UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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REGENERON PHARMACEUTICALS, INC.,
Petitioner

v.

NOVARTIS PHARMA AG,
NOVARTIS TECHNOLOGY LLC,
NOVARTIS PHARMACEUTICALS CORPORATION,
Patent Owners

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IPR2021-00816
U.S. Patent 9,220,631

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PATENT OWNERS' SURREPLY TO PETITIONER'S REPLY

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I. Introduction

The pre-filled syringes ("PFS") claimed in the '631 patent are a complex combination of elements that work together to solve the long-felt need for a safe, low silicone oil, terminally sterilized PFS for intravitreal injection of a VEGF-antagonist. Instead of looking at the invention as a whole, Petitioner attempts to meet its burden by reducing the invention to its component parts and arguing motivation and reasonable expectation of success of individual claim elements. Even that effort fails.

Petitioner has not rebutted the evidence that, as of the priority date, major pharmaceutical companies had tried and failed to make a PFS having the claimed characteristics. That objective evidence–demonstrating that making the claimed syringe was a difficult and unpredictable task–undermines Petitioner's simplistic arguments and exposes them as hindsight. This is especially true for the inventions of claims 21 and 24-26. The evidence, including admissions by Petitioner's expert, shows that a person of ordinary skill in the art ("POSA") would not have had a reasonable expectation of being able to terminally sterilize the claimed PFS to a sterility assurance level ("SAL") of 10^{-6} without unacceptably degrading the VEGF-antagonist active ingredient. Similarly, the evidence shows that a POSA would not have been motivated to use the Boulange syringes in a PFS to treat patients. Accordingly, the Board should confirm the patentability of the claims.

II. Petitioner Has Not Proven Motivation to Combine Boulange's Syringes with Sigg or Lam

A. A POSA Would Not Use a Parylene-C Coated Stopper With a VEGF-Antagonist

Petitioner's argument that a POSA would have been motivated to combine Boulange's Syringe B1 with Sigg or Lam rests on Mr. Koller's opinion that a POSA would have used Parylene-C in a PFS for intravitreal injection of a VEGF-antagonist. (Petition, 35; s*ee also*, Ex. 1103, ¶172.) As demonstrated in the Patent Owner Response ("POR"), however, Mr. Koller is not qualified to provide that opinion and failed to address the relevant prior art. (POR, 10.) Petitioner has therefore not met its burden on this issue. Petitioner's belated attempt to rectify the shortcomings in its prima facie case with the declaration of toxicologist Dr. Cohen (Ex. 1108) fails.

First, Dr. Cohen admits the prior art cited in the POR (Exs. 2030-2031) teaches that proteins adsorb to Parylene-C. (Ex. 1108.015, ¶30.) He argues a POSA would nevertheless not be deterred from using Parylene-C in a VEGF-antagonist-filled PFS because the references "encourage" its use "in medical applications." (Petitioner's Reply to Patent Owner's Response ("Reply"), 5; Ex. 1108.0014, ¶ 29.) As Dr. Cohen conceded, however, the known "medical applications" of Parylene-C were for implantable devices, and there was no

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