UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

REGENERON PHARMACEUTICALS, INC.
Petitioner,
v.

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

Case No. IPR2021-00816
U.S. Patent No. 9,220,631

DECLARATION OF JOEL M. COHEN

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I. INTRODUCTION

1. I have been retained by Petitioner Regeneron Pharmaceuticals, Inc. ("Petitioner" or "Regeneron"), as an independent expert witness in the above-captioned *inter partes* review ("IPR"), in which Regeneron has requested that the U.S. Patent and Trademark Office cancel as unpatentable all claims of U.S. Patent No. 9,220,631 ("the '631 patent").

2. This declaration sets forth my analyses and opinions in response to the declaration of Dr. John E. Dillberger (Ex. 2202). As I explain below, it is my opinion that a toxicologist, as a member of a product development team, would not have considered Parylene C to be unsafe, toxic, or unacceptable to be used as a stopper coating in a prefilled syringe for intravitreal injection of a VEGF antagonist drug.

II. QUALIFICATIONS AND COMPENSATION

3. I have a Sc.D. in Environmental Health from Harvard School of Public Health, a B.A. in Anthropology, Environmental Science, and Public Health from Tufts University, and am a certified Diplomate of the American Board of Toxicology (DABT).

4. In addition, I have worked in the field of toxicology since 2011, including 8 years working as a toxicology consultant at Gradient which provides

scientific consulting services specializing in toxicology, epidemiology, risk assessment, and product safety, among others. In 2021 I was promoted to Principal Scientist, and in 2022 I was promoted to Principal at the firm. My professional experience in toxicology includes work in the pharmaceutical, medical device, and product safety industries.

5. As a Principal at Gradient, I provide scientific consulting services related to medical device biocompatibility and toxicological risk assessment, consumer product risk assessment, and evaluations of toxicology studies in connection with human health risks. I have worked on pharmaceuticals, medical devices, consumer product safety, and toxicological risk assessments.

6. With respect to the pharmaceutical industry, I have evaluated the potential health risks from exposure to impurities in a drug product for juvenile patients. To determine the health risks, I evaluated the repeated dose toxicity, genotoxicity, and carcinogenicity of the components contained in the identified impurities, including those that had little toxicological data. I have also conducted human health hazard and risk assessments for potential impurities in cell-based cancer treatments. The evaluation was used as manufacturing guidance, as well as for regulatory applications. I have also evaluated the kinetics and biological effects of a new chemical platform for drug development. Specifically, I worked on understanding the potential off-target effects of the novel chemistry involved,

including known pharmacokinetics and potential for adverse health effects. Most recently I was hired to conduct a toxicological risk assessment on extractable and leachables from a pre-filled syringe, which involved chemical risk assessment for all compounds detected under aggressive extraction conditions (*e.g.* harsh polar solvents and at elevated temperatures), as well as chemicals detected having leached from the syringe into the drug formulation itself under more clinically relevant test conditions.

7. I have also worked on a number of medical device projects. I have provided ISO-compliant toxicological risk assessments for chemicals identified in extracts of implantable medical ports and catheter systems, a permanent implant screw, dialysis equipment, and leached compounds from a dialysis machine. In particular, I identified toxicological data for relevant endpoints and used the data to derive chemical and device specific safety margins, in accordance with ISO10993-17, ICH M7, and US FDA guidance. The risk assessments were used to support safety evaluations of the medical devices, and specifically for addressing potential risks related to systemic toxicity, genetic toxicity, carcinogenicity, and reproductive and developmental toxicity.

8. I have also established biocompatibility test plans involving experimental testing on medical devices for cytotoxicity, sensitization, irritation, genotoxicity, implantation, hemocompatibility, material mediated pyrogenicity,

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