

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

SANOFI-AVENTIS DEUTSCHLAND GMBH,
Patent Owner.

Case IPR2017-01526
Patent 7,476,652 B2

Before ERICA A. FRANKLIN, ROBERT A. POLLOCK, and
MICHELLE N. ANKENBRAND, *Administrative Patent Judges*.
ANKENBRAND, *Administrative Patent Judge*.

FINAL WRITTEN DECISION

Finding Claims 1–25 Unpatentable
35 U.S.C. § 318(a); 37 C.F.R. § 42.73

Denying-in-part and Dismissing-in-part as Moot Patent Owner's Motion to Strike
37 C.F.R. §§ 42.5(a), 42.20(a)

Dismissing Petitioner's Motion to Exclude and Denying-in-part and
Dismissing-in-part as Moot Patent Owner's Motion to Exclude
37 C.F.R. § 42.64(c)

Granting Petitioner's First Motion to Seal, Denying Petitioner's Second Motion to
Seal, and Granting Patent Owner's Motions to Seal
37 C.F.R. § 42.54

I. INTRODUCTION

This is a Final Written Decision in an *inter partes* review challenging the patentability of claims 1–25 (collectively, the “challenged claims”) of U.S. Patent No. 7,476,652 B2 (Ex. 1001, “the ’652 patent”). We have jurisdiction under 35 U.S.C. § 6. For the reasons that follow, we determine that Petitioner demonstrates, by a preponderance of the evidence, that the challenged claims are unpatentable.

A. Procedural History

Mylan Pharmaceuticals, Inc. (“Petitioner”) filed a Petition (Paper 2, “Pet.”) requesting an *inter partes* review under 35 U.S.C. § 311. Petitioner supported its Petition with the testimony of Samuel H. Yalkowsky, Ph.D. (Ex. 1003). On December 13, 2017, we instituted trial to determine whether:

1. Claims 1–25 of the ’652 patent are unpatentable under 35 U.S.C. § 103 as obvious over the combination of Lantus Label¹ and Lougheed²;
2. Claims 7 and 24 of the ’652 patent are unpatentable under 35 U.S.C. § 103 as obvious over the combination of Lantus Label and FASS³;

¹ Physicians’ Desk Reference, Lantus entry 709–13 (55th ed. 2001) (Ex. 1004). We refer in this decision to the corrected version of Exhibit 1004.

² W.D. Lougheed et al., *Physical Stability of Insulin Formulations*, 32 DIABETES 424–32 (1983) (Ex. 1006).

³ Farmaceutiska Specialiteter I Sverige (“FASS”), Summary of Product Characteristics Entry for Insuman Infusat (2000) (certified English translation provided as Ex. 1007A; original Swedish version provided as Ex. 1007).

3. Claims 7 and 24 of the '652 patent are unpatentable under 35 U.S.C. § 103 as obvious over the combination of Lantus Label and Grau⁴;
4. Claims 1–25 of the '652 patent are unpatentable under 35 U.S.C. § 103 as obvious over the combination of Owens⁵ and Lougheed;
5. Claims 7 and 24 of the '652 patent are unpatentable under 35 U.S.C. § 103 as obvious over the combination of Owens and FASS; and
6. Claims 7 and 24 of the '652 patent are unpatentable under 35 U.S.C. § 103 as obvious over the combination of Owens and Grau.

Paper 13 (“Institution Decision” or “Inst. Dec.”).

Following institution, Sanofi-Aventis Deutschland GmbH (“Patent Owner”) filed a Response (Paper 27, “Resp.”) and supporting declarations from Bernhardt Trout, Ph.D. (Ex. 2006) and Laurence C. Baker, Ph.D. (Ex. 2039). Petitioner filed a Reply (Paper 43, “Reply”) and supporting declarations from Dr. Yalkowsky (Ex. 1181), Robert S. Langer, Sc.D. (Ex. 1111), Deforest McDuff, Ph.D. (Ex. 1169), and William C. Biggs, M.D. (Ex. 1174).

During an interlocutory teleconference on July 17, 2018, we authorized Patent Owner to file a motion to strike certain arguments Petitioner made in the Reply. *See* Ex. 2055, 43:3–20 (Transcript of July 17, 2018 teleconference). We also authorized Patent Owner to file a sur-reply as to certain, but not all, arguments in Petitioner’s Reply. *Id.* at 42:13–43:2. Subsequently, Patent Owner filed a Sur-reply (Paper 46) and a Motion to Strike (Paper 47, “Mot. to Strike”). Petitioner

⁴ Ulrich Grau & Christopher D. Saudek, *Stable Insulin Preparation for Implanted Insulin Pumps – Laboratory & Animal Trials*, 36 DIABETES 1453–59 (1987) (Ex. 1008).

⁵ David R. Owens et al., *Pharmacokinetics of ¹²⁵I-Labeled Insulin Glargine (HOE 901) in Healthy Men – Comparison with NPH insulin and the influence of different subcutaneous injection sites*, 23 DIABETES CARE 813–19 (2000) (Ex. 1005).

filed an opposition to Patent Owner’s Motion to Strike (Paper 52, “Mot. to Strike Opp.”).

Petitioner and Patent Owner also filed several motions to seal certain briefs and exhibits. Paper 41 (Petitioner’s Motion to Seal and for Entry of Proposed Protective Order), Paper 45 (Patent Owner’s Supplemental Motion to Seal), Paper 78 (Patent Owner’s Motion to Seal), Paper 87 (Petitioner’s Motion to Seal). Both parties also filed motions to exclude, which have been fully briefed. *See* Papers 57, 64, 79 (briefing related to Petitioner’s Motion to Exclude); Papers 61, 67, 71 (briefing related to Patent Owner’s Motion to Exclude). Patent Owner also filed Observations on the Cross-Examination Testimony of Petitioner’s Reply Declarants, and Petitioner responded. Papers 60, 68. The record further includes a transcript of the final oral hearing conducted on September 27, 2018. Paper 77 (“Tr.”).

After the final oral hearing, we authorized Patent Owner to file a second sur-reply and additional evidence, and we authorized Petitioner to file a sur-sur-reply. Paper 75. Subsequently, Patent Owner filed the Sur-reply (Papers 79 (confidential version), 80 (public version)), and Petitioner filed the Sur-sur-reply (Papers 86 (confidential version), 88 (public version)).

B. *Related Matters*

The parties identify the following pending litigation involving the ’652 patent: *Sanofi-Aventis U.S. LLC v. Merck Sharp & Dohme Corp.*, C.A. No. 1:16-cv-00812-RGA (D. Del.); *Sanofi-Aventis U.S. LLC v. Merck Sharp & Dohme Corp.*, C.A. No. 2:17-cv-05914 (D.N.J.); *Sanofi- Aventis U.S. LLC v. Mylan N.V.*, C.A. No. 2:17-cv-09105-SRC (D.N.J); and *Sanofi- Aventis U.S. LLC v. Mylan N.V.*, C.A. No. 1:17-cv-00181-IMK (D.W.V.). Paper 7, 2; Paper 14, 1–2. The parties also identify the following concluded litigation involving the ’652 patent:

Sanofi-Aventis U.S. LLC v. Eli Lilly & Co., C.A. No. 1:14-cv-00113-RGA (D. Del.); *Sanofi-Aventis U.S. LLC v. Eli Lilly & Co.*, C.A. No. 1:14-cv-00884-RGA (D. Del.). Paper 7, 2; Paper 14, 1.

And the parties identify as related Case IPR2017-01528— an *inter partes* review involving claims 1–20 of U.S. Patent No. 7,713,930 (Ex. 1002), which issued from a continuation application to the application that issued as the ’652 patent. Paper 7, 2; Paper 14, 2. Concurrent with this decision, we issue a Final Written Decision in Case IPR2017-01528.

C. The ’652 Patent (Ex. 1001)

The ’652 patent, titled “Acidic Insulin Preparations Having Improved Stability,” issued on January 13, 2009. Ex. 1001, (45), (54). The ’652 patent relates to pharmaceutical formulations comprising a modified insulin—insulin glargine (Gly(A21)-Arg(B31)-Arg(B32)-human insulin) —and at least one surfactant. *See, e.g.*, Ex. 1001, Abstract, 1:11–19, 11:2–9. The formulation is used to treat diabetes, and is “particularly suitable for preparations in which a high stability to thermal and/or physicochemical stress is necessary.” *Id.* at 1:19–22. According to the specification, insulin glargine was a known modified insulin with a prolonged duration of action injected once daily as an acidic, clear solution that “precipitates on account of its solution properties in the physiological pH range of the subcutaneous tissue as a stable hexamer associate.” *Id.* at 2:56–61.

The specification explains that, at acidic pH, insulins exhibit decreased stability and increased susceptibility to aggregation in response to thermal and physicochemical stress, resulting in turbidity and precipitation (i.e., particle formation). *Id.* at 3:2–6. Such stresses can arise during use or shaking of the insulin solution. *Id.* at 5:34–56. Also contributing to aggregation are hydrophobic surfaces with which the insulin solution comes into contact during storage and

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