

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BAXTER HEALTHCARE CORP., APATECH, INC.,
AND APATECH LIMITED
Petitioners

v.

MILLENIUM BIOLOGIX, LLC
Patent Owner

Case IPR2013-00591
Patent 6,585,992

Before MICHELLE R. OSINSKI, SCOTT E. KAMHOLZ, and
BRIAN P. MURPHY, *Administrative Patent Judges*.

OSINSKI, *Administrative Patent Judge*.

DECISION

Denying Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

A. Background

Baxter Healthcare Corp. et al. (“Petitioners”) filed a petition (Paper 1, “Pet.”) requesting an *inter partes* review of claims 1, 2, 4, 9, 11, 16-18, 20, 25, 26, 36, 38, 43, and 44 of U.S. Patent No. 6,585,992 (Ex. 1001, “the ’992 patent”). Millenium Biologix, LLC (“Patent Owner”) filed a preliminary response (Paper 7, “Prelim. Resp.”). The Board has jurisdiction under 35 U.S.C. § 314. The standard for instituting an *inter partes* review is set forth in 35 U.S.C. § 314(a), which provides as follows:

THRESHOLD—The Director may not authorize an *inter partes* review to be instituted unless the Director determines that the information presented in the petition filed under section 311 and any response filed under section 313 shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.

We determine that the record before us does not demonstrate that there is a reasonable likelihood that Petitioners would prevail with respect to at least one challenged claim of the ’992 patent on the grounds in this petition. Consequently, we deny the petition and decline to institute an *inter partes* review of claims 1, 2, 4, 9, 11, 16-18, 20, 25, 26, 36, 38, 43, and 44 of the ’992 patent on the grounds in this petition.

B. Additional Proceedings

In addition to the petition filed in this proceeding, Petitioners filed another petition challenging the patentability of the same claims of the '992 patent on different grounds. *See* IPR2013-00590.

C. Related Proceedings

The parties represent that the '992 patent is involved in a civil action alleging infringement of the '992 patent, *Millenium Biologix, LLC v. Baxter Healthcare Corp.*, No. 1:13-cv-03084 (N.D. Ill.), filed April 24, 2013.

D. The '992 Patent

The '992 patent relates to methods of using a synthetic biomaterial compound comprising calcium, oxygen, and phosphorous, wherein a portion of at least one of these elements is substituted with an element having an ionic radius of approximately 0.1 to 0.6 Å. Ex. 1001, Abstr., 5:48-6:56. The synthetic biomaterial compound is “essentially insoluble in biological media but is resorbable when acted upon by osteoclasts.” *Id.* at 4:64-66. The compound “can be assimilated into natural bone during the natural course of bone remodeling through the activity of osteoclasts and osteoblasts.” *Id.* at 4:67-5:2. The compound has an interconnected microporosity and a globular morphology. *Id.* at 4:40-44; 11:7-11; 20:5-22. The size of particles comprising the microporous structure can range from about 0.1 to 2.0 μm. *Id.* at 13:14-17. One of the substituting elements having an appropriate ionic radius is silicon, resulting in silicon-substituted calcium phosphate created by substitution of silicon at phosphorous sites. *Id.* at 16:63-67.

The synthetic biomaterial compound can be prepared from a colloidal suspension (sol-gel) of calcium phosphate produced by mixing a calcium nitrate tetrahydrate and ammonium dihydrogen orthophosphate. *Id.* at 26:50-27:35. The compound can be prepared using the sol-gel as a thin film on a quartz substrate. *Id.* at 28:7-37. Alternatively, the compound can be prepared as a powder with a silicon additive that is introduced as a sol-gel metal-organic precursor in an organic carrier. *Id.* at 28:61-63. The precursor can be tetrapropyl orthosilicate or tetraethyl orthosilicate. *Id.* at 28:63-65. The preparation of the compound includes a sintering step at temperatures of about 1000°C. *Id.* at 28:30-33; 29:10-13. The synthetic biomaterial compound can be manufactured in many forms, one of which is a macroporous structure that can “serve as a scaffold for the integration of new bone tissue.” *Id.* at 22:21-22. “The macroporous structure is formed by the coating of the compound onto a reticulated polymer and subsequently removing the polymer through pyrolysis.” *Id.* at 22:23-26; *see* 29:65-30:29. The macroporous structure has interconnected voids having a pore size of approximately 50 to 1000 microns. *Id.* at 22:26-28.

E. Independent Claims

The challenged independent claims 1, 2, and 4 are illustrative of the claimed subject matter and are reproduced below.

1. A method for substituting natural bone at sites of skeletal surgery in human and animal hosts with a biomaterial compound comprising calcium, oxygen and phosphorous, wherein a portion of at least one of said elements is substituted with an element having an ionic radius of approximately 0.1 to 0.6 Å;
said method comprising the steps of:

implanting said biomaterial compound at the site of skeletal surgery wherein such implantation promotes the formation of new bone tissue at the interfaces between said biomaterial compound and said host, the progressive removal of said biomaterial compound primarily through osteoclast activity, and the replacement of that portion of said biomaterial compound removed by further formation of new bone tissue by osteoblast activity, such progressive removal and replacement being inherent in the natural bone remodeling process.

2. A method for repairing large segmental skeletal gaps and non-union fractures arising from trauma or surgery in human and animal hosts using a biomaterial compound comprising calcium, oxygen and phosphorous, wherein a portion of at least one of said elements is substituted with an element having an ionic radius of approximately 0.1 to 0.6 Å;

said method comprising the steps of:

implanting said biomaterial compound at the site of the segmental skeletal gap or non-union fracture wherein such implantation promotes the formation of new bone tissue at the interfaces between said biomaterial compound and said host, the progressive removal of said biomaterial compound primarily through osteoclast activity, and the replacement of that portion of said biomaterial compound removed by further formation of new bone tissue by osteoblast activity, such progressive removal and replacement being inherent in the natural bone remodeling process.

4. A method for providing tissue-engineering scaffolds for bone replacement in human or animal hosts using a biomaterial compound comprising calcium, oxygen and phosphorous, wherein a portion of at least one of said elements is substituted with an element having an ionic radius of approximately 0.1 to 0.6 Å;

said method comprising the steps of:

forming said biomaterial compound as a macroporous structure comprising an open cell construction with interconnected voids, combining mature and/or precursor bone

cells with said macroporous structure, and allowing the cells to infiltrate said structure in order to develop new mineralized matrix throughout said structure.

F. Prior Art Relied Upon in the Petition

Petitioners rely upon the following references, as well as the declaration of Dr. Antonios G. Mikos (Ex. 1003):

Leshkivich	4 J. MATER. SCI. 86	1993	Ex. 1013
Layrolle	6 PHOS. RES. BULL. 63	1996	Ex. 1018
Bigi	66 J. INORGANIC BIOCHEM. 259	1997	Ex. 1019
Hench	PROC. OF THE 7 TH INT'L. SYMP. ON CERAMICS IN MED. 3	1994	Ex. 1020
Bioceramics	1 INTRO. BIOCERAMICS 41:103; 139: 221	1993	Ex. 1021
Lynch	US 5,306,303	Apr. 26, 1994	Ex. 1026
Ohgushi	24 J. BIOMED. MAT. RES. 1563:1570	1990	Ex. 1073
Chaki	5 J. MAT. SCI.: MAT IN MED. 533:542	1994	Ex. 1130

G. The Asserted Grounds of Unpatentability

Petitioners assert that the challenged claims are unpatentable based on the following grounds:

Reference(s)	Basis	Claims challenged
Bigi, Hench, and Lynch	§ 103	1, 2, 9, 11, 16, 18, 20, 25
Bigi, Hench, Bioceramics, and Ohgushi	§ 103	4, 36, 38
Bigi, Hench, Bioceramics, Ohgushi, and Lynch	§ 103	43
Bigi, Hench, Lynch, and Chaki	§ 103	17, 26
Bigi, Hench, Bioceramics, Ohgushi, Lynch, and Chaki	§ 103	44
Layrolle, Hench, and Lynch	§ 103	1, 2, 9, 11, 16, 18, 20, 25
Layrolle, Hench, Bioceramics, and Ohgushi	§ 103	4, 36, 38
Layrolle, Hench, Bioceramics, Ohgushi, and Lynch	§ 103	43
Layrolle, Hench, Lynch, and Chaki	§ 103	17, 26
Layrolle, Hench, Bioceramics, Ohgushi, Lynch, and Chaki	§ 103	44
Leshkivich, Bigi, and Lynch	§ 103	1, 2, 9, 11, 16, 18, 20, 25
Leshkivich, Bigi, Bioceramics, and Ohgushi	§ 103	4, 36, 38
Leshkivich, Bigi, Hench, Bioceramics, Ohgushi, and Lynch	§ 103	43
Leshkivich, Bigi, Lynch, and Chaki	§ 103	17, 26
Leshkivich, Bigi, Bioceramics, Ohgushi, Lynch, and Chaki	§ 103	44

II. DISCUSSION

A. Effective filing date of the '992 patent

Petitioners argue that, although the '992 patent claims the benefit of an earlier international application filing date, the international application fails to support the challenged claims with adequate written description. Pet. 9-10. The '992 patent is a divisional of an application that claims priority to PCT/CA96/00585, published as WO97/09286 (Ex. 1017 (“Pugh”)), through a chain of continuation-in-part applications. Ex. 1001, 1:8-14. Pugh was filed August 30, 1996 and published March 13, 1997. Ex. 1017. Application 09/044,749, which led to the issuance of original U.S. Patent No. 6,324,146 prior to reissuance as RE 41,251, was filed on March 19, 1998. Ex. 1001.

Claims 1, 2, and 4 require a portion of at least one of the compound elements (Ca, O, or P) to be “substituted” with silicon. Petitioners argue that because Pugh does not disclose silicon substitution *per se* but rather discloses silicon stabilization, the challenged '992 patent claims are not entitled to Pugh’s August 30, 1996 priority date. Pet. 9-10. Petitioners rely on evidence that Patent Owner distinguished Pugh from then-pending claim 1 during prosecution by arguing that Pugh did not teach or suggest “substitution” but only taught “stabilization” of an alpha-TCP compound. *Id.* (citing Ex. 1009, 202; Ex. 1003 ¶¶ 323-325). Petitioners argue that because the concept of “substitution” was not included in Pugh, Pugh does not provide sufficient written description support for an August 30, 1996 priority date. *Id.*

Patent Owner notes an inconsistency in Petitioners’ position, given Petitioners’ argument in IPR2013-00590 to the effect that Pugh discloses each and

every element of the challenged claims and, therefore, anticipates those claims. Prelim. Resp. 2 (*see* IPR2013-590 Pet. 19-24). With regard to its supposed admission during prosecution that Pugh does not disclose “substitution,” Patent Owner explains that the claims then pending were materially different from those now challenged. Prelim. Resp. 9-17. In particular, then-pending claim 1 was broad enough to include substitution “with an element having an ionic radius of approximately 0.1 to 1.1 Å,” and this claim limitation included a range of stabilizing elements beyond those disclosed in Pugh. Ex. 1009, 62, 182-84; Prelim. Resp. 14-15; *cf.* Ex. 1001, 32:15-45, Table 2. Patent Owner also argues that statements made during prosecution are irrelevant to an inquiry into adequate written description, which is limited to the four corners of the application as of the filing date. Prelim. Resp. 2-3, 26-27 (citing *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed Cir. 2010) (en banc) (“[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.”)).

Petitioners’ argument and evidence do not persuade us that it is likely to prevail in showing that claims 1, 2, 4, 9, 11, 16-18, 20, 25, 26, 36, 38, 43, and 44 of the ’992 patent are not entitled to the benefit of Pugh’s filing date.

As a first matter, we emphasize the inconsistency of Petitioners’ argument here with their argument in IPR2013-00590, and do not see the logic of how Pugh could be an anticipatory reference disclosing each and every claim limitation in claims 1, 9, and 11, if Pugh fails to disclose the substitution limitation required by independent claim 1. We also are persuaded by Patent Owner’s argument. The claims at issue at the time of the prosecution argument in question were of materially broader scope than the claims now challenged, were rejected on a basis

different than the grounds of unpatentability proffered by Petitioners, and were amended during subsequent prosecution of the '749 application and during reissue proceedings. Therefore, even if we were to consider such evidence outside the four corners of the Pugh application, it would be of little probative value, given the materially different claim scope and basis for rejection of the prosecution claims.

For the foregoing reasons, we conclude that Petitioners have not demonstrated that claims 1, 2, 4, 9, 11, 16-18, 20, 25, 26, 36, 38, 43, and 44 are not entitled to the August 30, 1996, priority filing date of Pugh.

B. Obviousness of: claims 1, 2, 4, 9, 11, 16, 18, 20, and 25 under Bigi, Hench, and Lynch; claims 4, 36, and 38 under Bigi, Hench, Bioceramics, and Ohgushi; claim 43 under Bigi, Hench, Bioceramics, Ohgushi, and Lynch; claims 17 and 26 under Bigi, Hench, Lynch, and Chaki; and claim 44 under Bigi, Hench, Bioceramics, Ohgushi, Lynch, and Chaki; claims 1, 2, 4, 9, 11, 16, 18, 20, and 25 under Leshkivich, Bigi, and Lynch; claims 4, 36, and 38 under Leshkivich, Bigi, Bioceramics, and Ohgushi; claim 43 under Leshkivich, Bigi, Bioceramics, Ohgushi, and Lynch; claims 17 and 26 under Leshkivich, Bigi, Lynch, and Chaki; and claim 44 under Leshkivich, Bigi, Bioceramics, Ohgushi, Lynch, and Chaki

Bigi bears a publication date of 1997 on the face of the reference. Ex. 1019, 1. Petitioners assert that Bigi is prior art because it was published before March 1998.¹ Pet. 19. Patent Owner argues that Bigi is not prior art because the '992 patent claims being challenged are entitled to the benefit of Pugh's August 30, 1996 filing date. Prelim. Resp. 1-3, 9-16, 23-28, 35. As discussed above, Petitioners have not demonstrated that claims 1, 2, 4, 9, 11, 16-18, 20, 25, 26, 36,

¹ Petitioners acknowledge that the '992 patent is entitled to a priority date as early as March 1998. *See, e.g.*, Pet. 19.

38, 43, and 44 are not entitled to the benefit of Pugh's priority filing date. Petitioners have not demonstrated, therefore, that Bigi is available as prior art under any section of pre-AIA 35 U.S.C. § 102. Because Bigi is necessary to the above-referenced grounds of unpatentability asserted by Petitioners, we deny the petition as to these grounds.

C. Obviousness of: claims 1, 2, 4, 9, 11, 16, 18, 20, and 25 under Layrolle, Hench, and Lynch; claims 4, 36, and 38 under Layrolle, Hench, Bioceramics, and Ohgushi; claim 43 under Layrolle, Hench, Bioceramics, Ohgushi, and Lynch; claims 17 and 26 under Layrolle, Hench, Lynch, and Chaki; and claim 44 under Layrolle, Hench, Bioceramics, Ohgushi, Lynch, and Chaki

Layrolle bears a publication date of 1996 on the face of the reference. Ex. 1018, 1. Petitioners assert that Layrolle is prior art because it was published before March 1998. Pet. 39 (citing Ex. 1003, ¶ 485). Patent Owner argues that Layrolle is not prior art because the '992 patent claims being challenged are entitled to the benefit of Pugh's August 30, 1996 filing date. Prelim. Resp. 1-2. In particular, Patent Owner argues that Layrolle "has a publication date of 1996 with no further month or day detail. Petitioners have presented no evidence as to why Layrolle could be considered prior art to claims with a priority date of August 1996." *Id.* We agree with Patent Owner.

First, as discussed above, Petitioners have not demonstrated that claims 1, 2, 4, 9, 11, 16-18, 20, 25, 26, 36, 38, 43, and 44 are not entitled to the benefit of Pugh's August 30, 1996 priority filing date. Second, Petitioners have not demonstrated that the date on which Layrolle became accessible to the public was before Pugh's filing date. In particular, Petitioners have presented no evidence of when Layrolle was accessible to the public, except for the inclusion of "1996" on

the face of the reference, which spans a period of time both before and after Pugh's priority filing date of August 30, 1996. Ex. 1018, 1. Given the evidence of record, we have no basis on which to conclude that Layrolle was publicly accessible before Pugh's August 30, 1996 filing date. *See In re Lister*, 583 F.3d 1307, 1316-17 (Fed. Cir. 2009) ("Absent evidence of the date that the disclosure was publicly posted, if the publication itself does not include a publication date (or retrieval date), it cannot be relied upon as prior art under 35 U.S.C. 102(a) or (b)"). Petitioners have not demonstrated, therefore, that Layrolle is available as prior art under any section of pre-AIA 35 U.S.C. § 102. Because Layrolle is necessary to the above-referenced grounds of unpatentability asserted by Petitioners, we deny the petition as to these grounds.

III. CONCLUSION

Petitioners have not shown that there is a reasonable likelihood that they would prevail with respect to at least one of the claims challenged in the petition based on the grounds asserted therein. The petition is, therefore, denied.

IV. ORDER

For the reasons given, it is ORDERED that the Petition challenging the patentability of claims 1, 2, 4, 9, 11, 16-18, 20, 25, 26, 36, 38, 43, and 44 of the '992 patent is *denied*.

Case IPR2013-00591
Patent 6,585,992

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