UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/226,618	09/07/2011	Jason Schense	KUROS 142	3980

23579 7590 10/22/2019

Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER
BROWE, DAVID

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
10/22/2019	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JASON SCHENSE,
SILKE MARK, MONICA ALVISI,
and MARIA ANGELES MARTINEZ VARGAS

Appeal 2017-002307
Application 13/226,618
Technology Center 1600

Before JEFFREY N. FREDMAN, TAWEN CHANG, and DAVID COTTA, *Administrative Patent Judges.*

CHANG, *Administrative Patent Judge.*

DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellant[1] appeals from the Examiner's decision to reject claims 1, 2, 4, 5, 9, 10, 27, and 28. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

---

[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party in interest as Kuros Biosurgery AG. Appeal Br. 2.

BACKGROUND

Spinal fusion is "a surgical procedure aimed at achieving bone formation and thereby fusion between two or more adjacent vertebrae." (Spec. 10:12–14.) The Specification states that in spinal fusion "[a] bone graft is needed to create the appropriate environment in order for a solid bone bridge to form between the vertebrae" and that currently "[a] variety of materials . . . serve as bone grafts or bone graft substitutes, including autografts . . ., allografts, demineralised bone matrix, and various synthetic materials" such as "calcium phosphates or hydroxyapatites, stem cell containing products . . ., and . . . growth factor containing matrices." (*Id.* at 2:27–3:6.) According to the Specification, "[i]t is an object of the present invention to provide a bone graft substitute which effectively fuses vertebrae in spinal fusion procedures and is safer to use than the currently available bone graft substitutes." (*Id.* at 3:28–30.)

CLAIMED SUBJECT MATTER

The claims are directed to a spinal fusion method for treatment of a human patient. Claim 1 is illustrative:

> 1. A spinal fusion method for treatment of a human patient in need thereof, comprising
>
> administering to the patient at a site between two adjacent vertebrae in need of spinal fusion a pharmaceutical composition capable of forming under physiological conditions a bone graft substitute,
>
> wherein the pharmaceutical composition comprises one or more matrix forming materials and parathyroid hormone (PTH), wherein the composition does not contain any additional added peptide or protein bioactive factor with bone forming properties,

> wherein during or after administration, the pharmaceutical composition forms a bone graft substitute at the site,
>
> wherein the bone graft substitute comprises a matrix and the PTH, and does not contain any additional added peptide or protein bioactive factor with bone forming properties,
>
> and
>
> wherein the bone graft substitute locally delivers the PTH to the site in an effective amount to achieve bone formation between the vertebrae.

(Appeal Br. 31.)

The Examiner explains, and Appellant does not dispute, that

> Appellant's elected claims are directed to a spinal fusion method for treatment of a human patient in need thereof comprising administering to the patient at a site between two adjacent vertebrae a composition comprising *i)* fibrinogen and thrombin, as matrix precursor components, with a calcium source, wherein the components interact with each other to form a fibrin matrix during or after administration; *ii)* PTH_{1-34}, as the sole bioactive factor; and *iii)* hydroxyapatite. The spinal fusion is selected from the group consisting of cervical and lumbar vertebrae fusions.

(Ans. 3–4.) Our consideration of the merits of the appealed rejections is limited to the elected species. *See Ex parte Ohsaka*, 2 USPQ2d 1460, 1461 (BPAI 1987).

REJECTION(S)

A. Claims 1, 2, 4, 5, 9, and 10 are rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Schense[2] and Lane.[3] (Ans. 5.)

B. Claims 27 and 28 are rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Schense, Lane, and Zdeblick.[4] (Ans. 7.)

C. Claims 1, 2, 4, 5, 9, and 10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1–3, 5–12, 16, and 18 of U.S. Patent No. 8,575,101 (the '101 patent), in view of Lane. (Ans. 3.)

DISCUSSION

A. Issue

The same issue is dispositive of all of the rejections; we therefore consider the rejections together.

The Examiner finds that Schense, as well as claims 1–3, 5–12, 16, and 28 of the '101 patent, disclose almost all of the elements of the methods recited in appealed claims 1, 2, 4, 5, 9, and 10, except that they do not explicitly disclose that the bone segments or bones being joined are spinal lumbar vertebral bones. (Ans. 4, 6.) However, the Examiner finds that Lane discloses "a method of spinal fusion of two distinct lumbar vertebral bones comprising providing a . . . pharmaceutical composition comprising PTH_{1-34}

---

[2] Schense et al., US 2006/0148704 A1, published July 6, 2006.
[3] Joseph M. Lane et al., *PTH(1-34) Stimulates Spine Fusion*, Poster Abstract, The Sixth International Symposium on Osteoporosis: Current Status and Future Directions (Apr. 6–10, 2005), http://nof.confex.com/nof/2005/techprogram/P132.HTM.
[4] Thomas A. Zdeblick et al., *Interbody Cage Devices*, 28 SPINE S2 (2003).

in a bone graft matrix." (*Id.* at 4, 6.) The Examiner concludes that, "[s]ince Lane . . . disclose[s] that PTH_{1-34} significantly improves the rate and quality of lumbar spinal fusions, resulting in an improved quantity of bone mass formed in the fusion," a skilled artisan would be motivated to employ the method of Schense and/or claims 1–3, 5–12, 16, and 18 of the '101 patent for spinal fusion, "with the reasonable expectation that the resulting method will successfully facilitate spinal fusion with an improved rate and improved quantity of bone mass formed." (*Id.* at 5, 6–7.)

Appellant contends among other things that a skilled artisan would not have a reasonable expectation of success of combining Schense with Lane to arrive at the claimed invention. (Appeal Br. 15.) Citing to the Lane Declaration[5] and Boden,[6] Appellant argues that a skilled artisan would understand that "[t]he microenvironment of a bone fracture site is different from the microenvironment of a site in need of spinal fusion" and that a skilled artisan would expect such biological differences to "influence healing or the performance of a bone graft substitute at those sites." (*Id.* at 17.) Appellant makes similar arguments with respect to the obviousness-type double patenting rejection over certain claims of the '101 patent in view of Lane. (*Id.* at 28.)

The issue with respect to the rejections is whether a skilled artisan would have had a reasonable expectation of success of combining Schense or the claims of the '101 patent with Lane to arrive at the claimed invention.

---

[5] Declaration of Joseph M. Lane under 37 C.F.R. § 1.132 (Dec. 9, 2014).
[6] Scott D. Boden, *Overview of the Biology of Lumbar Spine Fusion and Principles for Selecting a Bone Graft Substitute*, 27 SPINE S26 (2002).

B. Analysis

On balance, we find Appellant has the better argument.

Schense teaches that matrices comprising PTH "decrease the time of healing compared to autograft and[/]or trigger healing of bone fractures which otherwise would not heal." Schense Abstract. Lane teaches that PTH_{1-34} stimulates spine fusion when administered after bilateral spine fusion surgery using iliac crest autograft as bone graft. Lane 1 (Materials and Methods); Lane Decl. ¶¶ 4, 6.

However, in light of Boden and the Lane Declaration, we agree with Appellant that these teachings do not provide a skilled artisan with a reasonable expectation that a pharmaceutical composition comprising matrix forming materials and PTH_{1-34}, without "any additional added peptide or protein bioactive factor with bone forming properties" such as those present in an autograft, *see, e.g.*, Lane Decl. ¶ 5 (stating that autograft contains bone-growing cells and proteins), would nevertheless successfully "achieve bone formation between the vertebrae[s]" as required by the claims.

In particular, Dr. Lane explains that spinal fusion differs from healing bone fracture because in "a bone fracture . . . the bone starts intact" and "[t]he body responds . . . with the production of several growth factors that attract stem cells and stimulate their proliferation and differentiation into osteoblasts that lead to bone healing," whereas "[s]pine fusion requires *de novo* production of bone in a location without any prior bone bridging." *Id.* ¶¶ 8, 10, 11. Dr. Lane states that, given the above, "[t]he fact that a composition was effective in inducing bone formation in bone fractures . . . provides no basis for expecting the same treatment to work in spinal fusions," and further provides an example of a factor (anti-sclerostin

antibodies) that enhances fracture healing but has no effect in spinal fusion. *Id.* ¶¶ 10, 11. Finally, Dr. Lane cites to Whitfield[7] as teaching that "[c]ontinuous systemic delivery of PTH is not known in the art to produce *de novo* bone synthesis in a void," because Whitfield states that "[n]o PTH can restore the original bone structure" and that "[t]hey cannot generate trabeculae *de novo* or make broken trabeculae rejoin if they have drifted too far apart." Lane Decl. ¶ 7; Whitfield 8.

The statements in the Lane Declaration are supported by the art cited by Appellant. Boden, for instance, teaches that

> different healing environments *(e.g.,* metaphyseal defect, long bone fracture, interbody spine fusion and posterolateral spine fusion) have increasing levels of difficulty in forming new bone. For example, a metaphyseal defect permits the successful use of many purely osteoconductive materials. In contrast, a posterolateral spine fusion environment generally does not tolerate the use of purely osteoconductive materials as stand-alone substitutes, and only sometimes permits their use as bone graft extenders. Thus, validation of any bone graft substitute in one clinical anatomic site may not be predictive of its performance in another location. Accordingly, surgeons must be very careful in using graft substitutes that have not been tested definitively in the particular healing environment wherein they are about to use it.

Boden 29, left column. Boden further teaches that "successful bone induction at any level does not infer success at the next most stringent level." *Id.* at S30, left column.

---

[7] James F. Whitfield et al., *The Parathyroid Hormones: Bone-Forming Agents for Treatment of Osteoporosis*, MEDSCAPE, http://www.medscape.com/viewarticle/408928 (last visited Oct. 15, 2019).

The Examiner asserts that Appellant improperly argues the references cited in the rejection separately and also misconstrued the prior art rejection of record. The Examiner asserts that

> the . . . prior art rejection of record is based on employing the Schense method, i.e. administering PTH_{1-34} in their "bone graft substitute", for spinal fusion, based on Lane's disclosure that administering PTH_{1-34} in a bone graft (i.e. autograft in their case) successfully stimulates spinal fusion, with the knowledge from Schense that their "bone graft substitute" is functionally equivalent to autograft as far as promoting successful bone formation, regeneration, and repair, but has the advantage over autograft of a decreased time of healing.

Ans. 12.

We are not persuaded. The explanation above fails to address the crux of Appellant's argument, namely that Schense and Lane address the use of PTH_{1-34} in two different physiological environments (i.e., bone fracture and spinal fusion, respectively), and there is no reasonable expectation that PTH_{1-34} would function in the same manner in both. Thus, even if Schense's PTH_{1-34}-containing bone graft substitute is considered functionally equivalent to autograft in the context of healing bone fractures, the Examiner has not persuasively explained why, in light of the evidence cited by Appellant, a skilled artisan would consider Schense's PTH_{1-34}-containing bone graft substitute to be functionally equivalent to autograft *in the context of a spinal fusion procedure*.

The Examiner asserts that

> [t]he Schense method and the presently claimed method both fundamentally involve the joining/fusing to two adjacent bones together by administering at the site between the two adjacent bones to be joined/fused the very same composition. Schense specifically joins two distinct bone segments together at a point of discontinuity, such as a fracture, via bone formation to thus

> repair the fracture. Anyone of ordinary skill in the art would know that a "discontinuity" is a "gap" between two bones. Schense does not expressly place any necessary limit on the size of the "discontinuity" or "gap" that can be treated. While PTH *alone* (i.e. in the absence of matrix) may not be effective in facilitating bone formation across larger gaps, as Appellant points out, in the instant case where PTH is associated with a bone graft matrix, and this composition is administered to fill the space within the gap, there would appear to be no limit on the size of the gap that can be successfully treated. Thus, one of ordinary skill in the art would find no reason why the Schense method could not be successfully employed for spinal fusion by administering their composition to fill the gap between the two vertebral bones.

Ans. 13–14.

We are not persuaded. The Examiner appears to be responding in part to the statements in Whitfield, cited in the Lane Declaration, that PTH cannot "restore the original bone structure," "generate trabeculae *de novo*," or "make broken trabeculae rejoin if they have drifted to far apart." Lane Decl. ¶ 7; Whitfield 8. However, the Examiner has not persuasively addressed the evidence provided by Appellant, in the form of Boden reference and the Lane Declaration, that even the same composition may not act in the same manner with respect to bone formation, depending on the particular environment—e.g., bone fracture versus spinal fusion—in which the bone formation is expected to take place. "[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (*quoting In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (internal quotation marks omitted)).

The Examiner also asserts that, even though Lane uses autograft in the spinal fusion, its title teaches that "PTH_{1-34} stimulates spine fusion," and it further reports that "'PTH administration . . . increases the rate of spine fusion by 170% and increases the mass of bone formation by 75%" and that "PTH has potential to . . . improve the rate of fusion and improve the quality of bone mass formed in the fusion'." Ans. 12. The Examiner asserts that,

> [c]learly, one of ordinary skill in the art would understand from this report that PTH is responsible for these reported effects, not specific cells or proteins in the autograft. Hence, there is absolutely no reason why one of ordinary skill in the art would not *reasonably expect* the PTH in Schense to have the very same affect, based on the understanding and evidence that their "bone graft substitute" is functionally an equivalent substitute for bone graft (i.e. iliac crest autograft in this case). In support of this, Schense discloses that PTH1-34 exhibits bone formation properties when included in either natural or synthetic matrices.

Id. at 12–13.

We are not persuaded. Although Lane teaches that PTH_{1-34} stimulates spine fusion, it does so in a context in which autograft is used as bone graft. Given Appellant's evidence that there is no reasonable expectation PTH_{1-34} would function in the same manner in healing bone fracture and in spinal fusion, the Examiner has not persuasively explained why a skilled artisan would reasonably expect PTH_{1-34} to stimulate spine fusion—which requires *de novo* bone formation, Lane Decl. ¶ 11—in the absence of autograft, merely because Schense teaches that PTH_{1-34}-containing matrices exhibit bone formation properties and may function as a bone graft substitute *in the context of healing bone fractures*.

The Examiner points out that the Specification teaches that patients in need of spinal fusion include those with spinal fracture. Ans. 13. The

Examiner states that, thus, "the microenvironment in which the Schense method has proven successful, i.e. fracture, is the very same as at least one microenvironment encompassed by the instant claims, i.e. fracture." *Id.*

We are not persuaded. The Specification defines spinal fusion as "a surgical procedure aimed at achieving bone formation and thereby fusion between two or more adjacent vertebrae." Spec. 10:12–14. While a spinal fracture may be *treated* with spinal fusion surgery, the Examiner cites no persuasive evidence that spinal fusion, as used in the treatment of a spinal fracture, is the same as the procedure of *healing* the fracture, which is the subject of the Schense reference.

Finally, the Examiner asserts that obviousness does not require an absolute guarantee or proof of success but rather a "reasonable expectation" of success. Ans. 14. While we agree with the Examiner that "the expectation of success need only be reasonable, not absolute," *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007), we agree with Appellant that the Examiner has not persuasively explained why, in light of the Lane Declaration and the Boden reference, a skilled artisan would have a *reasonable* expectation that a pharmaceutical composition comprising matrix forming materials and PTH_{1-34}, without "any additional added peptide or protein bioactive factor with bone forming properties," would successfully "achieve bone formation between the vertebrae[s]," as required by the claims.

Accordingly, we reverse the Examiner's rejection of claims 1, 2, 4, 5, 9, and 10 as obvious over Schense and Lane. The Examiner cites Zdeblick only for the limitations in dependent claims 27 and 28 regarding the use of an "interbody spinal fusion cage." Ans. 8–10.

We therefore reverse the rejection of claims 27 and 28 as obvious over Schense, Lane, and Zdeblick for the same reasons. *In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988) ("Dependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious."). Finally, the Examiner's obviousness-type double patenting rejection of claims 1, 2, 4, 5, 9, and 10 over claims 1–3, 5–12, 16, and 18 of the '101 patent largely tracks the rejection of these claims over the combination of Schense and Lane.[8] Thus, we reverse the obviousness-type double patenting rejection for the reasons already discussed.

CONCLUSION

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 2, 4, 5, 9, 10	103(a)	Schense, Lane		1, 2, 4, 5, 9, 10
27, 28	103(a)	Schense, Lane, Zdeblick		27, 28

[8] The Examiner points out that claim 3 of the '101 patent specifically recites a method of repairing a bone fracture wherein the bone fracture is a fracture of the vertebrae. Ans. 4. However, as discussed above with respect to the obviousness rejection over Schense and Lane, the Examiner has not persuasively shown that, in light of the evidence cited by Appellant, a skilled artisan would reasonably expect $PTH_{1\text{-}34}$ to function in the same manner with respect to *spinal fusion* as compared to repairing a *bone fracture*, even if the bone fracture is a fracture of the vertebrae.

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 2, 4, 5, 9, 10		Claims 1–3, 5–12, 16, 18 of U.S. Patent No. 8,575,101, Lane		1, 2, 4, 5, 9, 10
Overall Outcome				1, 2, 4, 5, 9, 10, 27, 28

REVERSED