

Internal distribution code:

- (A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

**Datasheet for the decision
of 14 June 2018**

Case Number: T 0765/12 - 3.3.01

Application Number: 05750580.2

Publication Number: 1768748

IPC: A61P19/10

Language of the proceedings: EN

Title of invention:

COMPOSITIONS COMPRISING STRONTIUM AND VITAMIN D AND USES
THEREOF

Patent Proprietor:

Mokwalo Pharma S.A.

Opponent:

Osteologix Inc.

Headword:

Strontium/MOKWALO

Relevant legal provisions:

EPC Art. 56

Keyword:

Inventive step - (yes)



Beschwerdekammern
Boards of Appeal
Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 0765/12 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 14 June 2018

Appellant: Mokwalo Pharma S.A.
(Patent Proprietor) 9, Place de Clairefontaine
1341 Luxembourg (LU)

Representative: Høiberg P/S
Adelgade 12
1304 Copenhagen K (DK)

Respondent: Osteologix Inc.
(Opponent) 4415 Cox Road
Glen Allen VA 23060 (US)

Representative: Hjelmencrantz, Anders
Chas. Hude A/S
H.C. Andersens Boulevard 33
1780 Copenhagen V (DK)

Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 31 January 2012
revoking European patent No. 1768748 pursuant to
Article 101(3) (b) EPC**

Composition of the Board:

Chairman A. Lindner
Members: M. Pregetter
L. Bühler

Summary of Facts and Submissions

I. European patent No. 1768748 is based on European patent application No. 05750580.2, filed as an international application published as WO2006/000224.

II. The following documents, cited during the opposition and appeal proceedings, are referred to below:

(6) Gryn timer et al., Bone, 1990, 11, 313-319

(7) Creger et al., Calc. Tis. Res. 1971, 8(1), 83-86

(15) Rodan et al., Science, 2000, 289, 1508-1514

(16) Skoryna et al., Trace substances in environmental health XIX, edited by D.D. Hemphill, University of Missouri, Columbia, Missouri, 1985, pp. 193-208

III. Claim 1 of the main request, filed with a letter dated 11 April 2018 as auxiliary request I and corresponding to the main request submitted with the statement setting out the grounds of appeal, reads as follows:

"1. A pharmaceutical composition comprising only two strontium salts, wherein said strontium salts consists (sic) of strontium carbonate and strontium chloride for oral administration in the form of a tablet, a capsule, or a dissolvable tablet."

Claims 8, 16, 17 and 21 read as follows:

"8. Use of the pharmaceutical composition according to any of the previous claims for the manufacture of a medicament for the prevention or treatment of cartilage or bone disorders/diseases."

"16. A pharmaceutical composition according to any of the previous claims 1-7 for use in a method of treatment."

"17. The pharmaceutical composition according to claim 16, wherein the method of treatment is treatment or prevention of a cartilage or bone disorder/disease."

"21. A kit of part comprising:

i) The pharmaceutical composition according to any one of claims 1-7 and
ii) a medicament comprising at least one calcium salt wherein the compositions i) and ii) are discrete units."

- IV. The patent proprietor (appellant) filed notice of appeal against the opposition division's decision to revoke the patent in suit, inter alia for lack of inventive step.
- V. Oral proceedings were held in the absence of the duly summoned respondent (opponent).
- VI. The appellant's arguments where relevant to the present decision may be summarised as follows:

The claims of the main request corresponded substantially to the set of claims of auxiliary request I of the opposition proceedings. For this set of claims the opposition division had acknowledged compliance with Articles 123, 84 and 54 EPC.

Osteoporosis was characterised by a general loss of bone density leading to increased fracturing of the bones from minimal trauma. The closest prior art was

document (6). It described an in vivo experiment performed on weaning rats in natural growth which were administered strontium chloride while on a low-calcium diet. Several measurements were performed and divergent results were obtained. Document (6) showed an increase in bone volume and "mineralization lag time". Osteoid thickness too was increased. A shift in mineralisation profile towards lower-density fractions was observed. The increase in bone volume was due to an increase in osteoid volume which was not aimed at in the treatment of osteoporosis. The skilled person would thus believe that the administration of strontium chloride would not be useful for the treatment of osteoporosis. The problem to be solved was how to provide an improved treatment for osteoporosis. It was not obvious that the combination of strontium chloride and strontium carbonate led to increased bone mineral density while having no side-effects. Also, the improved solubility of the combination of strontium salts was not obvious. Furthermore, document (6) provided no incentive to add strontium carbonate to the composition. An inventive step was to be acknowledged.

VII. The respondent's written arguments where relevant to the present decision may be summarised as follows:

Osteoporosis was a well-known disease caused by an imbalance between bone formation and bone resorption (see document (15)). As document (6) found reduced bone resorption (expressed as the activity of the osteoclasts) and the promotion of bone formation (enhanced number of osteoblasts) due to the administration of strontium chloride, it was the most promising starting point for the assessment of inventive step. Document (6) clearly mentioned that the deleterious effects of strontium could be avoided by

combining strontium chloride with calcium. It was even stated in document (6), page 317, right column, that under such conditions "osteoid tissue could mineralize properly which could lead to a marked elevation of bone density". The technical problem was how to provide a further strontium composition. It was known from documents (7) and (16) that strontium carbonate had effects on bone formation and could be used in the treatment of osteoporosis. The combination of the two strontium salts was thus obvious and consequently no inventive step could be acknowledged.

VIII. The parties' requests were as follows:

The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the claims of the main request or, alternatively, of the auxiliary request, filed with the letter dated 11 April 2018 as auxiliary requests I and II, respectively.

The respondent (opponent) had requested in writing that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.
2. In accordance with Rule 115(2) EPC, oral proceedings were conducted in the absence of the duly summoned respondent. In accordance with Article 15(3) RPBA the respondent has been treated as relying on its written case.

3. *Main request*

3.1 As its sole objection the respondent raised an objection of lack of inventive step against the set of claims filed together with the statement setting out the grounds of appeal, which corresponds to the present main request.

No objections under Articles 123(2) and (3), 83, 84 and 54 were raised by the respondent or are derivable from the decision under appeal, and the board sees no reason to raise objections of its own motion.

3.2 *Inventive step*

The present invention relates to pharmaceutical compositions intended for use in the treatment of cartilage and bone disorders, especially for use in the treatment of osteoporosis (paragraphs [0001] and [0009]). Specific strontium salts are used to provide an active ingredient having high availability and fewer side-effects (paragraph [0012]). In particular, the combination of strontium chloride and strontium carbonate has been found to be advantageous (paragraph [0050], examples 2 to 4, 6, 7, 11, 12 and 17, claims 5 to 8 as granted).

During the opposition proceedings and in appeal proceedings the only document discussed as the closest prior-art document and thus as a promising starting point for the skilled person is document (6).

The title of document (6) is "Effects of Low Doses of Strontium on Bone Quality and Quantity in Rats". In the abstract it is stated that strontium has been shown to increase bone mass when given at low doses (abstract,

first and last sentences). However, the information gained from the experimental section of document (6) does not support such a finding:

The data of table I relate to body weight and give indications of tibia and femur length; bone mass is not determined. Table II provides detailed information on bone volume, but without clarifying the mineralised bone content, thus making it impossible to determine effects on bone mass. From table III it can be learnt that the only significant increase lies in the "mineralization lag time". Figures 1 and 2 present mineralisation profiles of femur diaphyses and vertebrae. It is not indicated whether the differences in values are significant. It is thus unclear whether an actual shift towards lower bone density fractions is present. Table IV provides the information that a parameter concerning bone resorption (% endosteal surface covered by chondroclast and osteoclast surface) is significantly changed at 4 weeks of treatment, whereas no change is seen at 8 weeks of treatment. The data given in tables V and VI indicate that the mineralisation type (bone material includes less carbonate) and the bone crystals (X-ray diffraction data show shorter crystal length) are changed due to the administration of strontium chloride.

The experimental findings of document (6) are then analysed in view of other referenced scientific articles (pages 317 and 318). It seems to be clear from this discussion that bone mineralisation is negatively affected by the administration of strontium, whereas osteoblast surface is not diminished (page 317, left column, last paragraph). These findings lead the authors of document (6) to speculate about the influence of a possible calcium supplementation (page

317, right column, first paragraph, last seven lines).

In sum, from the data provided by document (6), which partly show non-significant findings, it is not clear how strontium, especially strontium chloride, will influence bone and cartilage disorders, specifically those that require strengthening of the bone material. Document (6) merely conveys the message that administration of strontium chloride may affect bone formation and resorption.

The problem underlying the patent in suit must thus be formulated as how to provide a composition for the treatment of bone and cartilage disorders.

The proposed solution is the provision of tablets, capsules or dissolvable tablets comprising strontium chloride and strontium carbonate.

Starting from document (6) the skilled person might have considered conducting further tests relating to the use of strontium chloride in the treatment of cartilage and bone disorders. The skilled person could, for example, take up the suggestion of document (6) to investigate the action of strontium chloride on bones when given in combination with a calcium supplement. There is however no straightforward and clear teaching in document (6) on a direct link between the administration of strontium chloride and physiologically significant effects on bone. It is thus not possible to assert that the skilled person would have administered strontium chloride in the hope of successfully treating a bone or cartilage disease. Since it cannot be clearly established what action the skilled person would have taken when considering document (6), it is not necessary to establish whether

the skilled person would have added a further strontium salt, particularly in the form of strontium carbonate, to the tablets, capsules or dissolvable tablets for administration to a patient suffering from a bone- or cartilage-related disease.

The subject-matter of claim 1 is thus not obvious when starting from document (6) as the closest prior art.

The same line of argument applies mutatis mutandis to the subject-matter of independent claims 8, 16, 17 and 21, which also involve an inventive step when starting from document (6) as the closest prior art.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the opposition division with the order to maintain the patent as amended in the following version:

Claims:

claims 1 to 22 of the main request filed as auxiliary request I with the letter dated 11 April 2018

Description:

pages 1 to 45 of the description received during the oral proceedings on 14 June 2018

Drawing:

sheet 1 of the patent specification

The Registrar:

The Chairman:



M. Schalow

A. Lindner

Decision electronically authenticated