UNITED STATES INTERNATIONAL TRADE COMMISSION
WASHINGTON, D.C.

In the Matter of	
CERTAIN PRE-FILLED SYRINGES FOR INTRAVITREAL INJECTION AND COMPONENTS THEREOF	Investigation No. 337-TA-[_]

COMPLAINT UNDER SECTION 337 OF THE TARIFF ACT OF 1930, AS AMENDED

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Exhibit No. 60	B. McEvoy, et. al., *Terminal sterilization of medical devices using vaporized hydrogen peroxide: a review of current methods and emerging opportunities*, Journal of Applied Microbiology 127, 1403-1420 (2019)
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Appendix No. 2	Cited references for Prosecution History of U.S. Patent No. 9,220,631

I. Introduction

1. This Complaint is filed by Novartis Pharma AG ("NPAG"); Novartis Pharmaceuticals Corporation ("NPC") and Novartis Technology LLC ("NT") (collectively, "Novartis" or "Complainants"), pursuant to Section 337 of the Tariff Act of 1930, as amended, 19 U.S.C. § 1337 ("Section 337"), against the Proposed Respondent Regeneron Pharmaceuticals, Inc. ("Regeneron"). Novartis respectfully requests that the United States International Trade Commission (the "Commission") institute an investigation relating to the unlawful sale for importation into the United States, importation into the United States, and/or the sale within the United States after importation of certain pre-filled syringes ("PFS"), such as Regeneron's EYLEA® (aflibercept) pre-filled syringe ("EYLEA PFS"), and/or components thereof, including but not limited to a glass body forming a barrel, a stopper, and a plunger (the "Accused Products").

2. Regeneron has engaged in unfair acts in violation of Section 337(a)(1)(B) through and in connection with the unlicensed importation into the United States, sale for importation, and/or sale within the United States after importation of the Accused Products that infringe certain claims of Novartis's U.S. Patent No. 9,220,631 (the "'631 patent" or "Asserted Patent"). (Exhibit No. 1 – Certified Copy of U.S. Patent No. 9,220,631). Regeneron directly infringes, and/or induces or contributes to the infringement of at least claims 1–6 and 11–26 of the '631 patent. (Exhibit 3) (Infringement Chart of Independent Claim 1).

3. Regeneron has violated and continues to violate Section 337 to the detriment of Novartis's domestic industry that exists or is in the process of being established in the United States relating to articles protected by the Asserted Patent.

4. Novartis has a domestic industry that exists or is in the process of being established with respect to its proprietary active pharmaceutical ingredient, brolucizumab, under the trade name, BEOVU® ("BEOVU"). On October 8, 2019, the United States Food & Drug Administration

("FDA") approved Novartis's biologics license application ("BLA") for its BEOVU vial presentation for the treatment of wet age-related macular degeneration. (Exhibit 4) (https://www.novartis.com/news/media-releases/novartis-receives-fda-approval-beovu-offering-wet-amd-patients-vision-gains-and-greater-fluid-reductions-vs-aflibercept).

5. The clinical studies supporting FDA approval utilized study centers and involved subjects and patients located in the United States. There are also ongoing clinical studies for additional potential indications, such as diabetic macular edema, taking place in study centers in the United States, and future clinical studies planned for the United States. Novartis has made and continues to make significant investments in the United States relating to clinical studies specific to BEOVU.

6. Novartis is currently seeking FDA approval for BEOVU in a PFS presentation ("BEOVU PFS"). (Confidential Exhibit 5) (Confidential Declaration of Meghan Brown). The BEOVU PFS practices at least one claim of the Asserted Patent. Novartis plans to commercialize the BEOVU PFS in the United States once approved as described in the Confidential Declaration of Dhaval Desai. (Confidential Exhibit 6). Novartis has conducted at least one observational in-use clinical study in the United States to test whether providers understood how to safely and effectively administer BEOVU in a PFS. The extensive clinical studies for the BEOVU vial presentation will also support the BEOVU PFS for reasons set forth in the Confidential Declaration of Meghan Brown. (Confidential Exhibit 5). Further, Novartis has made and continues to make significant investments in the United States relating to education and product support and regulatory oversight specific to the BEOVU PFS.

7. Additionally, Novartis licensed the '631 patent to Genentech, Inc. ("Genentech"). Genentech operates an industry in the United States relating to the Asserted Patent based on its

LUCENTIS® (ranibizumab) pre-filled syringe product ("LUCENTIS PFS"), which practices at least one claim of the Asserted Patent. On information and belief, Genentech has made and continues to make significant investments in the United States with respect to the LUCENTIS PFS, such as the employment of significant labor and capital and substantial investments in the exploitation of the Asserted Patent.

8. To remedy Regeneron's continuing and unlawful violation of Section 337, Novartis seeks, as permanent relief, a limited exclusion order, pursuant to 19 U.S.C. § 1337(d), barring from entry into the United States all infringing PFS and components thereof sold for importation, imported, or sold within the United States after importation by Regeneron.

9. Novartis also seeks cease and desist orders, pursuant to 19 U.S.C. § 1337(f), prohibiting Regeneron from engaging in the unlawful sale for importation into the United States, importation into the United States, and/or the sale within the United States after importation of PFS and components thereof that infringe, induce or contribute to the infringement of one or more claims of the Asserted Patent. Further, Novartis requests that the Commission impose a bond upon any importation by Regeneron of PFS and components thereof during the 60-day Presidential review period, pursuant to 19 U.S.C. § 1337(j).

A. Complainants

10. NPAG is a company organized and existing under the laws of Switzerland, with a principal place of business at Forum 1 Novartis Campus, CH-4056 Basel, Switzerland.

11. NPC is a Delaware corporation with a principal place of business at One Health Plaza, East Hanover, New Jersey, 07936.

12. NT is a Delaware corporation with a principal place of business at One Health Plaza, East Hanover, New Jersey, 07936.

B. Novartis's Licensee, Genentech

13. Genentech is a California corporation with its principal place of business at 1 DNA Way Mailstop, 258A South San Francisco, California 94080.

14. Genentech is licensed by Novartis to practice the Asserted Patent and is the exclusive U.S. provider of the LUCENTIS PFS, a domestic industry product. Copies of the license and related amendments are attached as Confidential Exhibits 7 through 10.

15. On information and belief, since its FDA approval in 2016 (Exhibit 11) (screen shot of https://www.gene.com/media/press-releases/14640/2016-10-14/fda-approves-genentechs-lucentis-ranibiz) and United States launch in 2017 (Exhibit 12) (https://eyewire.news/articles/lucentis-05-mg-prefilled-syringe-now-available-to-order-in-the-us/), the LUCENTIS PFS has been supported by Genentech's pharmaceutical operations in the United States.

C. Regeneron

16. Regeneron is a corporation organized and existing under the laws of New York state with its principal place of business at 77 Old Saw Mill River Road, Tarrytown, New York 10591. (Exhibit 13) (United States Securities and Exchange Commission Regeneron Form 10-K (2018)).

17. Regeneron currently markets the active pharmaceutical ingredient aflibercept under the brand name EYLEA® ("EYLEA") in the United States. EYLEA is a vascular endothelial growth factor ("VEGF") inhibitor that is approved by the FDA to treat four retinal indications, including diabetic retinopathy, diabetic macular edema, neovascular (wet) age-related macular degeneration, and macular edema following retinal vein occlusion. (Exhibit 14) (EYLEA prescribing information). On August 13, 2019, the FDA approved Regeneron's sBLA for its PFS presentation for EYLEA. The EYLEA PFS became available for purchase in the United States

beginning December 6, 2019. (Exhibit 15) (Regeneron Press Release entitled "FDA Approves EYLEA® (Aflibercept) Injection Prefilled Syringe"); (Exhibit 16) (screen shot of EYLEA® Healthcare Professional Website Available for Order in a Pre-filled syringe (https://hcp.eylea.us/)).

18. On information and belief, Regeneron's EYLEA PFS infringes claims 1–6 and 11–26 of the '631 patent.

19. On information and belief, Regeneron violates Section 337 through its sale for importation, importation, and/or sale after importation of EYLEA PFS or at least components of the infringing EYLEA PFS.

II. Background

A. Chronic Eye Disorders Affect Millions of Patients in the United States

20. Retinal diseases, such as diabetic retinopathy, diabetic macular edema and neovascular age-related macular degeneration are chronic eye disorders impacting millions of patients in the United States. For example, the National Eye Institute projects that by 2050, the estimated number of patients with neovascular age-related macular degeneration is expected to more than double from 2.07 million to 5.44 million. (Exhibit 17) (https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/age-related-macular-degeneration-amd-data-and-statistics). Patients diagnosed with these chronic eye diseases may experience symptoms such as distorted or blurry vision, spots or dark strings floating in vision, impaired color vision, or vision loss. Many of these chronic eye diseases are associated with an overexpression of VEGF, a signaling protein that promotes the growth of new blood vessels when, for example, the blood supply to cells and tissues are deprived of oxygenated blood due to impaired blood circulation.

21. Treatment of the chronic eye diseases discussed above require repeated intravitreal injections of a medication called an anti-VEGF. An intravitreal injection is a procedure to inject

the anti-VEGF medication directly into the space in the back of the eye called the vitreous cavity. This procedure is performed by a trained retinal specialist. In general, an anti-VEGF medication binds to, and inhibits the activity of, VEGF, thus discouraging or inactivating the growth of abnormal blood vessels.

B. Novartis and Its Licensee, Genentech, Have Each Developed PFS Products Containing Anti-VEGF Medications to Treat Chronic Eye Diseases

22. Novartis has developed an anti-VEGF medication, under the trade name BEOVU, containing the active ingredient brolucizumab. On October 8, 2019, the FDA approved Novartis's BLA for a vial presentation of BEOVU. (Exhibit 4) (https://www.novartis.com/news/media-releases/novartis-receives-fda-approval-beovu-offering-wet-amd-patients-vision-gains-and-greater-fluid-reductions-vs-aflibercept). An image of a BEOVU vial is shown below (image obtained from https://www.empr.com/slideshow/slides/new-drug-product-beovu/).

23. From approximately 2013 to 2018, before obtaining FDA approval, Novartis conducted at least seven clinical studies involving over 2,000 neovascular age-related macular degeneration subjects. (Confidential Exhibit 18) (excerpt of Clinical overview in neovascular age-related macular degeneration (nAMD)). Six of these clinical studies utilized study centers and

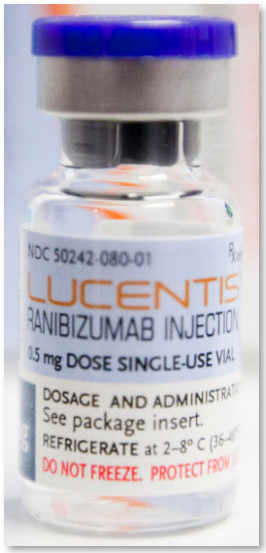
subjects located in the United States. Additionally, there are multiple ongoing and future clinical studies for potential additional indications, such as diabetic macular edema.

24. Novartis has also engaged in significant work to prepare for offering a PFS presentation for BEOVU in the United States upon FDA approval, and has an anticipated timeline for FDA approval of the BEOVU PFS and subsequent launch in the United States. *See* Confidential Declaration of Meghan Brown (Confidential Exhibit 5). As explained in detail in the Confidential Declarations of Meghan Brown (Confidential Exhibit 5) and Dhaval Desai (Confidential Exhibit 6), the BEOVU PFS presentation will be approved for the same indications as the BEOVU vial presentation. The BEOVU PFS embodies the inventions claimed in the '631 patent. (Confidential Exhibit 50) (Technical Prong Claim Chart).

25. An image of Novartis's BEOVU PFS is shown below. (Exhibit 20) (https://www.cphi-online.com/novartis-receives-ec-approval-for-nextgen-news082246.html).

26. Genentech's anti-VEGF medication, ranibizumab, sold under the trade name LUCENTIS, was originally available as a solution contained in a vial, as pictured below. On June 30, 2006, Genentech received initial approval for LUCENTIS in a vial presentation for intravitreal injection. (Exhibit 21) (copy of https://www.drugs.com/history/lucentis.html). (Image obtained

from https://www.nytimes.com/2014/04/10/business/eye-doctors-say-their-profits-are-smaller-than-medicare-data-makes-them-look.html.)



27. On October 14, 2016, Genentech received FDA approval for the LUCENTIS PFS product. (Exhibit 22) (screen shot of https://www.gene.com/media/press-releases/14640/2016-10-14/fda-approves-genentechs-lucentis-ranibiz). In January 2017, Genentech began marketing the LUCENTIS PFS product in the United States. (Exhibit 23) (https://eyewire.news/articles/lucentis-05-mg-prefilled-syringe-now-available-to-order-in-the-us/). An image of the 0.5 mg LUCENTIS PFS is below. (Exhibit 24) (screen shot of https://www.lucentis.com/hcp/prefilled-syringe.html).

28. The LUCENTIS PFS is the first anti-VEGF pre-filled syringe to be FDA-approved to treat three different eye diseases: wet age-related macular degeneration, macular edema after retinal vein occlusion, and myopic choroidal neovascularization. *Id.*

29. The LUCENTIS PFS uses Novartis's PFS technology, including the inventions recited in the '631 patent. Genentech's commercialization of the LUCENTIS PFS in the United States is pursuant to a license to that technology, including the '631 patent.

30. By 2018, the FDA had approved PFS options for all LUCENTIS indications. (Exhibit 25) (screen shot of https://www.gene.com/media/press-releases/14708/2018-03-21/fda-approves-genentechs-lucentis-ranibiz) (announcing the March 21, 2018 FDA approval of the LUCENTIS 0.3 mg PFS); (Exhibit 26) (https://eyewire.news/articles/lucentis-0-3-mg-prefilled-syringe-now-available-for-u-s-ophthalmologists/) (stating that ordering in the United States for the LUCENTIS 0.3 mg PFS began April 2018). An image of the 0.3 mg LUCENTIS PFS is below. (Exhibit 24) (screen shot of https://www.lucentis.com/hcp/prefilled-syringe.html).

C. Regeneron's EYLEA PFS

31. Regeneron received FDA approval for the EYLEA PFS on August 13, 2019 for four retinal indications including neovascular (wet) age-related macular degeneration, macular edema following retinal vein occlusion, diabetic macular edema, and diabetic retinopathy.

(Exhibit 14) (EYLEA prescribing information). The EYLEA PFS, like the vial presentation, contains aflibercept. An image of the EYLEA PFS is shown below.

(Exhibit 27) (image from screen shot of https://www.eyleamarketaccess.com/). On information and belief, the EYLEA PFS and its use infringe the '631 patent.

III. Non-Technical Description[1] of the '631 Patent

32. The '631 patent is entitled "Syringe" and names Juergen Sigg, Christophe Royer, Andrew M. Bryant, Heinrich M. Buettgen, and Marie Picci as inventors.

33. The '631 patent was legally and duly issued on December 29, 2015 and expires January 25, 2033.

34. Novartis owns by assignment the entire right, title, and interest in the '631 patent. A certified copy of the assignment is attached as Exhibit 2.

35. Together with this Complaint, Novartis has filed a certified copy of the prosecution history of the '631 patent as Appendix No. 1.

36. Novartis has also filed as Appendix 2 the technical references identified in the prosecution history of the application leading to the issuance of the '631 Patent.[2]

[1] This Complaint and the included non-technical descriptions are not intended to and do not construe either the specification or the claims of the Asserted Patent.

[2] Due to the ongoing COVID-19 pandemic, three additional hard copies of the certified copy of the prosecution history of the '631 patent and four copies of the technical references identified in the prosecution history of the patent application are currently not being filed. *See* 85 Fed. Reg. 15898 (Mar. 19, 2020).

37. The ’631 patent discloses and claims certain terminally sterilized small volume syringes for the injection of VEGF-inhibitors into the vitreous cavity of the eye to treat retinal indications. Figure 2 of the ’631 patent depicts one embodiment of the disclosed syringes. The PFS of Figure 2 includes, among other components, a [syringe] body (2), plunger (4), and stopper (10). (Exhibit 1) (’631 patent at 10:58-63].

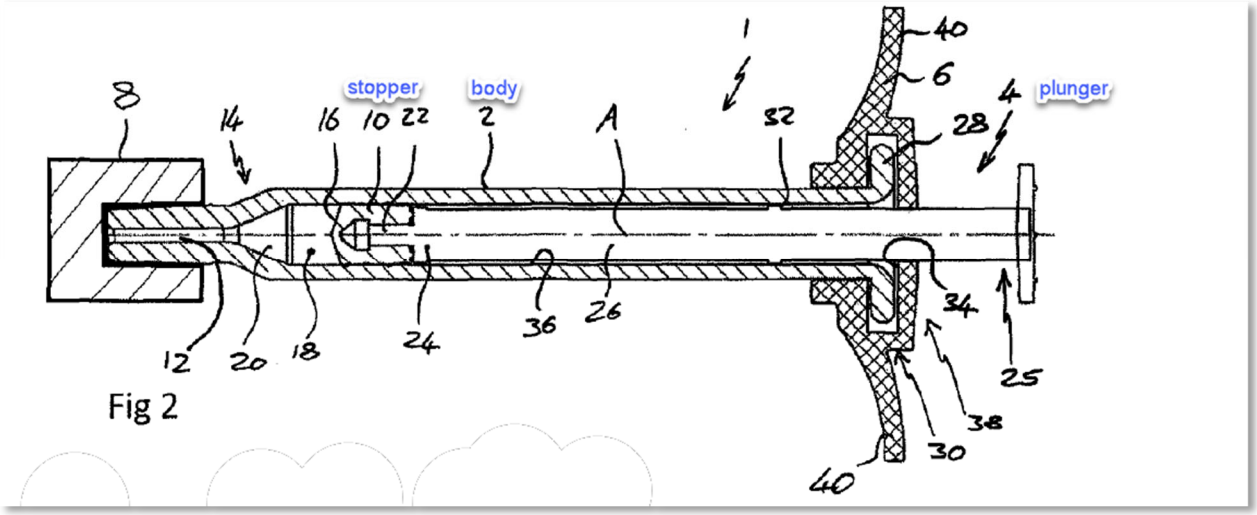


Fig 2

IV. Foreign Patents and Applications Corresponding to the ’631 Patent

38. A listing of all foreign patents and foreign patent applications corresponding to the Asserted Patent can be found as Exhibit 28. No other foreign patents or foreign patent applications corresponding to the Asserted Patent are known to Novartis at this time.

V. Licenses to the ’631 Patent

39. A listing of Novartis’s licensees to the ’631 Patent is attached as Exhibit 29. Novartis is not aware of any additional licenses to the ’631 Patent.

40. Copies of licenses and related amendments between Novartis and Genentech relating to Novartis’s PFS technology can be found as Confidential Exhibits 7 through 10.

VI. Unlawful and Unfair Acts of the Proposed Respondents

41. Regeneron manufactures and/or imports into the United States the aflibercept-filled EYLEA PFS and/or components of the EYLEA PFS. (Exhibit 14) (EYLEA prescribing information) (stating that EYLEA PFS is available for sale in the United States and is manufactured by Regeneron in the United States); (Exhibit 30) (notice of importation on November 6, 2019) (importing a product with description "S.L.A.C. EYLEA PFS H.S. CODE: 90183190."). Since December 6, 2019, Regeneron has sold the infringing EYLEA PFS in the United States. (Exhibit 16) (EYLEA Healthcare Professional Website) (announcing that EYLEA PFS is available for order in the United States (https://hcp.eylea.us/).

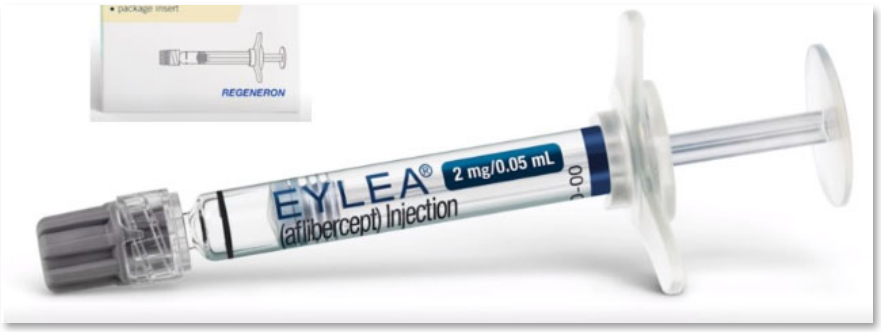
42. On information and belief, Regeneron sells its EYLEA PFS product to distributors in the United States, such as Besse Medical, CuraScript SD Specialty Distribution, McKesson Specialty Health, and McKesson Plasma & Biologics for hospitals (Exhibit 31) (screen shot of https://hcp.eylea.us/eylea4u/product-support), knowing that these distributors will sell or offer to sell EYLEA PFS in the United States.

43. At least one of these distributors sells or offers to sell the EYLEA PFS in the United States. (Exhibit 32) (order.besse.com/Orders/Search/ ProductSearch?query=eylea) (selling "EYLEA 2MG/0.05ML SINGLE-USE PRE-FILLED SYRINGE KIT").

44. Regeneron, either directly or indirectly, sells and/or provides its infringing EYLEA PFS to physicians with knowledge that they will use the product in an infringing manner. For example, on information and belief, Regeneron has actively encouraged infringement of at least claim 24 of the '631 patent by providing physicians with instructions to administer EYLEA PFS to treat patients suffering from choroidal neovascularization, wet age-related macular degeneration, macular edema secondary to retinal vein occlusion, choroidal neovascularization

secondary to pathologic myopia, diabetic retinopathy, diabetic macular edema, and/or proliferative retinopathy. (Exhibit 14) (EYLEA PFS prescribing information).

45. Many of the EYLEA PFS components have no substantial noninfringing uses. For example, the glass syringe barrel has printed on its body the product identifier for "EYLEA (aflibercept) Injection." (Exhibit 33) (screen shot of https://www.market-scope.com/pages/news/4010/regeneron-s-eylea-injection-prefilled-syringe-now-available). Accordingly, the glass syringe barrel for the EYLEA PFS cannot be filled with a drug solution other than aflibercept. *See, e.g.*, 21 C.F.R. § 201.6 ("Drugs; misleading statements").



46. Accordingly, Regeneron unlawfully sells for importation, imports, and/or sells after importation into the United States the aflibercept-filled EYLEA PFS or components thereof that directly and/or indirectly infringe the Asserted Patent in violation of Section 337. (Exhibit 3) (EYLEA PFS Infringement Claim Chart).

47. Contemporaneously with the filing of this Complaint, Novartis has provided Regeneron with a copy of the Complaint and the non-confidential exhibits to the Complaint. As a result, Regeneron received notice of the Asserted Patent and the infringement at issue no later than the filing of this Complaint.

48. As detailed in the cited infringement chart, Regeneron directly and/or indirectly infringes, either literally or under the doctrine of equivalents, the '631 patent under 35 U.S.C. § 271, including without limitation, Sections (a)-(c).

VII. Specific Acts of Unfair Importation and Sale

49. On information and belief, Regeneron is importing and will continue to import, sell for importation and/or sell after importation into the United States aflibercept-filled EYLEA PFS or components of the infringing EYLEA PFS.

50. Specific instances of importation, sale for importation into the United States, and/or sale within the United States after importation of the Accused Products by Regeneron are set forth below. These instances are exemplary in nature and are not intended to restrict the scope of any exclusion order or other remedy the Commission may order.

A. The Infringing EYLEA PFS or EYLEA PFS Components Are Manufactured in Germany and Are Imported Into the United States

51. On information and belief, Regeneron sells for importation, imports, and/or sells after importation aflibercept-filled EYLEA PFS and/or components thereof. In this regard, the pre-fillable glass syringe barrels and other components of Regeneron's EYLEA PFS are purchased from Gerresheimer Bünde GmbH ("Gerresheimer") located in Bünde, Germany and subsequently imported into the United States. (Exhibit 34) (notice of importation on October 31, 2019); (Exhibit 30) (notice of importation on November 6, 2019); (Exhibit 35) (notice of importation on November 21, 2019).

52. For example, on November 6, 2019, Regeneron imported into the United States a product with description "S.L.A.C. EYLEA PFS H.S. CODE: 90183190." (Exhibit 30) (notice of importation on November 6, 2019); (Exhibit 36) (Chapter 30 "Pharmaceutical Products" of the Harmonized Tariff Schedule of the United States (2020) Revision 1); (Exhibit 37) (excerpt of

Section XVIII of the Harmonized Tariff Schedule of the United States (2020) (Revision 1)). This importation appears to contain aflibercept-filled EYLEA PFS or at least one or more components of the infringing EYLEA PFS. The gross weight of this shipment was 2,303 kilograms (approximately 5,077 pounds). (Exhibit 30) (notice of importation on November 6, 2019); *see also* (Exhibit 38) (excerpt of Importation History Spreadsheet).

53. On information and belief, the pre-fillable glass syringes are labeled with the EYLEA brand and accordingly, have no substantial noninfringing uses. On information and belief, the EYLEA PFS incorporates a low quantity of silicone oil.

54. On information and belief, Regeneron knows and will continue to know after the filing of this Complaint that imported aflibercept-filled EYLEA PFS and/or components thereof infringe and will be used to infringe the asserted claims.

VIII. Harmonized Tariff Schedule Information

55. On information and belief, the articles subject to this Complaint are classifiable under at least the following heading and subheading of the Harmonized Tariff Schedule ("HTS") of the United States: (1) 9018.31.90; and/or (2) 3004.49.60.

56. This classification is intended for illustration only and is not intended to restrict the scope of this investigation.

IX. Related Litigation

57. Contemporaneously with the filing of this Complaint, Novartis is also filing a complaint against Regeneron in the U.S. District Court for the Northern District of New York alleging that Regeneron's EYLEA PFS infringes one or more claims of the Asserted Patent.

58. There are no other litigations involving the Asserted Patent known to Novartis.

59. For completeness, Novartis Vaccines and Diagnostics, Inc., Novartis Pharma AG, and Grifols Worldwide Operations Limited (collectively, the "Novartis Parties"") filed a lawsuit

against Regeneron in the United States District Court for the Southern District of New York, seeking a judgment of willful patent infringement of U.S. Patent No. 5,688,688 ("the '688 Patent") by Regeneron's manufacture of aflibercept (the active ingredient used in at least EYLEA). The case was dismissed on October 24, 2018. The '688 Patent expired on November 18, 2014.

X. Domestic Industry

60. A domestic industry related to the Asserted Patent, as required and defined by 19 U.S.C. § 1337(a)(2)-(3)(A), (B), and (C), exists and/or is in the process of being established by virtue of significant investments in plant and equipment; significant employment of labor and capital; and/or substantial investment in its exploitation, including engineering, research, and development by Novartis and its licensee, Genentech.

A. The Economic Prong

61. An industry, as defined in Section 337(a)(3)(A), (B), and (C), exists in the United States and/or is in the process of being established in the United States by virtue of Novartis's and Genentech's significant and substantial investments in the BEOVU PFS and the LUCENTIS PFS.

62. In particular, a domestic industry exists based on Novartis's significant investments in plant and equipment, employment of labor and capital, and substantial investment in exploitation of the patented technology, including research and development related to the technology underlying the BEOVU PFS. On information and belief, Genentech's significant investment in plant and equipment, employment of labor and capital, and substantial investment in exploitation of the patented technology, including research and development related to the LUCENTIS PFS further supports the existence of a domestic industry.

1. Novartis—BEOVU and BEOVU PFS

63. Novartis is a global pharmaceutical company that has enjoyed success around the world, including substantial success in the United States. BEOVU and BEOVU PFS add to Novartis's already robust pharmaceutical portfolio.

64. Novartis's United States-based medical team has already engaged in extensive clinical studies for BEOVU for treatment of wet age-related macular degeneration. All clinical studies related to BEOVU will also support BEOVU PFS. (Exhibit 5) (Confidential Declaration of Meghan Brown).

65. In total, more than 900 wet age-related macular degeneration subjects were enrolled across six major United States-concentrated clinical studies, some of which were completed as recently as 2018. For example, HAWK, an extensive Phase III clinical study, took place in approximately 126 study centers located in the United States from December 2014 through March 2018. (Confidential Exhibit 39) (Confidential Declaration of James Wheeler). The declaration of James Wheeler (Confidential Exhibit 39) provides an accounting of Novartis's domestic investments and expenditures for Novartis's clinical studies for BEOVU.

66. In 2019, Novartis also conducted an observational in-use clinical study that was carried out exclusively in the United States that verified that physicians understood how to safely administer BEOVU via the PFS presentation. (Confidential Exhibit 39) (Declaration of James Wheeler). Novartis's efforts and related investments are set forth in the declaration of James Wheeler, attached as Confidential Exhibit 39.

67. There are several ongoing clinical studies for additional potential indications, such as diabetic macular edema, taking place in over 300 study centers in the United States, and future clinical studies are planned. The declaration of James Wheeler (Confidential Exhibit 39) provides

a current accounting of Novartis's domestic investments and expenditures relating to the ongoing and future clinical studies.

68. Additionally, substantially all of Novartis's FDA regulatory work with respect to the BLA for BEOVU and the expected FDA approval of the sBLA for BEOVU PFS is handled in the United States. (Confidential Exhibit 5) (Declaration of Meghan Brown).

69. Once FDA approval for the PFS presentation is achieved, Novartis has tangible plans to introduce the PFS to the market. (Confidential Exhibit 6) (Declaration of Dhaval Desai); (Confidential Exhibit 5) (Declaration of Meghan Brown); (Confidential Exhibit 40) (Declaration of Chris Simms).

70. As outlined in the attached declarations, Novartis has made, and will continue to make, relevant and substantial investments, all of which are to support and improve BEOVU and the BEOVU PFS. (Confidential Exhibit 6) (Declaration of Dhaval Desai); (Confidential Exhibit 5) (Declaration of Meghan Brown); (Confidential Exhibit 39) (Declaration of James Wheeler); (Confidential Exhibit 40) (Declaration of Chris Simms); (Confidential Exhibit 41) (Declaration of Michelle Botts). An example of this is the continual and significant efforts of the United States-based medical affairs team working to support and improve BEOVU and the BEOVU PFS by, for example, educating physicians and the relevant industry about BEOVU. (Exhibit 6) (Confidential Declaration of Dhaval Desai). Not only are these expenditures quantitatively significant and substantial, they are also qualitatively so, at least because without Novartis's United States team, neither BEOVU nor BEOVU PFS would be commercially viable in the United States.

71. Based upon the activities set forth above and in the supporting exhibits, the investments made by Novartis satisfy the economic prong of the domestic industry requirement by establishing that a domestic industry exists and/or is in the process of being established.

2. Genentech – LUCENTIS PFS

72. "Genentech became a member of the Roche Group in March of 2009. As part of their merger agreement, Roche and Genentech combined their pharmaceutical operations in the United States. Genentech's South San Francisco campus now serves as the headquarters for Roche pharmaceutical operations in the United States. Genentech Research and Early Development operates as an independent center within Roche." (Exhibit 42) (https://www.gene.com/about-us).

73. Genentech is the exclusive provider of LUCENTIS PFS in the United States. On information and belief, LUCENTIS PFS is important to Genentech's success. For Genentech's LUCENTIS, 18% U.S.-based sales "growth was driven by sales of prefilled syringes and sales increases in all approved indications." (Exhibit 43) (Roche 2018 Annual report, at page 32).

74. LUCENTIS was one of five products that together accounted for a total of CHF 25.0 billion (nearly $26 billion) in sales in 2018 alone. (Exhibit 43) (Roche 2018 Annual report, at page 87). On information and belief, LUCENTIS accounts for multiple billions of dollars of U.S. sales revenue on an annual basis.

75. On information and belief, Genentech engages in a broad range of qualifying domestic industry activities in the United States related to the LUCENTIS PFS.

76. For example, on information and belief, Genentech has made and continues to make significant investments with respect to the LUCENTIS PFS. On information and belief, those are dedicated to at least regulatory work and various customer support activities focused on the LUCENTIS PFS.

77. Indeed, Genentech has facilities in Oceanside, California; Vacaville, California; San Francisco, California; and Hillsboro, Oregon. These facilities carry out manufacturing, research and development, and clinical operations to support Genentech's pharmaceutical products. (Exhibit 44) (https://www.gene.com/contact-us/visit-us); (Exhibit 45)

(https://www.gene.com/contact-us/visit-us/oceanside); (Exhibit 46) (https://www.gene.com/contact-us/visit-us/vacaville); (Exhibit 47) (https://www.gene.com/contact-us/visit-us/hillsboro). Additionally, in 2015, Genentech reportedly invested $125 million to expand its Hillsboro, Oregon research facility. (Exhibit 48) ("Genentech Invests More Than $125 Million To Expand Its Hillsboro, Oregon, Research Facility" (2015)). The Hillsboro site appears to include a fill and finish facility. (Exhibit 47) (https://www.gene.com/contact-us/visit-us/hillsboro).

78. On information and belief, Genentech has made and continues to make significant investments in labor and capital. Those activities include at least clinical studies, regulatory work, and various customer support activities focused on the LUCENTIS PFS. For example, Genentech appears to have conducted well over 100 United States-based clinical studies on the safety and efficacy of LUCENTIS, at least two of which specifically related to the efficacy of PFS delivery. (Exhibit 49) (print out from ClinicalTrials.gov as of January 27, 2020).

79. Throughout North America, Genentech and Roche employ over 25,000 workers, the vast majority of whom appear to be in the United States, and also have research and development facilities in the United States. (Exhibit 43) (Roche 2018 Annual report). On information and belief, certain LUCENTIS-specific work takes place in the United States, the only geographical area where Genentech is authorized to sell.

B. The Technical Prong

80. The BEOVU PFS practices claims 1-7 and 14-26 of the Asserted Patent. A chart of independent claim 1 is attached as Confidential Exhibit 50.

81. On information and belief the Lucentis PFS practices claims 1-10 and 14-26 of the Asserted Patent. A chart of independent claim 1 is attached as Confidential Exhibit 51.

XI. Request for Relief

WHEREFORE, Novartis respectfully requests that the Commission:

82. Institute an investigation pursuant to Section 337(b)(1) of the Tariff Act of 1930, as amended, 19 U.S.C. § 1337, into the violation by Regeneron of Section 337 arising from the importation into the United States and/or sale within the United States after the importation of the aflibercept-filled EYLEA PFS and/or components thereof that directly infringe or induce or contribute to the infringement of one or more claims of the '631 Patent;

83. Schedule and conduct a hearing pursuant to Section 337(c), for purposes of receiving evidence and hearing argument concerning whether there has been a violation of Section 337 and, following the hearing, determine that there has been a violation of Section 337;

84. Issue a permanent limited exclusion order pursuant to 19 U.S.C. § 1337 (d) forbidding entry into the United States of Regeneron's products or components that infringe or induce or contribute to the infringement of one or more claims of the '631 Patent;

85. Issue permanent cease and desist orders, pursuant to 19 U.S.C. § 1337(f), directing Regeneron to cease and desist from the importation, sale, offer for sale, advertising, packaging or solicitation of any sale by Regeneron of products or components that infringe or induce or contribute to the infringement of one or more claims of the Asserted Patent;

86. Impose a bond upon Regeneron should it continue to import infringing articles during the 60-day Presidential review period per 19 U.S.C. § 1337(j); and

87. Grant all such other and further relief as it deems appropriate under the law, based upon the facts complained of herein and as determined by the investigation.

Dated: June 19, 2020

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