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Paper 52
Date: September 20, 2018

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ARGENTUM PHARMACEUTICALS LLC,
Petitioner,

v.

ALCON RESEARCH, LTD.,
Patent Owner.

Case IPR2017-01053
Patent 8,268,299 B2

Before GRACE KARAFFA OBERMANN, SUSAN L. C. MITCHELL, and CHRISTOPHER M. KAISER, *Administrative Patent Judges*.

OBERMANN, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
Determining That Claims 1–28 Have Not Been Proven Unpatentable
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

I. INTRODUCTION

The Petition requests *inter partes* review of claims 1–28 of U.S. Patent No. 8,268,299 B2 (Ex. 1001, "the '299 patent"). Paper 2 ("Pet."). Patent Owner filed no preliminary response. After trial institution, Patent Owner filed a Response (Paper 22, "Resp.") and Petitioner filed a Reply (Paper 35). We held a final hearing on April 17, 2018. Paper 51 ("Tr.").

The Board has jurisdiction under 35 U.S.C. § 6. Petitioner bears the burden of demonstrating unpatentability by a preponderance of the evidence, a burden that never shifts to Patent Owner. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d); *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc*., 800 F.3d 1375, 1378 (Fed. Cir. 2015). We issue this decision pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73.

A. Related Matters

The '299 patent was the subject of seven district court actions and a prior *inter partes* review. *See Apotex Corp. v. Alcon Research, Ltd.*, IPR2013-00428 ("the Apotex IPR"). Pet. 1; Paper 3, 2–3. The Apotex IPR was terminated by settlement after trial institution. Apotex IPR, Papers 9, 58, 60. "Petitioner was not a party to any of these cases." Pet. 1.

B. Illustrative Claim

Claim 1, reproduced below, illustrates the claimed subject matter:

1. A multi-dose, self-preserved ophthalmic composition, comprising:

zinc ions at a concentration of 0.04 to 0.4 mM; and

borate and polyol, the borate being present in the composition at a concentration of 0.1 to 2.0% w/v and the polyol being present in the composition at a concentration of 0.25 to 2.5% w/v, the polyol comprising propylene glycol in the composition at a concentration of 0.25 to 1.25% w/v and sorbitol in the composition at a concentration of 0.05 to 0.5% w/v

wherein: (i) the composition has a concentration of anionic species less than 15 mM; and (ii) the composition exhibits sufficient antimicrobial activity to allow the composition to satisfy USP 27 preservative efficacy requirements.

Ex. 1001, 25:31–47.

C. Grounds of Unpatentability

We instituted trial on the following grounds of unpatentability:

(1) Whether claims 1, 2, 4–8, 16, 17, and 20 of the '299 patent are unpatentable under 35 U.S.C. § 103 over Xia[1], Schneider[2], and Chowhan[3];

(2) Whether claim 28 is unpatentable under 35 U.S.C. § 103 over Xia, Schneider, the Travatan® Label[4], and Chowhan;

(3) Whether claims 1–23, 25, and 26 are unpatentable under 35 U.S.C. § 103 over Xia, Schneider, Chowhan, and Gadd[5]; and

(4) Whether claims 24, 27, and 28 are unpatentable under 35 U.S.C. § 103 over Xia, Schneider, the Travatan® Label, Chowhan, and Gadd.

Dec. 17–18; *see* Pet. 2–3 (statement of grounds).

The Petition is supported by Declarations of Dr. Erning Xia (Ex. 1002) and Dr. Yvonne M. Buys (Ex. 1021). The Petition also is accompanied by Declarations of Dr. Richard P. Parrish (Ex. 1022) and Dr. Henry Grabowski (Ex. 1037), which previously were submitted by Patent

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[1] Xia *et al.*, WO 2005/097067, "Zinc Preservative Composition and Method of Use" (filed March 24, 2005; published October 20, 2005) ("Xia") (Ex. 1003).

[2] Schneider *et al.*, U.S. Patent No. 6,011, 062, "Storage-Stable Prostaglandin Compositions" (Filed February 9, 1999; issued January 4, 2000) ("Schneider") (Ex. 1007).

[3] Chowhan *et al.*, U.S. Patent No. 6,143,799, "Use of Borate-Polyol Complexes in Ophthalmic Compositions" (filed July 2, 1998; issued November 7, 2000) ("Chowhan") (Ex. 1004).

[4] FDA Approved Drug Label "TRAVATAN® (travoprost ophthalmic solution) 0.004% Sterile" (2001) ("TRAVATAN® Label") (Ex. 1006).

[5] Gadd *et al.*, "Microorganisms and Heavy Metal Toxicity," *Microbial Ecology*, 4:303–317 (1978) ("Gadd") (Ex. 1005).

Owner in the Apotex IPR. The Response to the Petition is supported by Declarations of Dr. Bhagwati P. Kabra (Ex. 2006), Dr. Stephen Shannon (Ex. 2007), Dr. Soumyajit Majumdar (Ex. 2023), Dr. George Zhanel (Ex. 2025), as well as newly-prepared Declarations of Dr. Parrish (Ex. 2027), and Dr. Grabowski (Ex. 2029). The Reply is supported by a Second Declaration of Dr. Yvonne M. Buys (Ex. 1092), a Second Declaration of Dr. Erning Xia (Ex. 1093) and a Declaration of Mr. John C. Staines, Jr. (Ex. 1094). Patent Owner filed three motions for observations pertaining to depositions of Dr. Xia, Dr. Buys, and Mr. Staines. Papers 43, 44, 45. Petitioner responded to each motion for observation. Papers 48, 49, 50. In making our final determinations, we have considered Patent Owner's observations concerning those depositions and Petitioner's responses.

II. ANALYSIS

We organize our analysis into four parts. First, we provide an overview of the invention claimed in the '299 patent. Second, we address the level of ordinary skill in the art. Third, we discuss claim construction. Fourth, we assess the merits of the patentability challenge asserted in the Petition, weighing the objective indicia of nonobviousness against the evidence of obviousness.

A. The Invention of the '299 Patent (Ex. 1001)

The '299 patent describes "multi-dose, self-preserved ophthalmic compositions." Ex. 1001, Abstract. The specification states that pharmaceutical compositions, such as irrigating solutions for the eye, "are typically utilized multiple times by the patient, and are therefore frequently referred to as being of a 'multi-dose' nature." *Id.* at 1:44–46. The

specification states that such compositions can be prepared under sterile conditions, but due to "frequent, repeated exposure of multi-dose products to the risk of microbial contamination, it is necessary to employ a means for preventing such contamination from occurring." *Id.* at 1:26–39, 47–50.

The '299 patent discloses "multi-dose products that do not require a conventional antimicrobial preservative" "yet are preserved from microbial contamination." *Id.* at 3:10–13. Such compositions are known in the art as "preservative free" or "self-preserved." *Id*. at 3:14, 19. According to the '299 patent, aqueous ophthalmic compositions may be preserved from microbial contamination, despite the absence of conventional preservatives, by combining low concentrations of zinc ions with a borate-polyol complex and limiting the concentration of anionic species (such as buffering anions and metal cations) other than zinc in the compositions. *Id.* at 3:33–62. The claimed composition is "able to satisfy the USP preservative efficacy requirements" and do so "without employing any conventional antimicrobial preservatives." *Id*. at 4:10–17. The specification identifies prostaglandin analogs (including "travoprost") as therapeutic agents suitable for use with the zinc-based preservation system of the invention. *Id*. at 8:60–65.

B. Level of Ordinary Skill in the Art

We consider each ground of unpatentability in view of the understanding of a person of ordinary skill in the art at the time of the invention. Petitioner submits that such a person would have had a Doctorate in microbiology or chemistry (or a related field) with at least a few years of experience in the development of ophthalmic formulations. Pet. 7. Alternatively, in Petitioner's view, that person would have had a Bachelor's

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