

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. IPR2020-01317  
U.S. Patent No. 9,220,631

---

PETITION FOR INTER PARTES REVIEW

## TABLE OF CONTENTS

|       |  |    |
|-------|--|----|
| I.    | INTRODUCTION .....   | 1  |
| II.   | MANDATORY NOTICES .....  | 4  |
|       | A. Real Party-in-Interest .....                                      | 4  |
|       | B. Related Matters.....  | 4  |
|       | C. Lead and Back-up Counsel and Service Information .....            | 4  |
| III.  | GROUNDS FOR STANDING.....  | 5  |
| IV.   | OVERVIEW OF THE TECHNOLOGY AT ISSUE .....                            | 5  |
|       | A. Pre-filled Syringes.....  | 5  |
|       | B. Siliconization of Syringe Barrels .....                           | 7  |
|       | C. Sterilization of Drug Products and Container Systems.....         | 10 |
|       | D. Particulate Content .....   | 13 |
| V.    | THE '631 PATENT.....   | 13 |
|       | A. The Challenged Claims .....                                       | 14 |
|       | B. The Specification.....  | 16 |
|       | 1. Siliconization Methods and Alleged Surprising Results .....       | 16 |
|       | 2. Terminal Sterilization .....                                      | 19 |
|       | 3. Particulate Content.....  | 19 |
|       | C. The Prosecution History.....                                      | 20 |
| VI.   | STATUTORY GROUNDS FOR THE CHALLENGES .....                           | 22 |
| VII.  | LEVEL OF ORDINARY SKILL IN THE ART .....                             | 26 |
| VIII. | CLAIM CONSTRUCTION .....   | 27 |
|       | A. “Stopper Break Loose Force” .....                                 | 27 |
|       | B. “Stopper Slide Force”.....  | 28 |
|       | C. “Terminally sterilized” .....                                     | 28 |
| IX.   | IDENTIFICATION OF HOW THE CHALLENGED CLAIMS ARE<br>UNPATENTABLE..... | 29 |
|       | A. Ground 1: Sigg in view of Boulange.....                           | 29 |

|    |  |    |
|----|--|----|
| 1. | Overview of Sigg .....   | 30 |
| 2. | Overview of Boulange .....   | 32 |
| 3. | Motivation to Combine and Reasonable Expectation of<br>Success .....   | 37 |
| 4. | Claim 1 .....  | 43 |
| 5. | Claims 2, 3, 5-9, 14, 16-22 and 24.....                                | 49 |
| 6. | Claim 15 .....   | 57 |
| B. | Ground 2: Sigg in view of Boulange and Fries.....                      | 59 |
| C. | Ground 3: Sigg in view of Boulange and Furfine.....                    | 61 |
| D. | Ground 4: Sigg in view of Boulange and Macugen <sup>®</sup> Label..... | 63 |
| E. | Ground 5: Sigg in view of Boulange and Dixon.....                      | 65 |
| X. | CONCLUSION.....  | 67 |

## PETITIONER'S EXHIBIT LIST

|          |   |
|----------|---|
| Ex. 1001 | U.S. Patent No. 9,220,631 (“the ’631 Patent”)   |
| Ex. 1002 | Prosecution File History of U.S. Patent No. 9,220,631   |
| Ex. 1003 | Declaration of Horst Koller under 37 C.F.R. § 1.68.   |
| Ex. 1004 | Curriculum Vitae of Horst Koller  |
| Ex. 1005 | Declaration of James Agalloco under 37 C.F.R. § 1.68.   |
| Ex. 1006 | Curriculum Vitae of James Agalloco  |
| Ex. 1007 | PCT Patent Publication No. WO 2011/006877 to Sigg <i>et al.</i> (“Sigg”)  |
| Ex. 1008 | PCT Patent Publication No. WO 2009/030976 to Boulange <i>et al.</i> (“Boulange”)  |
| Ex. 1009 | Internet Archive WayBack Machine, March 7, 2011 Record of Drugs.com, <i>Macugen Prescribing Information</i> , available at <a href="https://web.archive.org/web/20110307065238/http://www.drugs.com:80/pro/macugen.html">https://web.archive.org/web/20110307065238/http://www.drugs.com:80/pro/macugen.html</a> (“Macugen® Label”) |
| Ex. 1010 | <i>Certified English Translation of Bruno Reuter and Claudia Petersen. “Die Silikonisierung von Spritzen: Trends, Methoden, Analyseverfahren,” TechnoPharm 2, Nr. 4 (2012): 238-244. (“Reuter”)</i>   |
| Ex. 1011 | Bhavnes D. Shah & Bhupendra G. Prajapati, <i>Pre-Filled Syringes: A New Concept</i> , PHARMA BIO WORLD 51 (2009) (“Shah”)   |
| Ex. 1012 | Arno Fries, <i>Drug Delivery of Sensitive Biopharmaceuticals With Prefilled Syringes</i> , 9(5) DRUG DELIVERY TECH. 22 (2009) (“Fries”)   |
| Ex. 1013 | Thomas Schoenknecht, <i>Prefilled Syringes: Why New Developments Are Important In Injectable Delivery Today</i> , in PREFILLED SYRINGES INNOVATIONS THAT MEET THE GROWING DEMAND (OnDrugDelivery 2005) (“Schoenknecht”)   |
| Ex. 1014 | U.S. Patent Publication No. 2012/0091026 to Chacornac <i>et al.</i> (“Chacornac”)   |

|          |  |
|----------|--|
| Ex. 1015 | Sandeep Nema & John D. Ludwig, <i>Pharmaceutical Dosage Forms: Parenteral Medications, Volume 1: Formulation and Packaging</i> (3rd ed. 2010) (“Nema Vol. 1”)  |
| Ex. 1016 | Sandeep Nema & John D. Ludwig, <i>Pharmaceutical Dosage Forms: Parenteral Medications, Volume 2: Facility Design, Sterilization and Processing</i> (3rd ed. 2010) (“Nema Vol. 2”)  |
| Ex. 1017 | PCT Patent Publication No. WO 2007/035621 to Scypinski <i>et al.</i> (“Scypinski”)   |
| Ex. 1018 | U.S. Patent Publication No. 2003/0003014 to Metzner <i>et al.</i> (“Metzner”)  |
| Ex. 1019 | U.S. Pharmacopeia, <i>USP 789, Particulate Matter in Ophthalmic Solutions, USP 34 NF 29</i> (2011)   |
| Ex. 1020 | U.S. Patent Publication No. 2011/276005 to Hioki <i>et al.</i> (“Hioki”)   |
| Ex. 1021 | PCT Patent Publication No. WO 2007/149334 to Furfine <i>et al.</i> (“Furfine”)   |
| Ex. 1022 | Michael W. Stewart <i>et al.</i> , <i>Fresh From the Pipeline Aflibercept</i> , 11 NAT. REV. DRUG DISCOV. 269 (2012) (“Stewart”)   |
| Ex. 1023 | U.S. Patent No. 7,060,269 to Baca <i>et al.</i> (“Baca”)   |
| Ex. 1024 | Prosecution File History of U.S. Patent No. 7,060,269  |
| Ex. 1025 | Lu Liu <i>et al.</i> , <i>Silicone Oil Microdroplets and Protein Aggregates in Repackaged Bevacizumab and Ranibizumab: Effects of Long-term Storage and Product Mishandling</i> , 52(2) INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE 1023 (2011) (“Liu”) |
| Ex. 1026 | U.S. Patent No. 7,404,278 to Wittland <i>et al.</i> (“Wittland”)   |
| Ex. 1027 | U.S. Food and Drug Administration, <i>Lucentis® Highlights of the Prescribing Information</i> , (June 2010) (“Lucentis® Label”)  |
| Ex. 1028 | International Organization for Standardization, <i>ISO 11040-4 Prefilled Syringes – Part 4: Glass Barrels for Injectables</i> (2nd ed. 2007) (“ISO 11040-4”)   |

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.