



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.
12/891,240	09/27/2010	Solomon S. Steiner	SOLO 119 CIP	9988
23579	7590	10/26/2016	EXAMINER	
Pabst Patent Group LLP 1545 PEACHTREE STREET NE SUITE 320 ATLANTA, GA 30309			HELLMAN, KRISTINA M	
			ART UNIT	PAPER NUMBER
			1675	
			MAIL DATE	DELIVERY MODE
			10/26/2016	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 SOLOMON S. STEINER, ROBERT HAUSER, MING LI,
ROBERT FELDSTEIN, and RODERIKE POHL¹

Appeal 2014-005492
Application 12/891,240
Technology Center 1600

Before ERIC B. GRIMES, ULRIKE W. JENKS, and RACHEL H.
TOWNSEND, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a stabilized glucagon formulation, which have been rejected for obviousness and, provisionally, for obviousness-type double patenting. We have jurisdiction under 35 U.S.C. § 6(b). We reverse the obviousness rejections but affirm the double patenting rejections.

¹ Appellants identify the Real Party in Interest as Bidel, Inc. (Appeal Br. 2.)

STATEMENT OF THE CASE

“[G]lucagon increases the concentration of glucose in the blood.” (Spec. 1:19–20.) Glucagon is soluble in aqueous solution at low or high pHs, but “has low solubility in the pH range of 4 to 8. . . . It forms a gel in acidic aqueous conditions (pH 3-4) and precipitates within an hour of preparation in a neutral aqueous solution.” (*Id.* at 1:28–31.)

The Specification reports that the commercial preparation of glucagon is a two-part vial, to be reconstituted immediately before use. (*Id.* at 2:1–2.) An “artificial pancreas” for treatment of diabetes needs to be capable of keeping a patient within ideal glucose levels, providing insulin or glucagon as needed. (*Id.* at 2:31–3:11.) Thus, an artificial pancreas “requires a glucagon that is stable in solution for at least seven days at 30-37°C.” (*Id.* at 3:13–14.)

Claims 1–6 and 8–23 are on appeal. Claim 1 is the only independent claim and reads as follows:

1. A stabilized glucagon formulation comprising
Glucagon,
a surfactant, and
a monosaccharide,
wherein the surfactant and monosaccharide are in an effective amount to enhance the stability of glucagon, as compared to the stability of glucagon in combination with the surfactant, and
wherein the osmolarity is approximately 200 to 400 mOsm and the pH is between 2 and 8.

The claims stand rejected as follows:

Claims 1–6, 8–11, and 14–23 under 35 U.S.C. § 103(a) based on Kaarsholm² and Pedersen³ (Ans. 3);

Claims 12 and 13 under 35 U.S.C. § 103(a) based on Kaarsholm, Pedersen, and Weldele⁴ (Ans. 6);

Claims 1–6, 8–11, and 14–23, provisionally, for obviousness-type double patenting based on claims 1–17 of application 12/715,203 (Ans. 16); and

Claims 12 and 13, provisionally, for obviousness-type double patenting based on claims 1–17 of the '203 application in view of Weldele (Ans. 16).

I

The Examiner has rejected all of the claims on appeal as obvious based on Kaarsholm and Pedersen, either by themselves or further combined with Weldele. The same issue is dispositive for both rejections.

The Examiner finds that Kaarsholm discloses stabilized compositions of a peptide that can be glucagon comprising a detergent and an isotonic agent, but where the isotonic agent is mannitol rather than a monosaccharide as required by the claims. (Ans. 3–4.) The Examiner finds that Pedersen discloses a variety of tonicity agents, including mannitol and glucose, and their use in glucagon-containing pharmaceutical formulations. (*Id.* at 4.)

² US 6,384,016 B1, issued May 7, 2002.

³ US 2007/0010424 A1, published January 11, 2007.

⁴ US 2006/0293382 A1, published December 28, 2006.

The Examiner also finds that Pedersen discloses solutions having osmolarities within the range recited in claim 1. (*Id.*)

The Examiner finds that development of stabilized glucagon solutions was a recognized problem in the art, and Pedersen teaches that use of mannitol in peptide formulations improves their stability, but the mannitol crystallizes and clogs injection devices. (*Id.*) The Examiner concludes that it would have been obvious “to substitute the isotonicity agents taught by Pedersen et al. for the mannitol in the compositions taught by Kaarsholm and to screen for stable formulations. The optimization and screening would likely result in the selection of glucose.” (*Id.* at 5.)

Appellants argue, among other things, that Pedersen teaches away from including glucose in a glucagon-containing formulation because “Pederson expressly states that because glucose is a reducing saccharide, it is able to initiate unwanted degradation in the formulation, and **thus is ruled out as a suitable tonicity modifier**. See Pederson [sic], para. [0192] (emphasis added).” (Appeal Br. 16–17.) Appellants argue that “[o]ne o[f] ordinary skill in the art in selecting an agent to enhance the stability of glucagon, would consider Pederson’s [sic] disclosure highly relevant, and would be led to select a different agent to replace mannitol.” (*Id.* at 18.)

The Examiner discounts the foregoing because “the previous statement within the same paragraph [states] that glucose is a ‘suitable replacement’ candidate for mannitol” and concludes that “glucose is one of a finite number of tonicity modifying agents that would be obvious to test.” (Ans. 14.) However, we agree with Appellants that, when Pedersen is

considered as a whole, it would not have led a skilled worker to modify Kaarsholm's composition to include glucose.

The critical paragraph in Pedersen reads as follows (emphasis added):

In the simulated filling experiment xylitol, glycerol, glucose, maltose, PEG 400, propylene glycol, sorbitol, sucrose and glycine were found to be suitable replacements candidates for mannitol. However, as glucose is a reducing saccharide, and therefore is able to initiate unwanted degradation in the formulation, this tonicity modifier is ruled out. Furthermore, maltose is ruled out due to clogging of needles. This leads to the following candidates: glycerol, xylitol, sorbitol, sucrose, glycine, propylene glycol and PEG 400, which are found to have suitable properties as replacement[] candidates for mannitol in peptide formulations with regards to drop test, clogging of needles and simulated filling.

(Pedersen ¶ 192.)

Thus, Pedersen discloses that, with respect to its effect on a peptide formulation in a simulated filling experiment using a placebo formulation of preservative, buffer, isotonic agent, and pH adjuster (Pedersen ¶¶ 180, 181, 190), glucose is a suitable replacement for mannitol because it does not form deposits and clog injection devices. (*Cf. id.* ¶ 3.) However, Pedersen immediately cautions that, because glucose can cause unwanted degradation in peptide formulations, it is “ruled out” as an acceptable tonicity modifier for use in place of mannitol. In the critical paragraph, Pedersen lists the specific tonicity modifiers that have “suitable properties as replacement[] candidates for mannitol in peptide formulations” and the list does not include glucose. Considered as a whole, then, Pedersen would be understood to state that glucose does not have suitable properties as a

replacement for mannitol as a tonicity modifier, because it can cause unwanted degradation in peptide formulations.

In summary, we agree with Appellants that Kaarsholm and Pedersen, when considered as a whole, would not have led a person of ordinary skill in the art to replace the mannitol in Kaarsholm's formulation with glucose. The rejection of claims 1–6, 8–11, and 14–23 under 35 U.S.C. § 103(a) based on Kaarsholm and Pedersen is reversed.

The rejection of claims 12 and 13 depends on the same combination of Kaarsholm and Pedersen; Weldele is cited only as a basis for adding ethanol to the composition. (Ans. 6–7.) Thus, the rejection of claims 12 and 13 suffers from the same deficiency discussed above, and is reversed for the same reason.

II

In addition to the rejections under § 103(a), the claims have also been provisionally rejected for obviousness-type double patenting based on application 12/715,203. (Ans. 16.) Claim 1 of the '203 application reads as follows:

1. A stabilized glucagon formulation comprising
 between 0.8 and 1.5 mg/mL of glucagon,
 between 0.5 and 5 mg/mL of lyso myristoyl phosphocholine
(LMPC),
 between 20 and 100 mg of a monosaccharide or
disaccharide/ml,
 and
 between 0.2 and 3 mg/mL of a preservative,
 having enhanced stability of the glucagon in an aqueous
solution at physiological temperature as compared to glucagon not
formulated with LMPC or the monosaccharide or disaccharide.

Claim 1 of the instant application and claim 1 of the '203 application thus are both directed to a stabilized glucagon formulation comprising glucagon, a surfactant (LMPC specifically in the '203 application), and a monosaccharide (or disaccharide in the '203 application). We agree with the Examiner that these claims are directed to products that are not patentably distinct.

With regard to claims 12 and 13 on appeal, which additionally require ethanol in the claimed formulation, the Examiner finds that Weldele discloses that ethanol stabilizes warfarin in solution, and concludes that it would have been obvious to include ethanol in a glucagon-containing formulation for the same effect. (Ans. 7.) We agree, and we agree with the Examiner's conclusion that claims 12 and 13 are obvious variants of claim 1 of the '203 application, in view of Weldele.

Appellants state that "since the scope of the cited claims could change during prosecution, Appellants do not address these rejections in this Appeal Brief. However, Appellants will address the rejections when the current claims are otherwise found allowable." (Appeal Br. 6.)

As provided in the MPEP, however,

[i]f "provisional" ODP rejections in two applications are the only rejections remaining in those applications, the examiner should withdraw the ODP rejection in the earlier filed application thereby permitting that application to issue without need of a terminal disclaimer. A terminal disclaimer must be required in the later-filed application before the ODP rejection can be withdrawn and the application permitted to issue.

MPEP § 804(I)(B)(1)

Here, the present application is the later-filed of the two applications and therefore, “[a] terminal disclaimer must be required . . . before the ODP rejection can be withdrawn and the application permitted to issue.” *Id.*

SUMMARY

We reverse both the rejections under 35 U.S.C. § 103(a).

We affirm both of the provisional rejections for obviousness-type double patenting.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED