

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

PATENT OWNER ALCON RESEARCH, LTD.'S RESPONSE

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I. Introduction and Summary of Argument

The invention claimed in U.S. Patent No. 8,268,299 (“the ’299 patent”) combines particular concentrations of zinc ions, borate, sorbitol, and propylene glycol to achieve a “self-preserved” composition—*i.e.*, one that has sufficient antimicrobial activity to pass standard tests for “preservative efficacy” without needing a conventional preservative.¹ Argentum dismisses this invention as an obvious repackaging of well-known components. But while the ingredients in the claimed compositions were known, there is nothing obvious about the claimed combination. To the contrary, the person of ordinary skill in the art (“POSA”) would not have had reason to select and combine the claimed ingredients, let alone combine them at the claimed concentrations.

All the grounds at issue in this IPR center on the combination of three references—Xia, Schneider, and Chowhan—and all suffer from the same threshold defect. Argentum has failed to show that the POSA would have had reason to combine those references. Indeed, the obviousness of the ’299 patent over Xia and a Chowhan continuation patent with the identical specification was fully considered and rejected by the PTO during examination. Argentum’s assertion

¹ As used in the ’299 patent, “self-preserved” compositions “do not contain a conventional antimicrobial preservative, such as benzalkonium chloride, polyquaternium-1, chlorite, or hydrogen peroxide.” I.D. 7–8; Pet. 6.

that the addition of Schneider to the combination somehow renders the invention obvious is meritless. The premise of Argentum’s obviousness argument is that the POSA would have been motivated—as the first in a series of modifications—to replace the benzalkonium chloride (“BAK”) in Schneider’s formulation with the zinc disclosed in Xia. But Argentum admits (as it must) that Xia *by itself* teaches “multi-dose ophthalmic formulations containing a prostaglandin glaucoma agent that avoids the use of traditional preservatives, including BAC.”² Pet. 14. This admission belies any motivation the POSA would have had to combine Xia with any other reference. Yet, rather than simply using the self-preserved formulations disclosed in Xia, Argentum posits that it would have been obvious to the POSA to combine Xia with Schneider and then drastically alter the resulting Schneider/Xia formulation’s ingredients based on at least Xia, Schneider, and Chowhan.

Even assuming the POSA combined Xia and Schneider, Argentum cannot explain why the POSA would have been motivated to modify the Schneider/Xia formulation. Argentum’s own expert agreed that the POSA would have expected the Schneider/Xia formulation to pass preservative efficacy standards (“PET”). The best Argentum can muster is an unsupported assertion that the POSA would have “optimized” the preservative efficacy of the Schneider/Xia formulation by reducing its zinc concentration below the levels shown to pass PET in Xia, down to

² “BAC” and “BAK” are both accepted abbreviations for benzalkonium chloride.

the levels in the '299 patent's claims. But "optimizing" preservative efficacy would not have led the POSA to *decrease* the concentration of zinc; doing so would have been expected to reduce efficacy or encourage microbial growth, exactly the opposite of "optimizing" preservative efficacy.

Argentum also fails to show any teaching regarding why the POSA would substitute the single polyol—mannitol—present in the combined Schneider/Xia formulation, and replace it with a combination of two polyols—propylene glycol and sorbitol—each at the particular concentration that Alcon claims. Argentum's case is based entirely on hindsight. Although Chowhan lists propylene glycol and sorbitol among its preferred polyols, it gives no reason to combine polyols, much less a reason to select or combine these two particular polyols; it states that two other polyols—mannitol and glycerin—are each more preferred than either propylene glycol or sorbitol. Lacking any reason for the POSA to select the claimed combination of polyols at the claimed concentrations, Argentum's expert testified that the combination would be obvious because the POSA would "go through the iterations" of potential polyols and polyol combinations at various concentrations. But selecting particular concentrations of particular polyols would have required far more than routine optimization, even if it were clear what the POSA would be optimizing. There was no suggestion in the art that selecting more than one polyol, propylene glycol and sorbitol in particular, or any particular

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