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Paper No. 11
Date: April 23, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ETON PHARMACEUTICALS, INC.,
Petitioner,

v.

EXELA PHARMA SCIENCES, LLC,
Patent Owner.

PGR2020-00086
Patent 10,653,719 B1

Before ULRIKE W. JENKS, SUSAN L. C. MITCHELL, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge.*

DECISION
Denying Institution of Post-Grant Review
35 U.S.C. § 324

Eton Pharmaceuticals Inc. ("Petitioner") filed a Petition requesting a post-grant review of claims 1–27 ("the challenged claims") of U.S. Patent 10,653,719 B1(Ex. 1106, "the '719 patent"). Paper 1 ("Pet."). Exela Pharma Sciences, LLC ("Patent Owner") filed a Preliminary Response to the Petition. Paper 6 ("Prelim. Resp."). With our authorization (*see* Ex. 1124 at 14–20), Petitioner filed a reply to Patent Owner's Preliminary Response (Paper 8 ("Pet. Reply")), and Patent Owner filed a Sur-reply (Paper 10 ("Sur-reply")). We granted the additional briefing to allow Petitioner to file a copy of the request for rehearing it filed in related proceedings, PGR2020-00064 and PGR2020-00068, and to respond to assertions made in Patent Owner's Preliminary Response.

We have authority to determine whether to institute a post-grant review. 35 U.S.C. § 324. After considering all the papers submitted and cited evidence, for the reasons discussed below, we deny the Petition and do not institute a post-grant review.

I. BACKGROUND

A. Real Parties in Interest

Petitioner identifies itself as the real party in interest. Pet. 2. Patent Owner identifies itself as the real party in interest. Paper 3, 2.

B. Related Proceedings

The parties identify a related litigation matter, *Exela Pharma Sciences, LLC v. Eton Pharms., Inc.*, Case No. 1:20-cv-00365-MN (D. Del., filed March 16, 2020) (the "District Court Action"). Pet. 2; Paper 3, 2.

The parties also identify U.S. Patent No. 10/478,453, which is the subject of a post-grant review in PGR2020-00064, U.S. Patent No. 10,583,155, which is the subject of a post-grant Review in PGR2020-00068.

Pet. 3–4; Paper 3, 2. The parties also identify related applications U.S. Patent Appl. No. 16/746,028, U.S. Patent Appl. No.16/773,641, U.S. Patent Appl. No.16/850,726, U.S. Patent Appl. No.16/850,962, and U.S. Patent Appl. No.16/850,973. Pet. 3–4; Paper 3, 3.

C. The '719 Patent (Ex. 1106)

The '719 patent is titled "STABLE, HIGHLY PURE L-CYSTEINE COMPOSITIONS FOR INJECTION AND METHODS OF USE." Ex. 1106, code (54). The '719 patent issued from Application No. 16/773,563 ("the '563 application"), filed January 27, 2020. *Id.* at (21), (22).

The '719 patent describes stable L-cysteine compositions for injection, comprising: L-cysteine or a pharmaceutically acceptable salt thereof and/or hydrate thereof in an amount from about 10 mg/mL to about 100 mg/mL, and aluminum in an amount from about 1.0 parts per billion (ppb) to about 250 ppb. *Id.* at (57).

"L-cysteine is a sulfur-containing amino acid that can be synthesized de novo from methionine and serine in adult humans." *Id.* at 1:26–28. Because L-cysteine can be synthesized by the body, it is considered a non-essential amino acid. *Id.* at 1:33–34. "L-cysteine can be conditionally essential in preterm infants due to biochemical immaturity of the enzyme cystathionase that is involved in L-cysteine synthesis. Thus, there are a number of circumstances in which L-cysteine supplementation can be desirable." *Id.* at 1:37–42.

According to the specification, "[i]t has now been found that L–cysteine compositions for injection can be prepared using the methods described herein whereby the compositions unexpectedly comprise exceedingly low levels of Aluminum and other undesirable impurities, such

as cystine, pyruvic acid, certain heavy metals and certain ions." *Id.* at 4:37–43. Moreover, the specification discloses that:

> [T]he problems of safety, purity and stability are results not simply or directly from the level of Aluminum, but are also intertwined with dissolved oxygen levels in the composition and oxygen in the headspace as well as certain heavy metals and certain ions that may leach or be extracted out of the container closure.

Id. at 4:51–56.

The specification discloses that "known L-cysteine compositions contain up to 5000 ppb Aluminum." *Id.* at 7:21–22. In contrast, the specification describes "compositions that provide a therapeutically effective amount of L-cysteine, while containing less than 250 ppb Aluminum." *Id.* at 7:25–26. The specification discloses that reduced aluminum compositions "permit[ ] exposure to less than or equal to 4–5 micrograms per kilogram per day (µg/kg/d) to avoid or minimize Aluminum toxicity while still providing therapeutically effective L-cysteine in a stable composition." *Id.* at 7:35–38.

The specification expressly defines the term "stable."

> the term "stable" refers to a composition that has the component profiles described herein, for example. Aluminum, L-Cystine, and pyruvic acid, at the levels described and for the amount of time identified. In other words, a stable composition will coma.in the specified levels of all componentsfor [a] sufficient period of time to enable the composition to be commercially manufactured, stored, shipped, and administered in a clinical setting.

Id. at 16:41–48. For example, the specification discloses compositions wherein "cystine is present in the composition in an amount not more than 2.0 wt % relative to L-cysteine after storage at ambient temperature for a period of 6 months." *Id.* at 25:6–9. The specification also discloses

compositions wherein "pyruvic acid is present in the composition in an amount not more than 2.0 wt % relative to L-cysteine after storage at ambient temperature for a period of 6 months." *Id.* at 26:5–8.

Example 1 of the '719 patent describes a method of compounding an L-cysteine composition. *See id.* 41:60–42:32. Example 2 describes a test for aluminum levels in L-cysteine injections compounded as per Example 1. *Id.* at 42:34–60. The bulk solution was filled into uncoated Schott Type 1 USP glass vials. *Id.* Although "[t]he product was quite stable for all the time points tested up to 12 months[,] . . . the product resulted in an unacceptably high aluminum content." *Id.* at 42:43–49. The aluminum levels are shown in Table 6, reproduced below. *Id.*

TABLE 6

Aluminum Levels			
		6 Months	
Lot #	Release	25° C./60% RH	40° C./75% RH
XMHH1609	212 ppb	569 ppb	1,306 ppb
XMHH1610	199 ppb	748 ppb	1,374 ppb
XMHH1611	230 ppb	726 ppb	1,044 ppb

Example 6 also describes the stability of L-cysteine injections compounded as per Example 1. *Id.* at 49:55–50:22. The bulk solution was filled into Schott Type 1 USP Plus glass, which is internally coated with silicon dioxide. *Id.* Unlike Example 2, the L-cysteine compositions stored in coated glass vials did not show increased aluminum content when stored upright at room temperature for 9 months at 25° C/60% RH. *Id.* The stability data is shown in Table 18, reproduced-in-part below. *Id.*

TABLE 18

Characterization of L-Cysteine Composition for Injection			
Test	XMHJ1705	XMHJ1706	XMHJ1707

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