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Paper 9
Entered: March 21, 2014

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 IPR2013-00590
Patent 6,585,992

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

OSINSKI, *Administrative Patent Judge*.

DECISION

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 8, "Prelim. Resp."). 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 there is a reasonable likelihood that Petitioners would prevail with respect to claims 1, 2, 4, 9, 11, 16-18, 20, 25, 26, 36, 38, 43, and 44 of the '992 patent. Accordingly, we 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.

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* IPR2013-00591.

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 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 1000ºC. *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 pyrolosis." *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 Antonios G. Mikos (Ex. 1003):

Ruys '93a	42 INT'L CERAM. REV. 372:374	Dec. 1993	Ex. 1011
Ruys '93b	29 J. AUST. CERAM. 71:80	1993	Ex. 1014
Pugh	WO 97/09286	Mar. 13, 1997	Ex. 1017
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**
Pugh	§ 102	1, 9, 11
Pugh and Lynch	§ 103	1, 2, 9, 11, 16, 18, 20, 25
Pugh, Bioceramics, and Ohgushi	§ 103	4, 36, 38
Pugh, Bioceramics, Oghushi, and Lynch	§ 103	43
Pugh, Lynch, and Chaki	§ 103	17, 26
Pugh, Bioceramics, Ohgushi, Lynch, and Chaki	§ 103	44

Reference(s)	Basis	Claims challenged
Ruys '93a and Lynch	§ 103	1, 2, 9, 11, 16, 18, 20, 25
Ruys '93a, Bioceramics, and Ohgushi	§ 103	4, 36, 38
Ruys '93a, Bioceramics, Oghushi, and Lynch	§ 103	43
Ruys '93a, Lynch, and Chaki	§ 103	17, 26
Ruys '93a, Bioceramics, Ohgushi, Lynch, and Chaki	§ 103	44
Ruys '93b and Lynch	§ 103	1, 2, 9, 11, 16, 18, 20, 25
Ruys '93b, Bioceramics, and Ohgushi	§ 103	4, 36, 38
Ruys '93b, Bioceramics, Oghushi, and Lynch	§ 103	43
Ruys '93b, Lynch, and Chaki	§ 103	17, 26
Ruys '93b, Bioceramics, Ohgushi, Lynch, and Chaki	§ 103	44

II. DISCUSSION

A. Claim Construction

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,766 (Aug. 14, 2012). Claim terms are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art in the context of the

entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

1. *"biomaterial," "compound," and "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 and 0.6 Å"*

Although the parties propose differing constructions for these limitations, construction of these terms is not material to this decision. Consequently, we need not provide an express construction of these terms at this time.

2. *"implanting said biomaterial compound at the site of skeletal surgery," and "implanting said biomaterial compound at the site of the segmental skeletal gap or non-union fracture"*

Although Petitioners propose constructions of these limitations (Pet. 16-17), Patent Owner argues that the limitations need no construction in light of their straightforward nature (Prelim. Resp. 19-20). Again, construction of these terms is not material to this decision. Consequently, we need not provide an express construction of these terms at this time.

3. *"wherein" clauses of claims 1 and 2*

The parties propose constructions for various portions of the "wherein" clauses of claims 1 and 2. These clauses list various intended results of implanting the biomaterial compound at a specified site. They do not recite positive acts that are carried out as part of the claimed methods. Nor do they specify any limitation on the manner in which the "implanting" step is to be carried out. We determine, consequently, and for purposes of this decision, that they are to be given no patentable weight beyond requiring that the recited biomaterial compound be capable of producing the recited

intended results when implanted at the specified site. *See Minton v. Nat'l Ass'n of Sec. Dealers, Inc.*, 336 F.3d 1373, 1381 (Fed. Cir. 2003) (stating in a method claim, clause is not given weight when it simply expresses the intended result of a process step positively recited) (citing *Tex. Instruments Inc. v. U.S. Int'l Trade Comm'n*, 988 F.2d 1165, 1172 (Fed.Cir.1993))

B. Anticipation of claims 1, 9, and 11 by Pugh

Petitioners argue that, although the '992 patent claims the benefit of Pugh's filing date, Pugh is prior art to the challenged claims because it fails to support them with adequate written description. Pet. 9-10. The '992 patent is a divisional of a patent that claims priority to 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, 1:8-14.

Claim 1 requires 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 and should be considered § 102(b) art that anticipates the challenged claims. *Id*. at 9-10, 18-24, 33, 34.

Patent Owner emphasizes that Petitioners do not challenge Patent Owner's unbroken chain of claimed priority. Prelim. Resp. 2. 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. *Id*. at 9-11, 12-15. In particular, then-pending claim 1 was broad enough to include substitution "with an element having an ionic radius of approximately 0.1 to 1.1Å," 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, 25-26 (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 do not understand how Pugh could be an anticipatory reference that discloses each and every limitation in claims 1, 9, and 11, yet also 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 these reasons, we conclude that Petitioners have not demonstrated that Pugh is prior art to the '992 patent under 35 U.S.C. § 102(b). Accordingly, we decline to institute *inter partes* review of claims 1, 9, and 11 for anticipation by Pugh.

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

As described hereinabove, Petitioners have not made an adequate showing that Pugh is available as prior art under any section of pre-AIA 35 U.S.C. § 102. Because Pugh is necessary to the above-referenced grounds of unpatentability asserted by Petitioners, we decline to institute *inter partes* review of: claims 1, 2, 9, 11, 16, 18, 20, and 25 for obviousness over Pugh and Lynch; claims 4, 36, and 38 for obviousness over Pugh, Bioceramics, and Ohgushi; claims 17 and 26 for obviousness over Pugh, Lynch, and Chaki; and claim 44 for obviousness over Pugh, Bioceramics, Ohgushi, Lynch, and Chaki.

D. Obviousness of claims 1, 2, 9, 11, 16, 18, 20, and 25 over Ruys '93a and Lynch

1. Overview of Ruys '93a

Ruys '93a describes using a sol-gel process involving calcium nitrate ($Ca(NO_3)_2$) and diammonium hydrogen phosphate ($(NH_4)_2HPO_4$) to make hydroxylapatite (HAP) and then adding a solution of ethyl silicate in ethanol. Ex. 1011, 3:2.1. After the ethanol is removed by evaporation, the residual powder is cold pressed into pellets which are heat-treated (sintered) at 1100ºC for 1 hour. *Id*. Ruys '93a states that "silicon substitution probably occurred . . . at the phosphorous site since ionic radii restrictions favor this site to the exclusion of the three alternatives—the calcium, oxygen, and hydroxyl sites." *Id*. at 4:3.2. Ruys '93a describes that using greater amounts of silicon "resulted in the partial transition of the HAP phase to two new apatite phases, with a glassy phase forming at high additional levels." *Id*. The transition was from a "gradual formation of TCP at silicon to HA ratios of between 0.09 and 1.65; the formation of beta-predominantly TCP at ratios less than 0.36 and alpha-TCP at ratios greater than 0.36; and the formation of Si-P-O glass at ratios greater than 1.65," thereby "result[ing] in multi-phasic Ca-P mixtures that included HA and TCP." Ex. 1003 ¶¶ 361-362. Ruys '93a suggests the "suitability of silicon-doped HAP for clinical trials, using a sol-gel synthesized material with an optimal silicon content combining a negligible TCP level with adequate sintering." Ex. 1011, 5:4.

2. Obviousness of claims 1, 2, 9, 11, 16, 18, 20, and 25 over Ruys '93a and Lynch

Petitioners' position is that "[t]he methods disclosed in Ruys 1993a are equivalent to the methods disclosed in the '992 patent and therefore

necessarily resulted in products having the same physical, chemical, and biological properties, including 'biomaterial' properties." Pet. 41 (citing Ex. 1003 ¶¶ 369, 610). In other words, "Ca-P materials made by the process[] disclosed in Ruys 1993a are inherently the same 'biomaterial compounds' that are claimed in claims 1, 2, and 4." Pet. 42 (citing Ex. 1003 ¶¶ 614-615). With respect to the claimed method steps of "implanting" the biomaterial compound, Petitioners' position is that Lynch "describes a method of inducing bone growth by implanting a restorable Ca-P ceramic." Pet. 24 (citing Ex. 1003 ¶ 552). Petitioners cite the following passage from Lynch in particular:

> It is known that ceramics, especially calcium hydroxyapatite and other calcium phosphates and mixtures thereof, are osteoconductive (i.e., when placed next to viable bone they provide a framework for the rapid incorporation of connective tissue and subsequent bone ingrowth).

Ex. 1026, 1:14-19.

Petitioners argue:

> Given the known properties of Ca-P materials such as TCP and HA . . . and the guidance provided in [Lynch]—which discloses implantation of Ca-P material at the site of skeletal surgery in place of bone—the person of ordinary skill in the art would have been motivated to use the biomaterial compounds described in Ruys 1993a in methods that involved "substituting natural bone at sites of skeletal surgery in human and animal hosts" where the methods further involved "implanting said biomaterial compound at the site of skeletal surgery. . . . The person of ordinary skill in the art would have had a reasonable expectation of success given the extensive literature describing the clinical and surgical uses of Ca-P compounds.

Pet. 43-44 (citations omitted).

Petitioners have satisfactorily demonstrated, on the present record, that the methodology in Ruys '93a is the same as in the '992 patent, such that Ruys '93a's composition is identical in structure to that claimed. *See* Pet. 41-42. It is reasonable to expect, therefore, that Ruys '93a's composition would have the same biocompatibility and bioactivity as the claimed compound. *See In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990) (finding it reasonable to infer that polymerization of the same monomers using the same or similar techniques would produce polymers having the identical composition) (citing *In re Papesch*, 315 F.2d 381, 391 (CCPA 1963) (a chemical compound and its properties are inseparable)).

Patent Owner argues that Ruys '93a provides no testing or data as to whether any of the discussed materials are biocompatible or bioactive. Prelim. Resp. 34. This argument is not relevant to the analysis. A property inherent in a claimed composition may be assumed to exist in a prior-art composition of identical structure. *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 782 (Fed. Cir. 1985) (citing *In re Wilder*, 429 F.2d 447, 450 (CCPA 1970)). We are satisfied, on the present record, that Ruys '93a's method would have produced a composition with the claimed properties.

Patent Owner also argues that because of the unpredictability of biocompatibility and bioresorption, "one of skill in the art would have had no reason [to] take Ruys' work and try to move forward from there" (Prelim. Resp. 34; *see id.* at 39) and that obviousness cannot be predicated on what is unknown (even if it is inherent), and that there would be no reasonable expectation of success in modifying Ruys '93a. *Id.* at 36-37 (citing *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993)).

These arguments are unpersuasive. Ample case law establishes that inherent disclosure may be relied upon in finding that subject matter would have been obvious at the time of its invention. *E.g.*, *In re Napier*, 55 F.3d 610, 613 (Fed. Cir. 1995). It is not a requirement that the inherent properties were known at the time of invention. *E.g.*, *In re Huai-Hung Kao*, 639 F.3d 1057, 1072 (Fed. Cir. 2011) (affirming holding of obviousness even where "the only claim element not expressly disclosed in the prior art was the previously-unknown, yet inherent . . . property."); *In re Kubin*, 561 F.3d 1351, 1357-58 (Fed. Cir. 2009) (quoting *In re Wiseman*, 596 F.2d 1019, 1023 (C.C.P.A. 1979) as "rejecting the notion that 'a structure suggested by the prior art, and, hence, potentially in the possession of the public, is patentable . . . because it also possesses an inherent, but hitherto unknown, function which [patentees] claim to have discovered.'"). Unknown properties of the prior art may not, however, be relied upon to provide the rationale for modifying or combining the prior art to reach the claimed subject matter. *See In re Newell*, 891 F.2d 899, 901, (Fed.Cir.1989) ("a retrospective view of inherency is not a substitute for some teaching or suggestion which supports the . . . combination"). This is what is meant by the passage "obviousness cannot be predicated on what is unknown" that Patent Owner cites from *In re Rijckaert*, 9 F.3d at 1534 (quoting *In re Spormann*, 363 F.2d 444, 448 (C.C.P.A. 1966)). *See* Prelim. Resp. 36.

Petitioners' position is not based on modifying Ruys '93a's composition to render it biocompatible or bioactive. Rather, Petitioners assert that these properties are inherent in the chemically indistinguishable composition produced by the process of Ruys '93a. *See* Pet. 41-42. Petitioners do not predicate the obviousness of the modification on those

inherent properties. That is, Petitioners do not argue that the latent properties *themselves provide the rationale* for combining prior-art references to reach the claimed subject matter. Rather, they predicate obviousness on the suggestion in Ruys '93a, itself, to subject the composition to clinical trials, and also on the teachings of Lynch in support of a reasonable expectation of success in combining known elements.

Patent Owner also asserts that Ruys '93a "lacks any teaching or suggestion of the structural features that would be required to permit the claimed 'progressive removal of said biomaterial compound primarily through osteoclast activity, and the replacement of that portion of said biomaterial compound removed by . . . osteoblast activity, such progressive removal and replacement being inherent in the natural bone remodeling process." Prelim. Resp. 39. As discussed above, we assign these limitations no patentable weight, because they are presented in the claims as intended results of the "implanting" step, not as acts to be carried out as part of the claimed methods or as limitations on the manner in which the implanting is to be carried out. Ruys '93a's silence on these results consequently does not undermine Petitioners' argument.

Patent Owner also argues that Lynch was brought in to rectify Ruys '93a's purported failure to teach the progressive removal and replacement of said biomaterial compound (Prelim. Resp. 40), and that Lynch also fails to teach such a material since the disclosed compound of TCP dissolved in biological fluids and the disclosed compound of HA was non-bioresorbable (*Id*. at 41). These arguments are unpersuasive. Petitioners rely on Lynch for the limited purpose of showing that it was known to implant calcium phosphates and related compounds during skeletal surgery. *See* Pet. 43-44.

Lynch's silence as to other teachings is not relevant to the challenge Petitioners have presented.

We determine that Petitioners have demonstrated a reasonable likelihood that claims 1, 2, 9, 11, 16, 18, 20, and 25 are unpatentable for obviousness over Ruys '93a and Lynch. We are satisfied, on the present record, that there is a reasonable likelihood that one of ordinary skill in the art would have found it obvious to implant the compound of Ruys '93a in connection with skeletal surgery because of the reference to clinical trials in Ruys '93a itself, as well as the general teachings of Lynch directed to calcium phosphate compounds in skeletal surgery. Patent Owner's arguments do not dissuade us otherwise, on the present record. Accordingly, we institute *inter partes* review of claims 1, 2, 9, 11, 16, 18, 20, and 25 on the ground of obviousness over Ruys '93a and Lynch.

E. Obviousness of claims 4, 36, and 38 over Ruys '93a, Bioceramics, and Ohgushi

Petitioners argue that claims 4, 36, and 38 would have been obvious over Ruys '93a, Bioceramics, and Ohgushi. Pet. 45-47. Patent Owner opposes. Prelim. Resp. 42-46. Claim 4 recites the step of "forming said biomaterial compound as a macroporous structure comprising an open cell construction with interconnected voids." The '992 patent describes using a silicon-substituted, microporous, calcium phosphate material to form a "bulk ceramic having a globular microporous structure, an underlying internal microporous structure and an internal macroporous structure allowing cells to migrate and function throughout the entire bulk ceramic unit." *Id*. at 26:8-13. The open cell structure of interconnected macropores, best illustrated in

Figure 23, "encourages bone growth and subsequent remodeling in a system more closely resembling physiological in vivo bone." *Id*. at 25:64-66.

Petitioners assert that Bioceramics discloses that "[a]n ideal cancellous bone graft substitute would mimic osteon-evacuated cancellous bone and have a thin lattice interconnected by pores of 500-600 μm" (Ex. 1021, 110), and that "[p]orosity and interconnectivity are key determinants of amount and type of ingrowth" (*Id*. at 116-117). Pet. 45. Petitioners also assert that "[m]ethods of making a biomaterial compound having a macroporous structure . . . were well known." Ex. 1003 ¶ 699. Petitioners assert that forming Ruys '93a's compound "as an open cell structure with interconnected voids would have been an obvious design choice in order to facilitate bone ingrowth and vascularization within the implant material" (Pet. 45 (citing Ex. 1003 ¶697)).

With respect to the claimed step of "combining mature and/or precursor bone cells with said macroporous structure," (Ex. 1001, 34:61-63), Petitioners rely on Ohgushi's disclosure of combining porous Ca-P with bone cells to enhance implantation outcomes (*see* Ex. 1073, 3 ("[A]ll implants with marrow cells showed bone formation in the pore regions"); *id*. at 1566 ("the bone formation was active and progressive")), and assert that "it would have been obvious to pretreat Ca-P material comprising an open cell structure with interconnected voids with precursor and mature bone cells in a manner that would allow the cells to infiltrate the structure in order to develop new mineralized matrix throughout the structure." Pet. 33; Ex. 1003 ¶¶ 700-702. Petitioners assert that "[t]he person of ordinary skill in the art would have considered these references together as each relates to the

development and use of Ca-P bone implant material" and that "[t]he combination . . . therefore would have rendered claim 4 obvious." Pet. 45.

Patent Owner contends that "macroporosity [of the claimed invention] is added to confer the property of bioresorbability in a clinically relevant time frame" and that "[t]he addition of macroporosity made the compounds . . . particularly well suited for use as bone replacement material." Prelim. Resp. 8. Patent Owner argues that, in contrast, Bioceramics teaches that macroporosity does nothing to assist hydroxyapatite in being resorbed and replaced by bone. *Id*. at 42-43. Patent Owner asserts that while Bioceramics "showed that addition of macroporosity does nothing to improve the bioresorbability of a CaP material" (*Id*. at 45), the claimed macroporous structure unexpectedly improves the bioresorbability of the claimed compound. *See id*. at 8, 46; *see also id*. at 37 (citing *Procter & Gamble Co. v. Teva Pharmaceuticals USA, Inc.*, 566 F.3d 989, 995-98 (Fed. Cir. 2009) (noting that even if a prima facie case of obviousness had been established, nonobviousness can be shown when a claimed invention is shown to have unexpectedly superior properties when compared to the prior art)).

Patent Owner argues that, without any testing or data as to the bioactivity of Ruys '93a's compound, it would constitute hindsight to form Ruys '93a's compound into a macroporous structure. Prelim. Resp. 36-38. Patent Owner's argument does not explain why Petitioners' stated reasoning for forming Ruys '93a's compounds as a macroporous structure (i.e., "to facilitate bone ingrowth and vascularization within the implant material" (Pet. 45 (citing Ex. 1003 ¶ 697)) lacks rational underpinnings or must be based on hindsight. In particular, it does not address adequately why the Petitioners' stated reasoning lacks rational underpinnings in light of

Bioceramics' disclosure that a thin lattice, interconnected by pores in the macroporous range of 500-600 µm, would be "ideal" (Pet. 45 (citing Ex. 1021, 110); *see also* Ex. 1001, 22:26-28 (describing the pore size of macroporous structures to be approximately 50 to 1000 µm)), and would "mimic osteon-evacuated cortical bone" (Ex. 1021, 108).

Patent Owner also argues that the "additional two years" Petitioner Apatech took to find "the structure of macroporosity" supports the existence of secondary considerations of unexpected results, satisfaction of an unmet need, failure of others, commercial success, successful licensing, and praise of others. Prelim. Resp. 29-30, 35 (citing Ex. 2001). We have considered Patent Owner's argument and evidence in this regard, but find in this case that detailed review of the secondary consideration evidence need not be undertaken until after Patent Owner has had an opportunity to introduce new testimonial evidence, and Petitioners have had an opportunity to conduct cross-examination.

Patent Owner also argues that Professor Mikos is not qualified to give expert testimony in this matter, because, while he is an expert in bioengineering, he is not an expert in bioceramics, and has authored few papers on calcium phosphates, and no papers on elemental modification of calcium phosphates. Prelim. Resp. 30. This argument is unpersuasive. An expert need not have worked in precisely the same field as the subject matter in question to give credible evidence as to the knowledge and level of skill in the relevant art. Professor Mikos's curriculum vitae indicates a degree of familiarity with calcium phosphates sufficient to satisfy us that he has the qualifications and experience necessary to give expert testimony in this case.

We determine that, on the present record, Petitioners have demonstrated a reasonable likelihood that claims 4, 36, and 38 are unpatentable for obviousness over Ruys '93a, Bioceramics, and Ohgushi. Accordingly, we institute *inter partes* review of claims 4, 36, and 38 on the ground of obviousness over Ruys '93a, Bioceramics, and Ohgushi.

F. Obviousness of claim 43 over Ruys '93a, Bioceramics, Ohgushi, and Lynch

Claim 43 depends directly from claim 4. Petitioners argue that "combining the biomaterial compound . . . with an additional Ca-P component would have been an obvious design choice given that Ca-P materials having more than one Ca-P component (e.g., both TCP and HA) were well known and routinely used in clinical applications." Pet. 47-48. Petitioners point specifically to Lynch as identifying the benefits of a TCP/HA combination. *Id*. at 36. In particular, "TCP provides 'a soluble phase . . . which initiates the giant cell response, is resorbed and may initiate osteoblast differentiation . . . . The remaining hydroxyapatite appears to provide an appositional interface and scaffold for the new bone formation.'" *Id*. (citing Ex. 1026, 4:33-39; Ex. 1003 ¶ 724).

Patent Owner reiterates its arguments that there is "no appreciation of the bioactive properties of Si doped CaP and no reason to expect that addition of macroporosity would change this" and "[n]o argument for a reasonable expectation of success is provided." Prelim. Resp. 46. Petitioners do not predicate the obviousness of the modification of Ruys '93a into a macroporous structure on improved bioresorbability in particular. Rather, they predicate obviousness on Bioceramics' disclosure that forming calcium phosphate compounds into a macroporous structure is "ideal" as it

"mimic[s] the architecture of . . . interstitial or stromal bone." Pet. 47-48 (citing Ex. 1003 ¶ 745); *see* Ex. 1021, 108. Petitioners' reasoning appears to have rational underpinnings. We are satisfied that there is a reasonable likelihood, on the present record, that one of ordinary skill in the art would have found it obvious to form the compound of Ruys '93a with an additional calcium phosphate material for the different functions as taught by Lynch. Pet. 36, 47-58 (citing Ex. 1026, 4:33-39). Patent Owner's arguments do not dissuade us otherwise, on the present record. Accordingly, we institute *inter partes* review of claim 43 on the ground of obviousness over Ruys '93a, Bioceramics, Ohgushi, and Lynch.

G. Obviousness of claims 17 and 26 over Ruys '93a, Lynch, and Chaki

Petitioners contend that "[g]iven that it was known that increasing the mechanical strength and toughness of Ca-P implant materials was desirable in certain applications, the person of ordinary skill in the art would have been motivated to introduce additives to compositions containing the biomaterial compound" and "would have had a reasonable expectation of success." Pet. 49. Petitioners point specifically to Chaki as "recogniz[ing] the need to increase the mechanical strength and toughness of Ca-P implant material." *Id*. at 48. In particular, Chaki discloses the use of silver to reinforce HA, finding that flexural strength of the composite material was increased. *Id*. at 48-49 (citing Ex. 1130, 1, 8).

Patent Owner argues that Chaki fails to "render obvious the claimed Markush group of CaP materials" set forth in claims 16 and 25, from which claims 17 and 26 depend, respectively. Prelim. Resp. 47. However, Patent Owner does not address Petitioners' articulated rationale for adding at least

one calcium phosphate material in connection with claims 16 and 25. We determine that Petitioners have demonstrated a reasonable likelihood that claims 17 and 26 are unpatentable for obviousness over Ruys '93a, Lynch, and Chaki. We are satisfied, on the present record, that there is a reasonable likelihood that one of ordinary skill in the art would have found it obvious to form the compound of Ruys '93a with an additive to increase mechanical toughness and strength based on Chaki's teachings regarding the inclusion of additional materials to increase strength and fracture toughness. *See* Ex. 1130, 1. Patent Owner's arguments do not dissuade us otherwise, on the present record. Accordingly, we institute *inter partes* review of claims 17 and 26 on the ground of obviousness over Ruys '93a, Lynch, and Chaki.

H. Obviousness of claim 44 over Ruys '93a, Bioceramics, Ohgushi, Lynch, and Chaki

Claim 44 depends indirectly from claim 4. For the same reasons as described hereinabove in connection with claim 4 (relating to forming the compound in a macroporous structure), claims 16 and 25 (relating to adding an additional calcium phosphate material), and claims 17 and 26 (relating to adding an additive to increase mechanical toughness and strength), Petitioners contend that claim 44 would have been obvious. Pet. 49-50. Patent Owner again opposes on the basis that Petitioners "fail[] to explain how any of these references provide[] the additional materials of the claimed Markush group" of claims 16 and 26. Prelim. Resp. 48. Again, Patent Owner does not address Petitioners' articulated rationale for adding at least one calcium phosphate material in connection with claims 16 and 25. We determine that Petitioners have demonstrated a reasonable likelihood that claim 44 is unpatentable for obviousness over Ruys '93a, Bioceramics,

Ohgushi, Lynch, and Chaki. Accordingly, we institute *inter partes* review of claim 44 on the ground of obviousness over Ruys '93a, Bioceramics, Ohgushi, Lynch, and Chaki.

I. Obviousness of claims 1, 2, 9, 11, 16, 18, 20, and 25 over Ruys '93b and Lynch; Obviousness of claims 4, 36, and 38 over Ruys '93b, Bioceramics, and Ohgushi; Obviousness of claim 43 over Ruys '93b, Bioceramics, Ohgushi, and Lynch; Obviousness of claims 17 and 26 over Ruys '93b, Lynch, and Chaki; and Obviousness of claim 44 over Ruys '93b, Bioceramics, Ohgushi, Lynch, and Chaki

1. Overview of Ruys '93b

Ruys '93b describes doping hydroxyapatite (HAP) with silicon using a sol-gel route. Ex. 1014, 2. HAP is synthesized using calcium nitrate ($Ca(NO_3)_2$) and diammonium hydrogen phosphate ($(NH_4)_2HPO_4$), with silicon being added using tetraethyl orthosilicate (TEOS). *Id*.; *see id*. at 76. Ruys '93b further describes sintering the samples at 1100ºC for one hour. *Id*. at 71, 76. Ruys '93b states that "[i]onic radii considerations suggest that the most likely substitution site was that of phosphorous." *Id*. Ruys '93b suggests "future assessment of the effects of silicon on the bioactivity of Ha[P] through clinical trials." *Id*. at 79.

2. Redundancy

Patent Owner asserts that "Ruys 1993a is clearly cumulative of Ruys 1993b" (Prelim. Resp. 38) and points to Petitioners' statement that Ruys '93b is "a reference that discloses methods that are equivalent to Ruys 1993a" (*Id*. at 42 (citing Ex. 1003 ¶¶ 268-272, 616)). We agree with Patent Owner.

Pursuant to 35 U.S.C. § 316(b), rules for *inter partes* review were promulgated taking into account their effect on "the economy, the integrity

of the patent system, the efficient administration of the Office, and the ability of the Office to timely complete proceedings instituted under this chapter." The Board's rules provide that they be "construed to secure the just, speedy, and inexpensive resolution of every proceeding." 37 C.F.R. § 42.1(b). As a result, in determining whether to institute an *inter partes* review of a patent, the Board may "deny some or all grounds for unpatentability for some or all of the challenged claims." 37 C.F.R. § 42.108(b).

The focus of a redundancy designation is on whether Petitioners articulated a meaningful distinction in terms of relative strengths and weaknesses with respect to application of the reference disclosures to one or more claim limitations. *Liberty Mutual Ins. Co. v. Progressive Casualty Ins. Co.*, CBM2012-0003, slip op. at 2 (PTAB Oct. 25, 2012) (Paper No. 7) (Patent Review Processing System) (expanded panel). Petitioners did not articulate any meaningful distinction between the disclosures of Ruys '93a on the one hand, and Ruys '93b on the other hand. In fact, the underlying bases for grounds of rejection based on Ruys '93b are virtually identical to those for Ruys '93a. Because Petitioners allege that all of the features of the claims at issue would have been obvious over Ruys '93a, the grounds based on Ruys '93b are redundant in the absence of Petitioners' explanation as to why the combination of Ruys '93b, with the same additional references, is more preferred for satisfying some elements, while Ruys '93a with these references is more preferred for satisfying other elements.

As the grounds based on Ruys '93b are redundant to the grounds based on Ruys '93a on which we institute *inter partes* review of the same

claims, we do not institute *inter partes* review of any of the claims based on Ruys '93b.

III. CONCLUSION

For the foregoing reasons, based on the present record, we determine that Petitioners have demonstrated that there is a reasonable likelihood that Petitioners would 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 unpatentable. The Board has not made a final determination on the patentability of the challenged claims.

IV. ORDER

For the reasons given, it is

ORDERED that, pursuant to 35 U.S.C. § 314(a), *inter partes* review is instituted as to claims 1, 2, 4, 9, 11, 16-18, 20, 25, 26, 36, 38, 43, and 44 based on the following grounds of unpatentability:

A. Claims 1, 2, 9, 11, 16, 18, 20, and 25 as obvious over Ruys '93a and Lynch;

B. Claims 4, 36, and 38 as obvious over Ruys '93a, Bioceramics, and Ohgushi;

C. Claim 43 as obvious over Ruys '93a, Bioceramics, Ohgushi, and Lynch;

D. Claims 17 and 26 as obvious over Ruys '93a, Lynch, and Chaki; and

E. Claim 44 as obvious over Ruys '93a, Bioceramics, Ohgushi, Lynch, and Chaki;

FURTHER ORDERED that *inter partes* review commenced on the entry date of this Order, and pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial;

FURTHER ORDERED that the trial is limited to the grounds of unpatentability listed above, and no other grounds of unpatentability are authorized for *inter partes* review; and

FURTHER ORDERED that an initial conference call with the Board is scheduled for 11:00 AM Eastern Time on Tuesday April 8, 2014. The parties are directed to the Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,765-66 (Aug. 14, 2012) for guidance in preparing for the initial conference call, and should be prepared to discuss any proposed changes to the Scheduling Order entered herewith and any motions the parties anticipate filing during the trial.

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