IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

TEVA PHARMACEUTICALS USA, INC.,

400 Interpace Parkway,
Parsippany, NJ 07054,

TEVA PHARMACEUTICAL INDUSTRIES LTD.,

5 Basel St.,
Petach Tikva, Israel 4951033,

Plaintiffs,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION,

10903 New Hampshire Avenue,
Silver Spring, MD 20993,

STEPHEN M. HAHN, in his official capacity as COMMISSIONER OF FOOD AND DRUGS,

10903 New Hampshire Avenue,
Silver Spring, MD 20993,

UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES,

200 Independence Avenue, SW,
Washington, DC 20201,

ALEX M. AZAR II, in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES,

200 Independence Avenue, SW,
Washington, DC 20201,

Defendants.

Civil Action No. 1:20-cv-808

COMPLAINT

Plaintiffs Teva Pharmaceuticals USA, Inc. ("Teva") and Teva Pharmaceutical Industries Ltd. ("Teva Ltd.") (collectively, "Plaintiffs") bring this complaint for declaratory and injunctive relief against Defendants the United States Food and Drug Administration ("FDA"), Stephen M. Hahn (in his official capacity as Commissioner of Food and Drugs), the United States Department of Health and Human Services ("HHS"), and Alex M. Azar II (in his official capacity as Secretary of Health and Human Services). In support thereof, Teva states as follows:

INTRODUCTION

1. For many years, FDA has administered two different regulatory frameworks for medicines intended for human use. Drugs are approved through a New Drug Application (NDA) under Section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 355. "Biological products" are licensed through a Biologics License Application (BLA) under Section 351 of the Public Health Service Act (PHSA), 42 U.S.C. § 262. The two categories are not entirely distinct, and over time amendments expanding the definition of "biological product" have increased the overlap. This case is about the rules for handling a product that was approved as a drug but that today would be licensed as a biological product.

2. In 2010, Congress enacted the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), Pub. L. No. 111-148, tit. VII, subtit. A, 124 Stat. 119, 804, in an effort to promote competition in the marketplace for biological products. The BPCIA primarily created an abbreviated pathway by which products that are "biosimilar" to existing biological products may be licensed in an expedited manner. *See* 42 U.S.C. § 262(k).

3. The BPCIA also expanded the list of covered "biological products" to include "proteins." Today, the definition of "biological product" includes "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or

analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings." Thus, any "protein" or "analogous product" that is used to treat human beings is a biological product. 42 U.S.C. § 262(i)(1).

4. Congress recognized that many "proteins" had already been regulated as drug products subject to and approved under Section 505 of the FDCA, 21 U.S.C. § 355. So it gave FDA ten years from the date of the BPCIA's enactment to fully establish the BPCIA's implementing framework and convert existing drug products that meet the PHSA's definition into licensed "biological products."

5. Effective March 23, 2020—the BPCIA's ten-year anniversary—nearly 100 approved NDAs for drugs under the FDCA were "deemed to be a license" for biological products under the PHSA.

6. But FDA refused to transition the NDA for Teva's product COPAXONE® (glatiramer acetate). COPAXONE is a leading drug used for the treatment of multiple sclerosis. It meets the definition of a "biological product." Until late 2019, a "chemically synthesized polypeptide" was specially excluded from the definition of a "protein," and COPAXONE was excluded for that reason. But that exclusion has now been repealed. COPAXONE also meets FDA's other expectations for "proteins": it is a polymer that has at least 40 amino acids (meeting FDA's length requirement), and has a specific, defined sequence akin to other products that FDA treats as proteins. COPAXONE is at a minimum an "analogous product."

7. Because COPAXONE is now an eligible "biological product," the BPCIA required FDA to convert Teva's approved NDA for COPAXONE into a biological-product license by

March 23, 2020. The BPCIA provides FDA with no discretion in the matter: it says an approved NDA for a biological product "*shall* be deemed to be a license for the biological product."

8. Teva requested that FDA transition the COPAXONE NDA into a BLA. FDA refused to do so. That refusal is arbitrary, capricious, and contrary to law, and it thus should be set aside under the Administrative Procedure Act, 5 U.S.C. § 706(2)(A).

PARTIES

9. Plaintiff Teva Pharmaceuticals USA, Inc. ("Teva") is a Delaware corporation with a principal place of business in Parsippany, New Jersey.

10. Plaintiff Teva Pharmaceutical Industries Ltd. ("Teva Ltd.") is an Israeli corporation with a principal place of business in Petach Tikva, Israel.

11. Defendant FDA is an administrative agency of the United States government within HHS. It is the division of HHS specifically charged with administering the Public Health Service Act (PHSA), 42 U.S.C. § 201 *et seq.*, and the BPCIA. Its headquarters is located in Silver Spring, Maryland.

12. Defendant Stephen M. Hahn is the Commissioner of Food and Drugs and is responsible for overseeing FDA and administering the PHSA and the BPCIA. Commissioner Hahn is being sued in his official capacity only.

13. Defendant HHS is a Cabinet-level department of the United States government. Its headquarters is located in Washington, D.C.

14. Defendant Alex M. Azar II is the Secretary of Health and Human Services. He is ultimately responsible for the implementation of the PHSA and the BPCIA, as well as oversight of FDA. Secretary Azar is being sued in his official capacity only.

JURISDICTION AND VENUE

15. This action arises under and asserts violations of the Administrative Procedure Act ("APA"), 5 U.S.C. § 551 *et seq.*, and the BPCIA. The Court has subject-matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331, 1346, and 1361.

16. The Court is authorized to grant Plaintiffs' request for declaratory relief pursuant to the Declaratory Judgment Act, 28 U.S.C. §§ 2201–2202.

17. Venue in this judicial district is proper under 28 U.S.C. § 1391(b) and (e) and 5 U.S.C. § 703.

STATUTORY AND REGULATORY BACKGROUND

Drug Products and the FDCA

18. This case concerns the BPCIA-mandated transition of certain "drug products" to "biological products," so the appropriate starting point is the FDCA, which governs "drug products."

19. A drug product must be approved by FDA before it is manufactured and sold in the United States. Before obtaining approval, a sponsor of a new drug must show that the drug is effective and safe for use. *See* 21 U.S.C. § 355(d).

20. The FDCA provides the statutory framework for drug approvals. There are three pathways for approval. One pathway is a New Drug Application (NDA), a comprehensive, full-fledged application for which a manufacturer must undertake extensive scientific research demonstrating the safety and efficacy of the proposed drug. 21 U.S.C. § 355(b)(1). As part of an NDA, an applicant must provide information regarding "any patent which claims the drug . . . or which claims a method of using such drug." *Id.*

21. Another pathway for approval is an Abbreviated New Drug Application (ANDA), which can be used for "generic" versions of previously approved NDAs. ANDAs do not require an independent showing of safety and efficacy; rather, the applicant need only demonstrate that the new drug is "bioequivalent" to a previously approved drug (the "reference" drug). 21 U.S.C. § 355(j).

22. As part of an ANDA, an applicant must submit a certification addressing each patent for the reference drug listed in the FDA's publication *Approved Drug Products With Therapeutic Equivalence Evaluations*, also known as the "Orange Book." Not all patents are listed in the Orange Book; the Orange Book specifically excludes "[p]rocess patents, patents claiming packaging, patents claiming metabolites, and patents claiming intermediates." 21 C.F.R. § 314.53(b)(1). In addressing any listed patent, an ANDA applicant must certify one of four things: (I) no patent information has been submitted to the FDA, (II) the Orange Book-listed patent that is the subject of the certification has expired, (III) the patent will expire on a certain date; or (IV) the patent is invalid, or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA has been submitted. 21 U.S.C. §§ 355(j)(2)(A)(vii)(I)-(IV). The last category of certification is known as a "Paragraph IV certification."

23. Submitting an ANDA with a Paragraph IV certification seeking approval to manufacture, use, or sell a drug claimed in a patent or the use of which is claimed in a patent is an act of patent infringement. 35 U.S.C. § 271(e)(2)(A). An ANDA applicant that submits a Paragraph IV certification to FDA must also serve notice on the holder of the NDA for the reference drug and the owner(s) of the patent(s) to which the certification is directed. 21 U.S.C. § 355(j)(2)(B). If the NDA holder or patent owner files an infringement action within 45 days of receiving such notice, FDA may not approve the ANDA until the suit is resolved in the ANDA

applicant's favor, the patent expires, or after 30 months, whichever is earliest. *Id.* at § 355(j)(5)(B)(iii).

Biological Products, the PHSA, and the BPCIA

24. The PHSA, as amended by the BPCIA, requires a sponsor of a "biological product" to submit a Biologics License Application before manufacturing and marketing that product. 42 U.S.C. § 262. Before a BLA is approved, a sponsor must demonstrate that the biological product is "safe, pure, and potent." *Id.* § 262(a)(2)(C)(i)(I).

The Definition of "Biological Product"

25. Before the BPCIA's enactment, the PHSA defined "biological product" as "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound)." 42 U.S.C. § 262(i) (2006).

26. On March 23, 2010, Congress enacted the BPCIA. The BPCIA expanded the definition of "biological product" to add a "protein (except any chemically synthesized polypeptide)" to the list that precedes "or analogous product." BPCIA § 7002(b), 124 Stat. at 814; *see* 42 U.S.C. § 262(i)(1) (2012). The "analogous product" prong of the definition likewise expanded to include any "analogous product" to a protein.

27. In a Proposed Rule, FDA stated that it would interpret the BPCIA's use of the word "protein" as "any alpha amino acid polymer with a specific, defined sequence that is greater than 40 amino acids in size." Definition of the Term "Biological Product," 83 Fed. Reg. 63,817, 63,820 (Dec. 12, 2018).

28. FDA also defined the parenthetical exclusion for a "chemically synthesized polypeptide" as "any alpha amino acid polymer that (1) is made entirely by chemical synthesis

and (2) is greater than 40 amino acids but less than 100 amino acids in size." 83 Fed. Reg. at 63,818.

29. FDA took the view that although "peptides" are amino acid polymers, they are not proteins. A "peptide," FDA explained, "generally refers to smaller, simpler chains of amino acids, while protein is used to refer to longer, more complex chains." 83 Fed. Reg. at 63,820. The agency developed a "scientifically reasonable, bright-line rule" to distinguish covered "proteins" from uncovered "peptides": "a threshold of 40 amino acids" would be used to define "the upper size boundary of a peptide." *Id.* at 63,821. "[A]mino acid polymers that are greater than 40 amino acids," FDA observed, "may often assume several of the structural and functional characteristics that are generally associated with proteins, lending a higher level of complexity to these products." *Id.*

30. The Proposed Rule also acknowledged that a "chemically synthesized polypeptide," like a protein, would have a chain "greater than 40 amino acids but less than 100 amino acids in size." 83 Fed. Reg. at 63,821. Thus, the only meaningful difference between a "protein" and a "chemically synthesized polypeptide" was that the latter is "made entirely by chemical synthesis." *Id.* And any chemically synthesized polypeptides over 100 amino acids in length would be treated as proteins anyway, as such polypeptides had "a level of structural and functional complexity and sensitivity to environmental conditions that makes regulating such a protein under the same statutory authority as the majority of proteins more appropriate." *Id*.

31. After FDA published the Proposed Rule, Congress amended the definition of "biological product" to remove the parenthetical exclusion for "chemically synthesized polypeptides." Further Consolidated Appropriations Act, 2020, Pub. L. No. 116-94, § 605, 133 Stat. 2534, 3127 (2019) ("Appropriations Act").

32. In the Final Rule, FDA stated that, as a result of Congress's elimination of the parenthetical restriction for "chemically synthesized polypeptides," all "chemically synthesized polypeptides" that otherwise met the definition of "protein" would be treated as "biological products" under the PHSA and the BPCIA. *See* Definition of the Term "Biological Product," 85 Fed. Reg. 10,057, 10,059 (Feb. 21, 2020) ("[A]ll amino acid polymers that meet FDA's interpretation of the term 'protein' (including an amino acid polymer that previously would have fallen within the term 'chemically synthesized polypeptide' as interpreted by FDA) will be considered to fall within the statutory definition of 'biological product.'").

Biosimilars and Patent Dispute Resolution

33. A company seeking to manufacture a biological product that is "biosimilar" to an already-licensed biological product (the "reference product") may apply for a license under 42 U.S.C. § 262(k).

34. The biosimilar approval process is an abbreviated process that allows a biosimilar applicant to "piggyback" off of the showing of safety, purety, and potency made by the manufacturer of the reference product. *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1670 (2017). The biosimilar applicant is not required to show that its biosimilar is "safe, pure, and potent"; instead, its burden is only to show that the biosimilar is "highly similar to" the reference product, and there are "no clinically meaningful differences" between the two. 42 U.S.C. § 262(i)(2).

35. A biosimilar can be licensed, prescribed, and sold whether or not it is fully "interchangeable" with the reference product. But a biosimilar cannot be *substituted* for a reference product "without the intervention of the health care provider who prescribed the reference product," unless FDA takes the further step of deeming the biosimilar to be

"interchangeable." 42 U.S.C. § 262(i)(3). Biosimilars are unlike generic drugs in that respect: an approved generic drug generally can be substituted for the reference drug.

36. FDA will deem a biosimilar to be "interchangeable" if it "can be expected to produce the same clinical result as the reference product in any given patient," and, for multi-use biosimilars, the risk "in terms of safety or diminished efficacy" does not become greater because an individual has switched from the reference product to the biosimilar. 42 U.S.C. § 262(k)(4).

37. Like a drug, a biological product may be protected by various different types of patents, such as composition or formulation patents, method-of-treatment patents, or manufacturing process patents.

38. To ensure that a biosimilar product does not infringe a patent for a reference product, and to enable the parties to litigate and resolve any patent disputes *before* the actual launch of a biosimilar product (*i.e.*, before damages would accrue), the BPCIA requires the biosimilar applicant and the sponsor of the reference product to engage in a back-and-forth exchange about the patents relating to the product that the manufacture, marketing, and/or use of a biosimilar would implicate—an exchange that typically culminates in a patent-infringement lawsuit.

39. The exchange begins when the biosimilar applicant provides the reference product sponsor with its biosimilar application and the manufacturing information for the proposed biosimilar product. 42 U.S.C. § 262(*l*)(2).

40. If the biosimilar applicant does not provide the application and manufacturing information, that failure results in an artificial act of infringement, and allows the reference product sponsor to immediately bring a declaratory-judgment action for infringement. *See* 42 U.S.C. § 262(*l*)(9)(C); 35 U.S.C. § 271(e)(2)(C)(ii); *Sandoz*, 137 S. Ct. at 1675.

41. After receiving the application and manufacturing information, the reference product sponsor must provide to the biosimilar applicant a list of patents that the sponsor reasonably believes would be infringed if the biosimilar were to be manufactured and sold. 42 U.S.C. § 262(*l*)(3)(A)(i).

42. Once the reference product sponsor provides a list of affected patents, the biosimilar applicant must submit a "detailed statement" as to why the applicant believes each patent on the reference product sponsor's list is "invalid, unenforceable, or will not be infringed" by the biosimilar product. 42 U.S.C. § 262(*l*)(3)(B)(ii).

43. After engaging in this exchange, the reference product sponsor and the biosimilar applicant must engage in a good-faith effort to narrow the list of patents that would be the subject of an immediate patent-infringement lawsuit. The biosimilar applicant and the reference product sponsor exchange lists of patents that they would like to litigate immediately. 42 U.S.C. § 262(*l*)(4), (5).

44. Once the parties reach agreement on which patents should be the subject of an infringement lawsuit (or attempt to reach agreement but fail to do so), the reference product sponsor may file an infringement lawsuit seeking to enforce a predetermined number of patents. 42 U.S.C. § 262(*l*)(6); 35 U.S.C. § 271(e)(2)(C)(i). No independent act of infringement is necessary; the submission of the biosimilar application itself is an act of infringement. *Sandoz*, 137 S. Ct. at 1671 (citing 35 U.S.C. § 271(e)(2)(C)(i)). The biosimilar applicant's refusal to agree, or to negotiate, cannot prevent the reference product sponsor from suing based on the artificial act of infringement.

45. The biosimilar applicant must also provide to the reference product sponsor a notice of commercial marketing, i.e., a notice that it intends to begin selling the biosimilar to the public,

not less than 180 days before the date of the first commercial marketing of the biosimilar product. 42 U.S.C. § 262(*l*)(8)(A). This notice, which may be provided before or after FDA approval of the biosimilar product, potentially sets off another round of litigation covering the remainder of the patents not litigated as part of the first lawsuit. *Id.* § 262(*l*)(8)-(9).

Converting Approved Drugs into Biological Products

46. In addition to expanding the PHSA's definition of "biological product," and establishing a framework for biosimilar approval, the BPCIA also provides that "[a]n approved application for a biological product under section 505 of the [FDCA] (21 U.S.C. 355) shall be deemed to be a license for the biological product under [PHSA] section 351," *i.e.*, "deemed" to be an approved BLA. BPCIA § 7002(e)(4)(A), 124 Stat. at 817. The transition took place ten years after the BPCIA's enactment, *i.e.*, on March 23, 2020.

47. On December 31, 2019, FDA released a preliminary list of approved NDAs to be converted to BLAs. U.S. Dep't of Health & Human Servs., Food & Drug Admin., *The "Deemed to be a License" Provision of the BPCI Act: Questions and Answers—Draft Guidance for Industry; Preliminary List of Approved NDAs for Biological Products That Will Be Deemed to Be BLAs on March 23, 2020* (Dec. 31, 2019), https://www.fda.gov/media/119229/download ("Preliminary Transition List").

48. In a March 2020 Guidance, FDA stated that, for any approved NDA that FDA now deems to be a license for a biological product under the PHSA, FDA would send a letter on March 23, 2020, confirming to the NDA's holder that the NDA has transitioned into a BLA. U.S. Dep't of Health & Human Servs., Food & Drug Admin., *The "Deemed to be a License" Provision of the BPCI Act: Questions and Answers Guidance for Industry* 6 (Mar. 2020), https://www.fda.gov/media/135838/download ("March Guidance").

FACTUAL AND PROCEDURAL BACKGROUND

COPAXONE Is a "Biological Product"

49. Teva owns the NDA for COPAXONE (glatiramer acetate), an injectable used for the treatment of multiple sclerosis. FDA approved the NDA for COPAXONE in 1996.

50. Teva Ltd. owns several U.S. patents on aspects of the process for manufacturing glatiramer acetate. These patents include U.S. Patent No. 9,155,775 (the '775 Patent) and U.S. Patent No. 9,763,993 (the '993 Patent). Teva is the exclusive U.S. licensee of these patents. Both the owner and the exclusive licensee of a U.S. patent may be plaintiffs in an action for infringement.

51. FDA approved the COPAXONE NDA well before the BPCIA's enactment. But even after the BPCIA, and as recently as 2019, COPAXONE was not a "biological product," because it is a "chemically synthesized polypeptide" and thus fell within the exclusion from the definition.

52. After Congress removed the parenthetical exclusion for "chemically synthesized polypeptides" and included such polypeptides in the definition of "protein," COPAXONE was an eligible "biological product." Under the BPCIA's transition mandate, FDA should have deemed the COPAXONE NDA to be a "license" under the PHSA.

53. COPAXONE meets the regulatory definition of "biological product" because it is a protein. The active ingredient in COPAXONE is glatiramer acetate, which is a complex mixture of synthetic polypeptides with four different amino acids: L-glutamic acid, L-alanine, L-tyrosine, and L-lysine.

54. The average length of each glatiramer acetate polypeptide is 40 to 100 amino acids. COPAXONE therefore meets FDA's length requirement for proteins: a chain that meets or exceeds the "threshold of 40 amino acids." 83 Fed. Reg. at 63,821.

55. COPAXONE also has a "specific, defined sequence." Glatiramer acetate is chemically synthesized through a process of polymerization and partial depolymerization. The resulting mixture contains polymers of varying length and sequence, dictated by the composition of the reaction mixture and the conditions under which the reaction occurs. While the exact order of amino acids can vary amongst the individual polymers, the sequence is not random: alanine, for example, is the most reactive and most concentrated of the amino acids and is typically found closer to the start of a polymer chain. Tyrosine, by contrast, is the least reactive and least concentrated amino acid, and tends to be found at the end of the polymer chain. This phenomenon, known as a propagational shift, allows Teva to manufacture well-controlled and consistent amino acid sequences for COPAXONE.

56. FDA's Preliminary Transition List demonstrates that it is not necessary to know the exact chemical structure for a polymer to be a qualifying "protein." One of the converted NDAs is for Vitrase (hyaluronidase for injection), "a preparation of purified ovine testicular hyaluronidase, a protein enzyme." Vitrase Prescribing Information at 8 (May 2018), https://www.bausch.com/Portals/77/-/m/BL/United%20States/Files/Package%20Inserts/Pharma/Vitrase-Prescribing-Info.pdf?ver=2018-07-31-131432-430. FDA has identified Vitrase as a "biological product" despite the fact that "[t]he exact chemical structure of [the protein] enzyme is unknown." *Id.*

57. Another product treated as a "biological product" is Creon (pancrelipase). Creon's active ingredient is pancrelipase, an extract derived from the pancreatic glands of pigs. Creon

Prescribing Information at 9 (Nov. 2019), https://www.rxabbvie.com/pdf/creon_PI.pdf. The active ingredient is a "very crude mixture of digestive enzymes" that are "not well characterized or controlled." Center for Drug Evaluation and Research, Application No. 20-725, Chemistry Review(s), at 8 (Mar. 20, 2009), https://www.accessdata.fda.gov/drugsatfda_docs/nda/2009/020725s000ChemR.pdf.

58. FDA has also stated that the "structural or functional attributes" of a product are not controlling in determining whether the product is a "protein." 85 Fed. Reg. at 10,060. To the contrary, FDA concluded that focusing on such attributes "would lead to regulatory uncertainty due to the lack of a bright-line rule." *Id.* In defining "protein," FDA placed its focus on "the number of amino acids in the amino acid polymer (irrespective of the method of manufacture)." *Id.*

59. COPAXONE therefore meets FDA's definition of "protein": "any alpha amino acid polymer with a specific defined sequence that is greater than 40 amino acids in size." 85 Fed. Reg. at 10,057.

60. At a minimum, COPAXONE is an "analogous product" to others listed in the definition. Glatiramer acetate has a structure similar to that of myelin base protein (MBP), a naturally occurring protein found in the central nervous system, and has many of MBP's characteristics. The two have many of the same polypeptide sequences, to the point where glatiramer acetate polypeptides have been found to "mimic certain properties of MBP." Romualdas Stapulionis et al., *Structural Insight into the Function of Myelin Basic Protein as a Ligand for Integrin αMβ2*, 180 J. of Immunology 3946, 3950 (2008). Glatiramer acetate also functions in an analogous way to the other biological products listed in the definition: it modulates

an immune response, is absorbed through the lymphatic system, and has a molecular weight far greater than that associated with the typical small-molecule drug.

FDA Denies Teva's Request for COPAXONE to Be Treated as a Biological Product

61. Because COPAXONE's active ingredient is a protein, FDA should have classified it as a biological product. Yet the Preliminary Transition List did not include COPAXONE as a previously approved NDA set for transition to a license. FDA requested that interested parties provide comments on the Preliminary Transition List by February 19, 2020.

62. Teva provided timely comments on the Preliminary Transition List, requesting that FDA "correct [the] oversight" of failing to list COPAXONE "on the list of biological products whose approvals will be deemed to be a license under section 351 of the PHSA" ("Transition Request") (attached as Exhibit A). It explained that COPAXONE was a chemically synthesized polypeptide under the pre-Appropriations Act definition of "protein," which parenthetically excluded "chemically synthesized polypeptides." Because "chemically synthesized polypeptides" were to be treated as "proteins" after the enactment of the Appropriations Act, Teva submitted that COPAXONE should have been listed on the Preliminary Transition List as an approved NDA to be transitioned into a deemed license.

63. Teva also stated that, even if chemically synthesized polypeptides were not categorically "proteins," COPAXONE met the length and specificity requirements set forth in FDA's definition of "protein."

64. In the alternative, Teva contended that COPAXONE was an "analogous" product. Glatiramer acetate is a synthetic analogue of MBP, a naturally occurring protein. Teva also argued that glatiramer acetate was analogous to biological products more generally; like a vaccine, for instance, glatiramer acetate induces an immune response to achieve its therapeutic effect.

65. Teva received no response to its Transition Request as of March 23, 2020, the date on which approved NDAs were to be converted to deemed licenses.

66. Teva did not receive a letter like the one described by the March Guidance on March 23, 2020. Under the March Guidance, the agency's failure to send such a letter indicates that the COPAXONE NDA will not transition into a deemed license.

67. FDA denied Teva's Transition Request by failing to respond to it by March 23, 2020 and by failing to provide Teva with a notice of transition on March 23, 2020.

Plaintiffs' Ongoing Injury from FDA's Failure to Reclassify COPAXONE

68. Plaintiffs have been, are being, and will continue to be injured by FDA's denial of Teva's Transition Request.

69. Had FDA transitioned the COPAXONE NDA to a deemed license, an applicant seeking to rely on COPAXONE's approval to make an equivalent product would have to undergo the biosimilar application process. The PHSA would require such an applicant to provide a copy of its application to both Teva and Teva Ltd.

70. Under the ANDA process, by contrast, an applicant seeking to rely on COPAXONE's approval to make a generic product need not notify Plaintiffs or provide Plaintiffs with a copy of its application, because the process patents are not eligible for listing in the Orange Book.

71. Had FDA transitioned the COPAXONE NDA to a deemed license, Plaintiffs could assert the Teva Ltd. process patents against any biosimilar applicant based upon the filing of a biosimilar application, because the filing of the application is an artificial act of infringement with respect to (inter alia) the process patents. The parties would initially negotiate which patents to litigate, but that negotiation process would not be able to preclude Teva from asserting its patents.

72. Under the ANDA process, by contrast, Plaintiffs cannot sue for an artificial act of infringement based upon the filing of an ANDA, because Teva Ltd.'s patents are not for "a drug" or "the use of [a drug]." 35 U.S.C. § 271(e)(2)(A). Instead, Plaintiffs must wait to sue until a generic applicant actually infringes a patent by "us[ing]" or "sell[ing]" the patented process; or "sell[ing]," "offer[ing]," or "import[ing]" glatiramer acetate made with the patented process; or until such an infringement is certainly impending. *Id.* § 271(a), (g).

73. Plaintiffs have a concrete need for the notice and greater enforcement opportunity for the process patents that the PHSA affords. A generic pharmaceutical manufacturer has expressed to Teva that it will soon file an ANDA for a new generic version of COPAXONE. The generic company has asked Plaintiffs for a covenant not to assert the COPAXONE patents—including the process patents—against the generic company. Teva has not agreed to such a covenant; to date, Plaintiffs and the generic company have not been able to negotiate the information exchange necessary to consider such a covenant. If that manufacturer files an ANDA, it will not be required to notify Plaintiffs, and Plaintiffs will not be able to assert their process patents against that manufacturer based on the submission to FDA.

74. For Teva, litigating a claim of actual infringement not only would entail delay, but would also be more expensive than litigating a claim of artificial infringement. A claim of artificial infringement would require only a bench trial to resolve, and would not require proof of damages. A claim of actual infringement would require proof of damages, and would require a jury trial if either Plaintiffs or the opposing party elects it. In previous litigation to enforce the COPAXONE process patents, Plaintiffs invoked their right to a jury trial.

COUNT I
Violation of the Administrative Procedure Act, 5 U.S.C. § 706(2)(A), PHSA Section 351(i)(1), and BPCIA Section 7002(e)(4)

75. Plaintiffs repeat and reallege the allegations contained in the preceding paragraphs as if fully set forth herein.

76. The Administrative Procedure Act prohibits FDA from taking an action that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A).

77. FDA's denial of Teva's Transition Request is a "final agency action." *See* 5 U.S.C. § 704.

78. FDA's denial of Teva's Transition Request causes Plaintiffs injuries-in-fact that are redressable by the relief sought.

79. FDA's denial of Teva's Transition Request is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law" because it is contrary to the BPCIA, which states that a previously approved NDA for a biological product "*shall* be deemed to be a license for the biological product under [section 351 of the PHSA] on the date that is 10 years after the date of [the BPCIA's enactment]," *i.e.*, March 23, 2020. BPCIA § 7002(e)(4)(A), 124 Stat. at 817 (emphasis added). The BPCIA gives FDA no discretion: it must convert a qualifying NDA for a "biological product" to a deemed license.

80. COPAXONE is a "biological product" for at least two reasons. First, it is a "protein." Its active ingredient, glatiramer acetate, is a "chemically synthesized polypeptide" that necessarily falls within the definition of "protein" as used in Section 351(i)(1). Even without the context provided by the now-repealed exclusion for chemically synthesized polypeptides, glatiramer acetate would independently be a "protein." In particular, it satisfies the definition of

"protein" set forth by FDA: (a) the polymer chain is greater than 40 amino acids, and (b) the chain has a "specific, defined sequence." Second, COPAXONE is an "analogous product." Glatiramer acetate is an analogue of myelin basic protein, a naturally occurring protein, and is functionally analogous to a vaccine.

81. In light of these reasons, FDA's refusal to classify COPAXONE as a "biological product" and convert the COPAXONE NDA into a deemed license is contrary to the plain text of the BPCIA (which now includes "chemically synthesized polypeptides" like COPAXONE as eligible "proteins"), and the FDA's own regulatory guidance on the meaning of the terms "biological product" and "protein." That inconsistency is arbitrary and capricious, and is otherwise not in accordance with governing law.

82. FDA's denial of Teva's Transition Request is arbitrary and capricious, contrary to law, and exceeds FDA's statutory authority under the BPCIA. It must be set aside.

83. Teva has exhausted its administrative remedies, or, to the extent that it has not, it is excused from exhausting those remedies because further pursuit of administrative remedies would not further the goals that exhaustion is intended to further.

84. Teva has no other adequate remedy at law.

COUNT II
Violation of the Administrative Procedure Act, 5 U.S.C. § 706(2)(A)

85. Plaintiffs repeat and reallege the allegations contained in the preceding paragraphs as if fully set forth herein.

86. FDA's denial of Teva's Transition Request is arbitrary and capricious because it lacks a sufficient explanation.

87. FDA has treated other products as "proteins," satisfying FDA's requirement of a "specific, defined sequence," even though—like COPAXONE—they are mixtures of different polypeptides and/or their sequence is unknown or not well characterized.

88. To the extent FDA now seeks to apply a "specific, defined sequence" requirement that is so rigid as to exclude COPAXONE, that requirement would reflect an unacknowledged, unexplained change in agency interpretation that must be set aside as arbitrary and capricious.

89. To the extent FDA now seeks to apply a "specific, defined sequence" requirement that is so rigid as to exclude COPAXONE, that requirement would be contrary to law because the term "protein" as used in the PHSA contains no such rigid requirement.

PRAYER FOR RELIEF

Teva respectfully prays for the following relief:

1. An order holding unlawful, vacating, and setting aside FDA's denial of Teva's Transition Request.

2. A declaration pursuant to 28 U.S.C. § 2201 that COPAXONE is a "biological product" under the BPCIA; that the approved COPAXONE NDA is deemed to be a license under Section 351 of the PHSA; and that FDA's denial of Teva's Transition Request is arbitrary, capricious, and contrary to law.

3. An injunction ordering FDA to take all steps necessary to effect the conversion of the approved COPAXONE NDA into a deemed license, and to place COPAXONE on the final list of Approved NDAs for Biological Products That Will Be Deemed to Be BLAs;

4. An award of costs for pursuing this action pursuant to 28 U.S.C. § 2412; and

5. Such other relief as the Court deems just and proper.

Respectfully submitted,

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