Regeneron's Initial Invalidity Contentions in Inv. No. 337-TA-1207

Exhibit A: Invalidity of U.S. Patent No. 9,220,631 Under 35 U.S.C. §§ 102-103

Regeneron contends that each of the references set forth below, either alone or in combination with other prior art, invalidates the claims of the 631 Patent under 35 U.S.C. §§ 102-103:

Prior Art Reference	Date of Publication or Other Prior Art Date	Statutory Provision of Prior Art[1]
A. Fries, Drug Delivery of Sensitive Biopharmaceuticals with Prefilled Syringes, Drug Delivery Technology, Vol. 9, No. 5 (May 2009) ("Fries")	2009	102(b)
Bruno Reuter and Claudia Petersen. "Die Silikonisierung von Spritzen: Trends, Methoden, Analyseverfahren," TechnoPharm 2, Nr. 4 (2012): 238-244. ("Reuter")	2012	102(a)
Bryon Lambert, et al. Radiation and Ethylene Oxide Terminal Sterilization Experiences with Drug Eluting Stent Products, American Association of Pharmaceutical Sciences, December 2011, 12(4):1116-1126 ("Lambert")	December 2011	102(a); 102(b)
Carl Hultman, et al. The Physical Chemistry of Decontamination with Gaseous Hydrogen Peroxide, Pharmaceutical Engineering, January/February 2007, 27(1):1-6 ("Hultman")	2007	102(b)
Dow Corning® 365 35% Dimethicone NF Emulsion – Frequently Asked Questions (2002) ("DC365 FAQ")	2002	102(b)
European Patent Application No. EP2371406 to Hioki et al. ("Hioki")	2011	102(a); 102(b); 102(e)
Macugen PFS: *see e.g.*, Internet Archive WayBack Machine, March 7, 2011 Record of Drugs.com, Macugen Prescribing Information, available at https://web.archive.org/web/20110307065238/http://www.drugs.com:80/pro/macugen.html ("Macugen® Label")	2011	102(a); 102(b)

[1] In light of Novartis' failure to provide any basis to support its effective filing date and conception contentions with respect to the 631 Patent, Regeneron reserves the right to identify different statutory provisions under which each reference qualifies as prior art.

Prior Art Reference	Date of Publication or Other Prior Art Date	Statutory Provision of Prior Art[1]
John R. Gillis & Gregg Mosley, Validation of Pharmaceutical Processes, Chapter 16 – Validation of Ethylene Oxide Sterilization Processes (2011), pp.241-262. ("Gillis")	2011	102(a); 102(b)
K. Kereluk, et al. Microbiological Aspects of Ethylene Oxide Sterilization: I. Experimental Apparatus & Methods, Applied Microbiology 1970, 19(1):146-151. ("Kereluk")	1970	102(b)
Pamela Carter, et al. The lowdown on low temperature sterilization for packaged devices, Healthcare Purchasing News, July 2008, 42-45. ("Carter")	2008	102(b)
PCT Patent Publication No. WO 2007/035621 to Scypinski et al. ("Scypinski")	2007	102(b)
PCT Patent Publication No. WO 2007/149334 to Furfine et al. ("Furfine")	2007	102(b)
PCT Patent Publication No. WO 2008/077155 to Lam et al. ("Lam")	2008	102(b)
PCT Patent Publication No. WO 2009/030976 to Boulange et al. ("Boulange")	2009	102(b)
PCT Patent Publication No. WO 2011/006877 to Sigg et al. ("Sigg")	2011	102(b)
PCT Patent Publication No. WO 2011/159975 to D'Souza et al. ("D'Souza")	December 2011	102(a); 102(b); 102(e)
PCT Patent Publication No. WO1994/013328 to Hagen ("Hagen")	1994	102(b)
Sandeep Nema & John D. Ludwig, Pharmaceutical Dosage Forms: Parenteral Medications, Volume 1: Formulation and Packaging (3rd ed. 2010) ("Nema Vol. 1")	2010	102(b)
Sandeep Nema & John D. Ludwig, Pharmaceutical Dosage Forms: Parenteral Medications, Volume 2: Facility Design, Sterilization and Processing (3rd ed. 2010) ("Nema Vol. 2")	2010	102(b)
Sandeep Nema & John D. Ludwig, Pharmaceutical Dosage Forms: Parenteral Medications, Volume 3: (3rd ed. 2010) ("Nema Vol. 3")	2010	102(b)
U.S. Patent Application No. 2007/0253984 to Khandke et al. ("Khandke")	2007	102(b)

Prior Art Reference	Date of Publication or Other Prior Art Date	Statutory Provision of Prior Art[1]
U.S. Patent Publication No. 2012/0091026 to Chacornac et al. ("Chacornac")	April 19, 2012	102(a); 102(e)
U.S. Department of Labor, Occupational Safety & Health Administration, Ethylene Oxide (EtO): Understanding OSHA's Exposure monitoring Requirements, 2007 OSHA3325-01N (2007), available at https://www.osha.gov/Publications/ethylene_oxide.html ("OSHA Guidelines")	2007	102(b)
U.S. Food and Drug Administration, Eylea® Highlights of the Prescribing Information (Nov. 2011) ("the Eylea® Label")	November 2011	102(a); 102(b)
U.S. Food and Drug Administration, Lucentis® Highlights of the Prescribing Information, (June 2010) ("the Lucentis® Label")	June 2010	102(b)
U.S. Patent No. 6,790,410 to Metzner et al. ("Metzner")	2004	102(b)
United States Patent No 8,221,353 to Cormier et al. ("Cormier")	July 17, 2012	102(a); 102(b); 102(e)
United States Patent No. 7,404,278 to Wittland et al. ("Wittland")	2008	102(b)
United States Patent Publication No. 2007/0190058 to Sharms ("Sharms")	2007	102(b)
William Leventon, "Medical Device Sterilization: What Manufacturers Need to Know" (MDDI online, Sept. 1, 2002), available at https://www.mddionline.com/medical-devicesterilization-what-manufacturers-need-know ("Leventon")	2002	102(b)
Bhavnesh Shah, "Pre-filled Syringes: A New Concept," Pharma Bio World (August 2009) ("Shah")	2009	102(b)
EYLEA Vial	On sale no later than November 21, 2011	102(a); 102(b)
EYLEA PFS	*See* Exhibits C1 and C2 for conception and reduction to practice dates	102(g)
U.S. Food and Drug Administration, Lucentis® Highlights of the Prescribing Information, (June 2010) ("Lucentis® Label")	June 2010	102(b)

Prior Art Reference	Date of Publication or Other Prior Art Date	Statutory Provision of Prior Art[1]
Vetter Syringes		102(f)
Dr. Thomas Schoenknecht, "Pre-Filled Syringes: Why New Developments are Important to Injectable Delivery Today," Prefilled Syringes: Innovations that meet the growing demand (2005) ("Schoenknecht")	2005	102(b)
Advait Badkar, "Development of Biotechnology Products in Pre-filled Syringes: Technical Considerations and Approaches," AAPS PharmSciTech, Vol. 12 No. 2 (June 2011) ("Badkar")	June 2011	102(b)
U.S. Pharmacopeia, USP 789, Particulate Matter in Ophthalmic Solutions, USP 34 NF 29 (2011) ("USP 789")	2011	102(b)
James A. Dixon, et al. "VEGF Trap-Eye for the treatment of neovascular age-related macular degeneration." Expert opinion on investigational drugs 18.10 (2009): 1573-1580. ("Dixon")	2009	102(b)

Each of the prior art references identified in Exhibits A1-A13, B1-B3, and C1-C2 of Regeneron's initial invalidity contentions either anticipates one or more of the claims of the 631 Patent and/or renders obvious one or more of the claims of the 631 Patent when viewed in combination with other prior art references. Regeneron reserves the right to contend that each of the anticipatory references renders the claims obvious either in view of the reference alone or in combination with other references. The identification of any patent or patent application should be deemed an identification of any counterpart patent, application, or associated product; the identification of any article or publication should be deemed a disclosure of any substantially similar article if published in some other form, or of any patent or patent application whole, as understood by a POSITA. For example, a reference to a figure should be deemed to refer to the text describing the figure and vice versa.

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