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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ANJA C. GEMPERLI and OLEH ANDRUKHOV[1]

Appeal 2018-004488
Application 14/787,941
Technology Center 1600

Before ERIC B. GRIMES, JOHN G. NEW, and JAMIE T. WISZ, *Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a wound-healing composition, which have been rejected as lacking adequate written description and as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

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

STATEMENT OF THE CASE

"The present invention relates to the field of enamel matrix proteins and to the use of them in wound healing. In particular, the invention relates to the disclosure of a new active amelogenin polypeptide ((SEQ.ID.NO: 1) TRAP 63) that in particular stimulates the tissue formation phase of a wound healing process." Spec. 1:3–6.

Claims 1, 3, 4, and 8–14 are on appeal. Claims 1 and 4 are illustrative and reproduced below (emphasis added):

> 1. A pharmaceutical composition which stimulates the tissue formation phase of a wound healing process, said composition comprising a mixture of enamel matrix polypeptides and/or proteins with a molecular weight < 8 kDa, wherein said mixture is *free of enamel matrix polypeptides and/or proteins with a molecular weight > 8 kDa*, and a suitable pharmaceutical carrier, wherein said mixture comprises the enamel matrix polypeptide of SEQ ID NO: 1 (TRAP63).
>
> 4. A pharmaceutical composition which stimulates the tissue formation phase of a wound healing process, said composition comprising an acid-extraction of enamel proteins and/or polypeptides derived from developing mammalian tooth buds, which is *at least 2x enriched* in an enamel matrix polypeptide which has the amino acid sequence as shown in SEQ ID NO: 1 (TRAP63), or a pharmaceutically acceptable salt thereof.

The claims stand rejected as follows:

Claims 1, 3, and 8–14 under 35 U.S.C. § 112(a) as failing to comply with the written description requirement (Ans. 3) and

Claim 4 under 35 U.S.C. § 102(a)(1) as anticipated by, or alternatively under 35 U.S.C. § 103 as obvious based on, Gestrelius[2] as evidenced by UniProt[3] (Ans. 5).

OPINION

Written Description

The Examiner finds that claim 1 "has been amended to exclude all enamel matrix polypeptides and/or proteins having a molecular weight above 8 kDa," and "the issue is whether or not the original disclosure provided support specifically for mixtures that are completely free of all enamel matrix polypeptides and/or proteins having a molecular weight above 8 kDa." Ans. 3–4.

The Examiner finds that "the amended claim scope is not supported by express disclosure" because "the specification does not include the actual language 'free of enamel matrix polypeptides and/or proteins with a molecular weight > 8 kDa', the term 'free' in the context of protein components, or terms equivalent to 'free' in the context of protein components." *Id*. at 4.

The Examiner also finds that the Specification exemplifies an "LMW fraction," which includes proteins with molecular weights below 8 kDa, but "the specification presents data that suggests that proteins with a molecular weight above 8 kDa are in fact present in the LMW fraction." *Id*. The Examiner points to Figures 9 and 10 as "clearly show[ing] that Fraction LMW comprises polypeptides with molecular weights of approximately 12,

[2] Gestrelius et al., US 2002/0169105 A1, published Nov. 14, 2002.
[3] UniProt database, entry Q9TQY2_PIG (2000).

15, and 20 kDa." *Id*. The Examiner also points to the Specification's statements that the LMW fraction contained "significantly less" or "insignificant amounts" of 20 kDa amelogenin protein, both of which indicate that the LMW fraction is not "'free of' components with a molecular weight above 8 kDa." *Id*. at 4–5.

Appellant argues that, "although actual reduction to practice may serve as evidence of possession, actual reduction to practice is *not required*." Appeal Br. 5. Appellant argues that, "[e]ssentially, the Examiner's argument is that the Examples in the specification do not evidence an actual reduction to practice of the claimed invention. But this is not the standard. *See, e.g., Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926 (Fed. Cir. 2004)." Reply Br. 3. "Working examples are explicitly *not required*." *Id*. at 4 (citing *Falkner v. Inglis*, 448 F.3d 1357 (Fed. Cir. 2006).)

Appellant also argues that "the specification as filed . . . describe[s] a process for producing a composition that includes the step of 'removing any protein with a molecular weight (M.W.) ≥ 8 kDa from' a preparation of isolated enamel proteins." Appeal Br. 7. Appellant argues that a composition "from which proteins with a molecular weight ≥ 8 kDa *have been removed*, is a *literal* description of a composition that does not include proteins with a molecular weight > 8 kDa." *Id*. at 7–8. Appellant thus argues that "the inventors, at the time the application was filed, were in possession of the claimed invention, if not in actual physical possession, then at least by providing sufficient '[w]ords, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention.' *Lockwood v. American Airlines, Inc.*, 107 F .3d 1565, 1572 (Fed. Cir. 1997)." Reply Br. 4–5.

We agree with Appellant that the Specification satisfies the 35 U.S.C. § 112(a) requirement that the "description must 'clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'" *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (alteration in original). "In other words, the test for sufficiency [of the written description] is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id*.

"The term 'possession,' however, has never been very enlightening." *Id*. "[T]he written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that *in a definite way identifies the claimed invention* can satisfy the written description requirement." *Id*. at 1352 (emphasis added). That is, based on "the perspective of a person of ordinary skill in the art . . . the specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed." *Id*. at 1351.

Here, the Specification states that "[t]he enamel matrix is composed of a number of proteins," and "[e]namel matrix proteins and enamel matrix derivatives (EMD) have previously been described in the patent literature to be able to . . . promote open wound healing." Spec. 2:5–8, 2:17. The Specification describes Appellant's invention as follows:

> The present invention now for the first time discloses all components of a newly identified low molecular weight fraction of isolated enamel matrix derivatives that can clearly be shown to be more effective in reducing the inflammatory response in a targeted soft tissue than the complete enamel matrix extract (EMD).

Id. at 4:13–16. The Specification also states that "the invention relates to the disclosure of a new active amelogenin polypeptide ((SEQ.ID.NO: 1) TRAP 63) that in particular stimulates the tissue formation phase of a wound healing process." *Id*. at 1:4–6. These passages identify Appellant's invention as being low molecular weight enamel matrix proteins, including TRAP 63, that reduce inflammation and stimulate wound healing, as recited in claim 1.

The Specification also states that an aspect of the disclosed invention is a process for producing a pharmaceutical composition, comprising isolating enamel proteins from developing animal tooth buds, and "removing any protein with a molecular weight (M.W.) ≥ 8 kDa from said isolate," thus producing "a pharmaceutical composition comprising proteins with a molecular weight (M.W.) < 8 kDa, such as ≤ 7 kDa." *Id*. at 6:24 to 7:2. This passage identifies a molecular weight of 8 kDa, as recited in claim 1, as a threshold for the "low molecular weight" enamel matrix proteins described as part of the disclosed composition.

In our view, the Specification adequately describes the composition defined by claim 1 in a manner that is understandable to a skilled artisan and demonstrates that Appellant invented what is claimed. No more is required to satisfy the written description requirement of 35 U.S.C. § 112(a). *See Ariad*, 598 F.3d at 1351.

It is true, as the Examiner has pointed out, that the "LMW" fraction characterized in the Specification's working examples is not completely free of proteins with molecular weights above 8 kDa. Figure 10, for example, identifies one of the proteins in Fraction LMW as "Amelogenin (20 kDa)." Claim 1, however, is not directed to "Fraction LMW," or limited to

compositions made by the same process. Claim 1 simply requires that the composition be free of proteins above a molecular weight of 8 kDa, and the Examiner has not shown that a skilled artisan would not have been able to use conventional protein purification techniques to "remov[e] any protein with a molecular weight (M.W.) ≥ 8 kDa from [an] isolate" of enamel proteins, as described in the Specification (page 6).

We conclude that the Specification adequately describes the composition of claim 1. We therefore reverse the rejection of claims 1, 3, and 8–14 under 35 U.S.C. § 112(a).

Prior Art

The Examiner rejects claim 4 as anticipated by, or obvious based on, Gestrelius with evidence provided by UniProt. The Examiner finds that Gestrelius discloses "a pharmaceutical composition for wound healing . . . comprising main protein bands at 20 kDa, 12–14 kDa and around 5 kDa." Ans. 6. The "composition may mainly or exclusively contain up to 70–90% amelogenins with a molecular weight (MW) between 40,000 and 5,000 Daltons." *Id*.

The Examiner finds that Gestrelius teaches that "the enamel matrix may be obtained from . . . a mammal in which teeth are under development. A suitable source is developing teeth from slaughtered animals such as, e.g., calves, pigs or lambs." *Id*. The Examiner cites UniProt as evidence that "[p]orcine amelogenin comprises an amino acid sequence that is identical to instant SEQ ID NO: 1 (TRAP63) at positions 1–63." *Id*.

The Examiner finds that Gestrelius teaches preparing its composition by scraping off enamel matrix and "extraction with aqueous solution such as

a buffer, a dilute acid or base or a water/solvent mixture, followed by size exclusion, desalting or other purification steps, optionally followed by freeze-drying." *Id*. The Examiner concludes that

> Gestrelius et al. explicitly teaches acid extraction, and a composition having at least 2x enrichment in an enamel matrix polypeptide (i.e. up to 70–90% amelogenins with a molecular weight (MW) between 40,000 and 5,000 Daltons) (¶ [0105]), which appears to meet all of the structural requirements of and to anticipate the instant claim.

Id. In the alternative, the Examiner concludes that

> it would have been obvious to use acid extraction of . . . a mammal in which teeth are under development as taught by Gestrelius et al., and in doing so one of ordinary skill in the art would prepare a composition that is at least 2x enrich[ed] in an enamel matrix polypeptide. The reference does not name a polypeptide TRAP63 but the compositions disclosed in or suggested by the reference would contain TRAP63.

Id. at 6–7.

Appellant argues that "Gestrelius teaches that the . . . proteins in the mixture prepared therein 'typically have a molecular weight of at the most about 120 kDa such as, e.g., at the most 100 kDa, 90 kDa, 80 kDa, 70 kDa or 60 kDa as determined by SDS Page electrophoresis.'" Appeal Br. 8 (quoting Gestrelius ¶ 95). "Such a composition would contain both the high and low molecular weight proteins identified by the present inventors, and would not be relatively enriched in TRAP63." *Id*. at 9.

Appellant argues that, therefore, "Gestrelius does not inherently describe a composition which meets the limitations of the present claims. What is more, there is no teaching or suggestion in Gestrelius to use size

exclusion to prepare a composition which is specifically enriched in the low molecular weight material TRAP 63." *Id*.

We agree with Appellant that the Examiner has not shown that the composition of claim 4 is either anticipated by or obvious based on Gestrelius as evidenced by UniProt. With respect to anticipation, the Examiner has not provided evidence or sound technical reasoning to support the conclusion that the composition described at ¶ 105 of Gestrelius—a composition "up to 70–90% amelogenins with a molecular weight (MW) between 40,000 and 5,000 Daltons" (Ans. 6)—is inherently "at least 2x enriched in" TRAP63 relative to the starting material, as required by claim 4. *See In re King*, 801 F.2d 1324, 1326 (Fed. Cir. 1986) ("It is axiomatic that anticipation of a claim under § 102 can be found only if the prior art reference discloses every element of the claim.").

With respect to obviousness, the Examiner has not shown that acid extraction of enamel matrix from pig teeth, as suggested by Gestrelius, inherently results in a composition that is at least two-fold enriched in TRAP63, as claimed. "The inherent result must inevitably result from the disclosed steps; '[i]nherency . . . may not be established by probabilities or possibilities.'" *In re Montgomery*, 677 F.3d 1375, 1379–80 (Fed. Cir. 2012) (citations omitted, alterations in original).

Nor has the Examiner shown that a skilled artisan would have had a reason, based on the prior art or the knowledge of those skilled in the art, to use "size exclusion, desalting, or other purification steps" (Gestrelius ¶ 88) to produce a composition at least two-fold enriched in TRAP63. "Obviousness requires more than a mere showing that the prior art includes

. . . each separate limitation in a claim under examination." *Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1360 (Fed. Cir. 2011). "Rather, obviousness requires the additional showing that a person of ordinary skill at the time of the invention would have selected and combined those prior art elements in the normal course of research and development to yield the claimed invention." *Id.*

We therefore reverse the rejection of claim 4 as anticipated by, or obvious based on, Gestrelius with evidence provided by UniProt.

DECISION SUMMARY

In summary:

Claims Rejected	**35 U.S.C. §**	**Reference(s)/Basis**	**Affirmed**	**Reversed**
1, 3, 8–14	112(a)	Written Description		1, 3, 8–14
4	102(a)(1)	Gestrelius, UniProt		4
4	103	Gestrelius, UniProt		4
Overall Outcome				1, 3, 4, 8–14

REVERSED