the disclosure. The board judges therefore that the application as amended complies with the requirements of Articles 76(1) and 123(2) EPC.

*Sufficiency of disclosure, support, clarity (Articles 83 and 84 EPC)*

4. The board has no objections to the clarity of the terms of the present claims nor to sufficient support and disclosure of the claimed invention in the application. The board considers furthermore that the description as amended does not introduce new issues to be considered in this respect.
5. Accordingly, the board judges that the requirements of Articles 83 and 84 EPC are fulfilled.

*Novelty (Article 54 EPC)*

6. The board is satisfied that none of the prior art documents cited disclose the administration of human PTH(1-34) at a dose of 20 µg/day supplemented with calcium and vitamin D for the prevention or reduction of vertebral and non-vertebral fracture in human patients. Accordingly, the claimed subject-matter is novel in accordance with Article 54 EPC.

*Inventive step (Article 56 EPC)*

7. Claim 1 relates to the prevention or reduction of the incidence of vertebral and non-vertebral fracture in a human with or at risk of progressing to osteoporosis. The effect is obtained by subcutaneous injection of human PTH(1-34) at a dose of 20 µg/day whereby the patient also receives effective doses of calcium and vitamin D.
8. Document D8 (Lindsay *et al* (1997), *The Lancet*, Vol. 350, pages 550-555) discloses a three year randomised controlled study of the effect of PTH on



vertebral bone mass and fracture incidence among postmenopausal women who suffer from osteoporosis and receive hormone replacement therapy (oestrogen). Human PTH(1-34) was administered subcutaneously at a dose of 25 µg/day to 17 of the 34 patients taking part in the study. In the discussion section the document reports that the observed effect of the studied PTH(1-34) treatment was most prominent in the spine in these osteoporotic postmenopausal women taking hormone replacement therapy (see page 554, left-hand column, lines 8 to 10), *i.e.* significantly fewer vertebral fractures were found in the PTH-treated group (see Table 4 and page 554, right-hand column, lines 11 to 16). At page 554, right-hand column, lines 18 to 21 document D8 continues that the observed anabolic effects of PTH were significantly lower in the total hip region and forearm, but that there was no evidence, however, of a detrimental effect of PTH at these sites as previously suggested as bone mass was at least preserved at these sites. It had in this respect "*been suggested that PTH may increase vertebral bone mass at the expense of cortical bone by inducing increased intracortical and perhaps endocortical-junction remodelling, leading to weakened bone at primarily cortical sites.*" (see page 554, right-hand column, lines 31 to 34).

9. The board is satisfied that the disclosure in document D8 represents the closest prior art for the assessment of inventive step as it discloses the effects of the administration of human PTH(1-34) in a daily dose to osteoporotic patients on the incidence of vertebral and non-vertebral fracture in these patients.
10. As compared to the disclosure in document D8 and in accordance with the invention of claim 1, a lower dose

of PTH(1-34) is administered daily (*i.e.* 20 µg rather than 25 µg) and the patients further receive an effective dose of vitamin D and calcium. The technical effect of these differences is that both the incidence of vertebral *and* non-vertebral fracture in these patients was reduced (see example 3, in particular the sentence bridging pages 52 and 53 and Tables 15 and 16 of the application as filed).

11. Accordingly, starting from the disclosure in document D8, the problem to be solved may be formulated as the provision of an improved therapy for the prevention or reduction of the incidence of vertebral fractures in osteoporotic patients whereby also non-vertebral fracture incidence is prevented or reduced.
12. Neither document D8, representing the closest prior art, nor any of the other prior art documents on file suggest to the skilled person that by reducing the daily dose of PTH(1-34) and combining the therapy with effective doses of calcium and vitamin D this problem can be solved. The subject-matter of the claims can therefore not be considered as having been obvious to the skilled person.
13. In view of the above considerations the board judges that the subject-matter of claim 1 to 4 involves an inventive step (Article 56 EPC).

## Order

### For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the examining division with the order to grant a patent in the following version:
  - Claims 1 to 4 of the sole claim request, as filed at the oral proceedings,
  - Description: pages 2, 12, 15 to 29, 31 to 46 and 48 to 52 of the application as filed, pages 1, 3 to 11, 13, 14, 30, 47 and 53 as filed at the oral proceedings,
  - Drawings: Sheets 1 - 10 of the application as filed.

The Registrar:

The Chairwoman:



P. Cremona

G. Alt

Decision electronically authenticated