aam
Association for Accessible Medicines

Your Generics and Biosimilars Industry

October 17, 2018

The Honorable Robert E. Lighthizer
U.S. Trade Representative
600 17th Street, NW
Washington, DC 20508

The Honorable Alex M. Azar II
Secretary of Health and Human Services
Department of Health and Human Services
Hubert H. Humphrey Building
200 Independence Avenue, SW
Washington, DC 20201

Dear Ambassador Lighthizer and Secretary Azar:

On behalf of the Association for Accessible Medicines (AAM), I am writing to express the serious concerns of manufacturers of generic and biosimilar medicines about the recently negotiated U.S.-Mexico-Canada Free Trade Agreement (USMCA). This trade agreement, if left in its current form, will decrease competition, inevitably leading to increased drug prices in the United States, harming American patients, job creators, workers, and taxpayers. Furthermore, several provisions within the agreement are inconsistent with U.S. law, and if left unchanged, could lead to inappropriate changes in U.S. law or cause the United States to be in violation of the agreement on day one of its enactment. We call on each of you to work with us to improve this agreement before it is finalized in order to help achieve President Trump's goal of lowering prescription drug prices for Americans by facilitating biosimilar and generic drug competition. The changes to the USMCA text that we propose are all consistent with U.S. law, and we believe would be readily accepted by the other treaty parties.

AAM represents manufacturers and distributors of finished generic pharmaceuticals and biosimilar medicines. In 2016, AAM members manufactured over 61 billion doses of prescription medicines in the United States across 149 facilities located in 16 states. Our members manufacture generic medicines in the U.S. for both domestic use as well as export, including to Canada and Mexico.

AAM and its members are driven by the belief that access to safe, effective and affordable generic and biosimilar medicines can improve people's lives and provide significant savings to the U.S. health care system. Generic medicines make up 90% of prescriptions dispensed in the United States, but only 23% of total drug spending. In the last decade the availability of low cost generic medicines has saved U.S. patients, taxpayers, and insurers $1.67 trillion. Thanks to U.S. law intended to foster the development of new cures while encouraging competition from more affordable medicines, America's patients and our health care system have realized trillions of dollars in savings from generic medicines. In 2017 alone, generic medicines saved $265 billion and the potential for savings from biosimilars is projected to reach nearly the same level.[1]

Yet, the American biosimilar market lags far behind markets in other developed countries, due in large part to the gaming of existing intellectual property and exclusivity provisions by brand-name manufacturers. This means that U.S. patients are *already* denied access to the same life-saving biosimilars that are available in other countries. Adoption of the USMCA will exacerbate

[1] Association for Accessible Medicines, 2018 Generic Drug Access & Savings in the U.S. – Access in Jeopardy, available at https://accessiblemeds.org/resources/blog/2018-generic-drug-access-and-savings-report ; Grewal S, et al.,Cost-savings for biosimilars in the United States: a theoretical framework and budget impact case study application using filgrastim, Expert Rev Pharmacoecon Outcomes Res. 2018.

the lagging biosimilar market in the U.S. The USMCA should not put patient access to, or savings from, generic and biosimilar medicines at risk here in the United States.

I. AAM Supports the Administration's Efforts to Lower Drug Prices

AAM strongly supports the Administration's efforts, as stated in President Trump's drug pricing blueprint, to enhance the "availability, competitiveness, and adoption of biosimilars as affordable alternatives to branded biologics." Generic drug and biosimilar competition is a centerpiece of the President's blueprint, because fair competition is the best way to bring down the cost of prescription drugs in the U.S. Erecting barriers through trade agreements delays patient access to competitive generic and biosimilar medicines. We are deeply concerned that requiring brand-name biologic exclusivity to be ten years in the USMCA, as well as adding other barriers to generic and biosimilar access, will have the exact opposite effect by slowing the development of biosimilars that we need in the U.S., thereby decreasing prescription drug competition.

For example, while Mexico does not currently have specific biologic exclusivity, we understand that patients in Mexico may access biosimilar medicines after five years of new chemical entity exclusivity granted to brand-name biologics, assuming all other patents and exclusivities have expired. The proposed agreement doubles this delay to at least ten years of time for patients to wait before they may access biosimilars. Delaying patient access to biosimilars in Mexico and Canada is bad for patients because U.S. biosimilar exporters would be blocked from potential markets, hampering their ability to invest in the development of biosimilars for the U.S. market – thus striking a new blow to the nascent and fragile biosimilars industry in this country.

At a time when the U.S. generics and biosimilars markets are under intense pressure domestically, access to other markets is crucial for providing companies with the capital needed to invest in their U.S. pipelines. The net effect of slowing biosimilar and generic development, as USMCA will do, will likely be increased prescription drug prices borne by patients in the U.S., which again is inconsistent with President Trump's Blueprint to Lower Drug Prices, and not a desirable outcome of the trade agreement. Accordingly, expanding brand-name drug monopolies and creating barriers to both generic drug and biosimilar competition will harm public health as well as the U.S. economy. Moreover, this provision would mean that the Trump Administration would be hand-cuffed by an international agreement from lowering biologic exclusivity to fewer years, if it were ever determined that such a change would be necessary to create a vibrant biosimilar market competition in the U.S. – a severe infringement on U.S. sovereignty and policy options.

II. Improving USMCA to Enhance Access to Affordable Medicines

AAM supports trade agreements that balance the need for medical innovation as well as enhancing access to medicines, including the bi-partisan trade policy negotiated in 2007. AAM is extremely concerned that the proposed USMCA Intellectual Property Rights (IPR) chapter fails to achieve one of the principal objectives of the Bipartisan Congressional Trade Priorities and Accountability Act of 2015 (TPA), because the proposed provisions – which will almost uniformly protect and extend the patent monopolies of brand name drug companies – do not

adequately balance innovation with access to medicine as Congress has required.[2] Importantly, in reviewing the text of the USMCA, the ITAC-13 advisors, including representatives of the innovative pharmaceutical industry, unanimously supported inclusion of provisions "which facilitate market entry for generic drugs and biosimilars (e.g., exemptions from infringement to generate test data to support generic drug and biosimilar approvals, provision of generic exclusivity periods and measures that provide transparency in patent status for drug products)."

While the proposed USMCA text includes many monopoly protections and deterrents to competition (*e.g.,* extended biologics exclusivity, broad exclusivities for drugs, patent term extensions and patent term adjustments, etc.), the agreement lacks critical features of U.S. laws that encourage generic and biosimilar competition. By including such provisions, the USMCA can ensure that competition from affordable generic and biosimilar medicines is available to American patients, taxpayers, and healthcare payers. Without such provisions necessary to accomplish the TPA objective, the USMCA will increase drug prices for American patients and taxpayers.

U.S. law seeks to balance innovation and access by providing 180 days of exclusivity to the first generic drug applicant to challenge a brand name drug patent – thus providing a critical incentive to challenge non-innovative brand drug patents.[3] Similarly, U.S. law provides an incentive to the first biosimilar applicant to prove interchangeability with the brand name biologic drug. The proposed USMCA lacks such critical balance that Congress has adopted in the U.S. through the Hatch-Waxman amendments and the Biologics Price Competition and Innovation Act (BPCIA).[4] Yet the proposed USMCA rewards brand name pharmaceutical companies with the ability to block generic and biosimilar drug competition in a manner inconsistent with the balance in U.S. law, which encourages generic drug development and biosimilar interchangeability.

At a minimum, AAM believes that the imbalance in the IPR chapter of USMCA should be addressed with the following changes that are consistent with the TPA negotiating objective as well as U.S. law:

- **Ensuring a clear and robust regulatory review ("Bolar") provision.** While USMCA provides for regulatory review, the existing language does not provide necessary certainty and clarity. A stronger regulatory review clause is needed to allow generic and biosimilar manufacturers to use a patented invention during the period of patent term without the consent of the patent holder for the purposes of developing information to obtain marketing approval from health regulatory authorities. The regulatory review clause is a crucial provision that facilitates the production and introduction of generics and biosimilars manufacturers into the market on the date of patent expiry. Without these changes, USMCA will prevent rapid development of generics and biosimilars and sales with our trading partners. As the ITAC-13 advisors (including representatives of the innovative drug manufacturers) unanimously agreed, USMCA should provide for a Bolar provision that is just as clear and robust as that granted in U.S. law to ensure the timely launch of generics and

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[2] Bipartisan Congressional Trade Priorities and Accountability Act of 2015, Pub.L. No. 114-26, Sec. 102(b)(5)(C) (creating a principle trade objective "to ensure that trade agreements foster innovation and promote access to medicines.")
[3] 21 U.S.C. § 355(j)(5)(B)(iv).
[4] 42 U.S.C. § 262(k)(6).

biosimilars upon patent or exclusivity expiry.[5] I have included the U.S. provision in the footnote below, and we would recommend adopting its terms in the USMCA.

- **Enhance generic competition by requiring an incentive to challenge patents/exclusivities and granting a reward to those that successfully do so.** Currently, the U.S. is one of the only countries in the world that has an intellectual property framework that includes a reward to promote generic competition. It is commonly agreed that this framework, which is a centerpiece of the Hatch-Waxman amendments, has served as a successful incentive to challenge the validity or applicability of weak patents, thus helping to ensure the expedited entry of generic drugs to the market for the benefit of patients, insurers, and U.S. taxpayers. This mechanism has been, since its implementation, a driver of generic access and has contributed greatly to the number of patent challenges. Establishing a formal system, akin to 180-day exclusivity in the U.S. and consistent with U.S. law, will enhance the market for U.S. made generic medicines in Mexico and Canada.

- **Enhancing patent transparency by including a best mode requirement.** According to the TRIPS Agreement, patent authorities may require the applicant to indicate the best mode for carrying-out the invention known to the inventor at the filing date or, where priority is claimed, at the priority date of the application. Therefore, under the 'best mode' requirement if there are several ways in which the invention may be put into practice, the applicant can be required to disclose that which is most practicable in order to facilitate introduction of other versions of the product once the patent expires. This is particularly important to ensure competition in the biologics market once patents expire. The USMCA patent provisions should make disclosure of the best mode mandatory, in order to enhance the transparency of patents and support the creation of generics and biosimilars.

- **Requirement of full transparency and a public registry for all patents and exclusivities granted to a drug.** USMCA should include a requirement that each signatory adopt a transparent system with a public listing of all patents and exclusivities. Such a system would include creation of a public registry of applicable pharmaceutical patents as currently exists in the U.S. (i.e., FDA's Orange Book).

The improvements discussed above will increase the likelihood that USMCA is consistent with TPA and adequately balanced between protection for innovators as well as patients seeking access to affordable medicines. These changes also help ensure that USMCA is consistent with the Administration's goals of lowering drug prices and facilitating competition through generic and biosimilar medicines. This is the only outcome that is worthy of the bipartisan majorities in Congress that have worked diligently to providing meaningful relief to patients that are facing ever-increasing overall prescription drug costs.

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[5] 35 U.S.C. § 271(e)(1) ("It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention ... solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.")

III. Aspects of the Proposed USMCA are Inconsistent with U.S. Law and Create Significant Additional Barriers for Generic and Biosimilar Products in the US and Other Countries

Aspects of the proposed USMCA conflict with U.S. law, which could necessitate either changes to U.S. law or immediate non-compliance with the agreement. Because these provisions could serve as a template for future trade agreements, these inconsistencies should be addressed now to avoid possible necessary changes to U.S. law in the future.

While these are technical issues that may require technical revisions or clarification, their potential impact on generics and biosimilars, and access to affordable medicine in the U.S. is substantial. I have attached a list of such inconsistencies as Attachment A, but I would like to note perhaps the most important inconsistency here. The proposed text of the USMCA would mandate that countries provide at least 10 years of biologic exclusivity for certain pharmaceutical products that Congress has chosen to exclude from biologic exclusivity under U.S. law. Specifically, in defining a biologic subject to exclusivity, section 351(i)(1) of the Public Health Service Act expressly excludes a protein that is a "chemically synthesized polypeptide." Article 20.F.14.2 of the proposed USMCA contains no such exception. Accordingly, a protein that is a chemically synthesized polypeptide would appear to be entitled to biologic exclusivity under the agreement, even though those products are not biologics in the U.S. and therefore not entitled to biologic exclusivity under our statute. Assuming FDA continues not to provide biologic exclusivity to such a protein under the Public Health Service Act, as dictated by Congress, the U.S. would likely be in violation of the USMCA and any other future trade agreement that adopted its definition of a biologic entitled to exclusivity.

As noted in Attachment A, the USMCA also expands the scope of biologic, five-, and three-year drug exclusivities beyond U.S. law in multiple significant ways. All of these issues should be conformed to the Hatch-Waxman amendments and the BPCIA to avoid a major disruption of the careful balance struck by Congress in enacting the approval pathways for generic and biosimilar medicines in the United States.

In conclusion, AAM looks forward to working with you and Congress to foster a free and fair-trade agreement with Mexico and Canada while ensuring an adequate balance between access and innovation.

Sincerely,

Chester "Chip" Davis Jr.
President and CEO

CC: The Honorable Scott Gottlieb, M.D., Commissioner of Food and Drugs
The Honorable Seema Verma, Administrator, Centers for Medicare and Medicaid
The Honorable C.J. Mahoney, Deputy U.S. Trade Representative

Your Generics and Biosimilars Industry

Attachment A

United States-Mexico-Canada Agreement ("USMCA")
Chapter 20: Intellectual Property Rights
Subsection C: Measures Relating to Pharmaceutical Products
Section-By-Section Comparison

USMCA Section/Text	FDC Act/PHS Act Section/Text	Comments
Article 20.F.11: Patent Term Adjustment for Unreasonable Curtailment		
1. Each Party shall make best efforts to process applications for marketing approval of pharmaceutical products in an efficient and timely manner, with a view to avoiding unreasonable or unnecessary delays.	***FDA User Fee Programs:*** • Prescription Drug User Fee Act (PDUFA) • Generic Drug User Fee Amendments (GDUFA) • Biosimilar User Fee Act (BsUFA)	It is unclear what might constitute "unreasonable or unnecessary delays."
2. With respect to a pharmaceutical product that is subject to a patent, each Party shall make available an adjustment *[39]* of the patent term to compensate the patent owner for unreasonable curtailment of the effective patent term as a result of the marketing approval process. *([39] For greater certainty, a Party may alternatively make available a period of additional sui generis protection to compensate for unreasonable curtailment of the effective patent term as a result of the marketing approval process. The sui generis protection shall confer the rights conferred by the patent, subject to any conditions and limitations pursuant to paragraph 3.)*	***35 U.S.C. § 156 - Extension of Patent Term*** (a) The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent, which shall include any patent term adjustment granted under section 154(b) . . . . (c) The term of a patent eligible for extension under subsection (a) shall be extended by the time equal to the regulatory review period for the approved product which period occurs after the date the patent is issued. . . .	It is unclear what is meant by "unreasonable curtailment." Is this intended to refer to a new or additional patent term restoration?

USMCA Section/Text	FDC Act/PHS Act Section/Text	Comments
4. With the objective of avoiding unreasonable curtailment of the effective patent term, a Party may adopt or maintain procedures that expedite the processing of marketing approval applications.	Various statutory provisions, regulations, and policies; described and discussed in: FDA, Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics (May 2014).	It is unclear what would constitute "unreasonable curtailment" under this USMCA provision.
Article 20.F.12: Regulatory Review Exception		
Without prejudice to the scope of, and consistent with, Article 20.F.4 (Exceptions), each Party shall adopt or maintain a regulatory review exception for pharmaceutical products.	***35 U.S.C. § 271(e)(1) ("Bolar Exemption")*** (1) It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.	The USMCA provision is less clear 35 U.S.C. § 271(e)(1).

USMCA Section/Text	FDC Act/PHS Act Section/Text	Comments
Article 20.F.13: Protection of Undisclosed Test or Other Data		
1. (a) If a Party requires, as a condition for granting marketing approval for a new pharmaceutical product, the submission of undisclosed test or other data concerning the safety and efficacy of the product *[40]*, that Party shall not permit third persons, without the consent of the person that previously submitted such information, to market the same or a similar *[41]* product on the basis of: (i) that information; or (ii) the marketing approval granted to the person that submitted such information, for at least five years *[42]* from the date of marketing approval of the new pharmaceutical product in the territory of the Party. *([40] Each Party confirms that the obligations of this Article, and Article 20.F.14 (Biologics) apply to cases in which the Party requires the submission of undisclosed test or other data concerning: (a) only the safety of the product, (b) only the efficacy of the product or (c) both.)* *([41] For greater certainty, for the purposes of this Section, a pharmaceutical product is "similar" to a previously approved pharmaceutical product if the marketing approval, or, in the alternative, the applicant's request for such approval, of that similar pharmaceutical product is based upon the undisclosed test or other data* concerning *the*	***FDC Act §§ 505(c)(3)(E)(ii) (505(b)(2) NDAs) and 505(j)(5)(F)(ii) (ANDAs)*** (ii) If an application submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), is approved after the date of the enactment of this subsection, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.	This USMCA provision has the potential to conflict with Hatch-Waxman. FDC Act § 505(j)(5)(B) governs the effective date of ANDA approval when there is not a timely filed patent infringement lawsuit made in response to the notice of a Paragraph IV certification contained in an ANDA submitted beginning at year 4 of the 5-year NCE exclusivity period. FDC Act § 505(j)(5)(B)(iii), states, in relevant part: "If the applicant made a [Paragraph IV certification], ***the approval shall be made effective immediately*** unless, before the expiration of 45 days after the date on which the notice described in [FDC Act § 505(j)(2)(B)] is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under [FDC Act §§ 505(b)(1) or (c)(2)] before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted." Thus, ANDA approval is made effective "immediately" (i.e., possibly prior to the expiration of 5-year exclusivity) if there is not a timely filed patent infringement lawsuit made in response to notice of a Paragraph IV certification. The USMCA provision appears

USMCA Section/Text	FDC Act/PHS Act Section/Text	Comments
safety and efficacy of the previously approved pharmaceutical product, or the prior approval of that previously approved product.) *([42] For greater certainty, a Party may limit the period of protection under paragraph 1 to five years, and the period of protection under Article 20.F.14.1(a) (Biologics) to 10 years.*		to make the 5-year period applicable in all cases. USMCA also has the potential to conflict with FDA's implementing regulations to the extent "the same or a similar product" is interpreted to include a product containing a different active moiety.
(b) If a Party permits, as a condition of granting marketing approval for a new pharmaceutical product, the submission of evidence of prior marketing approval of the product in another territory, that Party shall not permit third persons, without the consent of a person that previously submitted such information concerning the safety and efficacy of the product, to market a same or a similar product based on evidence relating to prior marketing approval in the other territory for at least five years from the date of marketing approval of the new pharmaceutical product in the territory of that Party.	No specific FDC Act or PHS Act provision.	This USMCA provision has the potential to conflict with both Hatch-Waxman and the Biosimilars Act. To the extent this provision would prohibit an applicant seeking approval of a literature-based 505(b)(2) NDA for a NCE that is marketed elsewhere in the world, it would conflict with Hatch-Waxman. To the extent this provision would prohibit a biosimilar applicant from using a foreign-sourced reference product for purposes of demonstrating biosimilarity/interchangeability, it would conflict with the Biosimilars Act and FDA's implementation of the statute.
2. Each Party shall: *[43]* (a) apply paragraph 1, *mutatis mutandis*, for a period of at least three years with respect to new clinical information submitted as required in support of a marketing approval of a previously approved pharmaceutical product covering a new indication, new formulation or new method of administration; or, alternatively,	***FDC Act §§ 505(c)(3)(E)(iii), (iv) (505(b)(2) NDAs) and 505(j)(5)(F)(iii), (iv) (ANDAs)*** (iii) If an application submitted under subsection (b) for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b), is approved after the date of enactment of this subsection and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the	This USMCA provision has the potential to conflict with Hatch-Waxman. It is unclear what constitutes "new clinical information" under this provision and whether that information must be from studies conducted/sponsored by the applicant. Both the FDC Act and FDA's implementing regulations require that, to obtain 3-year exclusivity, the applicant must have conducted or sponsored "new clinical investigations (other than bioavailability studies)" that FDA considers essential to the approval of the

USMCA Section/Text	FDC Act/PHS Act Section/Text	Comments
([43] A Party that provides a period of at least 8 years of protection pursuant to paragraph 1 is not required to apply paragraph 2.)	application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) for such drug. (iv) If a supplement to an application approved under subsection (b) is approved after the date of enactment of this subsection and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b).	application. The broad reference to "new clinical information" in this USMCA provision could extend beyond the type of data that could lead to 3-year exclusivity under the statute. It is also unclear whether USMCA would extend 3-year exclusivity to bar the approval of applications that are not seeking approval for the new indication, new formulation or new method of administration approved for the previously-approved product. To the extent USMCA were interpreted to allow this, that would conflict with current US law.
(b) apply paragraph 1, *mutatis mutandis*, for a period of at least five years to new pharmaceutical products that contain a chemical entity that has not been previously approved in that Party. *[44]* *([44] For the purposes of Article 20.F.13.2(b) (Protection of Undisclosed Test or Other Data), a Party may choose to protect only the undisclosed test or other data concerning the safety and efficacy relating to the chemical entity that has not been previously approved.)*	***FDC Act §§ 505(c)(3)(E)(ii) (505(b)(2) NDAs) and 505(j)(5)(F)(ii) (ANDAs)***	See above comments (Article 20.F.13.1).

USMCA Section/Text	FDC Act/PHS Act Section/Text	Comments
Article 20.F.14: Biologics		
1. With regard to protecting new biologics, a Party shall, with respect to the first marketing approval in a Party of a new pharmaceutical product that is or contains a biologic, *[45] [46]* provide effective market protection through the implementation of Article 20.F.13.1 (Protection of Undisclosed Test or Other Data) and Article 20.F.13.3 (Protection of Undisclosed Test or Other Data), *mutatis mutandis*, for a period of at least ten years from the date of first marketing approval of that product in that Party. *([45] Nothing requires a Party to extend the protection of this paragraph to: (a) any second or subsequent marketing approval of such a pharmaceutical product; or (b) a pharmaceutical product that is or contains a previously approved biologic.)* *([46] Each Party may provide that an applicant may request approval of a pharmaceutical product that is or contains a biologic under the procedures set forth in Article 20.F.13.1(a) (Protection of Undisclosed Test or Other Data subparagraph 1(a)) and Article 20.F.13.1(b) (Protection of Undisclosed Test or Other Data subparagraph 1(b)) on or before March 23, 2020, provided that other pharmaceutical products in the same class of products have been approved by that Party under the procedures set forth in in Article 20.F.13.1(a) (Protection of Undisclosed Test or Other Data subparagraph 1(a)) and Article 20.F.13.1(b) (Protection of Undisclosed Test or Other Data*	***PHS Act § 351(k)(7)*** (7) EXCLUSIVITY FOR REFERENCE PRODUCT.— (A) EFFECTIVE DATE OF BIOSIMILAR APPLICATION APPROVAL.— Approval of an application under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a). (B) FILING PERIOD.—An application under this subsection may not be submitted to the Secretary until the date that is 4 years after the date on which the reference product was first licensed under subsection (a). (C) FIRST LICENSURE.—Subparagraphs (A) and (B) shall not apply to a license for or approval of— (i) a supplement for the biological product that is the reference product; or (ii) a subsequent application filed by the same sponsor or manufacturer of the biological product that is the reference product (or a licensor, predecessor in interest, or other related entity) for— (I) a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form,	This provision has the potential to conflict with the Biosimilars Act. This USMCA provision refers to Article 20.F.13.1 and states that a Party must "provide effective market protection through the implementation" of that article. Although this provision refers to "market protection," Article 20.F.13.1 refers to data protection, and to a period of 5-year data protection. This could appear to conflict with the 4-year "data protection" period under the Biosimilars Act preventing aBLA submission. Furthermore, to the extent this provision allows for a 10-year period of "data protection" prohibiting aBLA submission, it could conflict with the Biosimilars Act. USMCA also has the potential to conflict with the way FDA has interpreted the transition rules under the Biologics Price Competition and Innovation Act (BPCIA) governing biologics approved as NDAs. Footnote 46 of USMCA includes its own transition rules for biologic products, which allows biologic applicants to seek approval on or before March 23, 2020 under the procedures set forth in Article 20.F.13.1 (and thus be eligible for, or subject to, 5-year and 3-year exclusivity) under certain circumstances. But footnote 46 does <u>not</u> state whether new biologic applications submitted during this period will be eligible upon approval for 5-year exclusivity under Article 20.F.13 *only*, or if they will also be eligible for 3-year exclusivity under Article 20.F.13, or if

USMCA Section/Text	FDC Act/PHS Act Section/Text	Comments
subparagraph 1(b)) before the date of entry into force of this Agreement for that Party.)	delivery system, delivery device, or strength; or (II) a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. BPCIA § 7002(e) (e) PRODUCTS PREVIOUSLY APPROVED UNDER SECTION 505.— (1) REQUIREMENT TO FOLLOW SECTION 351.—Except as provided in paragraph (2), an application for a biological product shall be submitted under section 351 of the Public Health Service Act (42 U.S.C. 262) (as amended by this Act). (2) EXCEPTION.—An application for a biological product may be submitted under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) if— (A) such biological product is in a product class for which a biological product in such product class is the subject of an application approved under such section 505 not later than the date of enactment of this Act; and (B) such application— (i) has been submitted to the Secretary of Health and Human Services (referred to in this subtitle as the ''Secretary'') before the date of enactment of this Act; or	they will also be eligible for 10-year exclusivity under Article 20.F.14. USMCA could conflict with the way FDA interprets the transition rules under Section 7002(e) of the BPCIA[1] if footnote 46 were interpreted such that a new biologic sponsor may be eligible for exclusivities available under both Article 20.F.13 and Article 20.F.14, and thus entitled to both 5-year exclusivity under one pathway and at least 10 years of exclusivity under another (though these would likely overlap), and also to 3-year exclusivity for each new indication, formulation change or method of administration.

[1] *See* FDA Draft Guidance, *Implementation of the "Deemed to be a License" Provision of the Biologics Price Competition and Innovation Act of 2009*, at 6 (Mar. 2016) (Stating that "any unexpired period of exclusivity associated with an approved NDA for a biological product subject to section7002(e) of the BPCI Act (e.g., 5-year exclusivity, 3-year exclusivity, or pediatric exclusivity) would cease to have any effect" after March 23, 2020); *id*. at 6-7 (noting that "an approved application for a biological product under section 505 of the FD&C Act that will be *deemed* to be a license for the biological product . . . will not receive a period of exclusivity under section 351(k)(7)(A) and (B) of the PHS Act").

USMCA Section/Text	FDC Act/PHS Act Section/Text	Comments
	(ii) is submitted to the Secretary not later than the date that is 10 years after the date of enactment of this Act. (3) LIMITATION.—Notwithstanding paragraph (2), an application for a biological product may not be submitted under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) if there is another biological product approved under subsection (a) of section 351 of the Public Health Service Act that could be a reference product with respect to such application (within the meaning of such section 351) if such application were submitted under subsection (k) of such section 351. (4) DEEMED APPROVED UNDER SECTION 351.—An approved application for a biological product under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) shall be deemed to be a license for the biological product under such section 351 on the date that is 10 years after the date of enactment of this Act.	
2. Each Party shall apply this Article to, at a minimum *[47]*, a product that is produced using biotechnology processes and that is, or, alternatively, contains, a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, for use in human beings for the prevention, treatment, or cure of a disease or condition. *([47] For greater certainty, for the purposes of this Article, the Parties understand that "at a minimum" means that a Party may limit the*	***PHS Act § 351(i)(1)*** (1) The term ''biological product'' means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), 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.	The definition of "Biologics" in Article 20.F.14.2 should be amended to comport with the PHS Act (bold/italics typeface): "Each Party shall apply this Article to, at a minimum, a product that ~~is produced using biotechnology processes and that is, or, alternatively,~~ contains, a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein ***(except any chemically synthesized polypeptide)***, or analogous product, for use in human beings for the prevention, treatment, or cure of a disease or condition."

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application to the scope specified in this paragraph.)		
Article 20.F.16: Measures Relating to the Marketing of Certain Pharmaceutical Products		
1. If a Party permits, as a condition of approving the marketing of a pharmaceutical product, persons, other than the person originally submitting the safety and efficacy information, to rely on evidence or information concerning the safety and efficacy of a product that was previously approved, such as evidence of prior marketing approval by the Party or in another territory, that Party shall provide: (a) a system to provide notice to a patent holder *[48]* or to allow for a patent holder to be notified prior to the marketing of such a pharmaceutical product, that such other person is seeking to market that product during the term of an applicable patent claiming the approved product or its approved method of use; (b) adequate time and sufficient opportunity for such a patent holder to seek, prior to the marketing of an allegedly infringing product, available remedies in subparagraph (c); and (c) procedures, such as judicial or administrative proceedings, and expeditious remedies, such as preliminary injunctions or equivalent effective provisional measures, for the timely resolution of disputes concerning the validity or infringement of an applicable patent claiming an approved pharmaceutical product or its approved method of use.	***FDC Act §§ 505(c)(3)(C) (505(b)(2) NDAs) and 505(j)(5)(B)(iii) (ANDAs)*** (B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii) . . . . (iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—	Article 20.F.16.1(a) should be clarified such that a generic drug manufacturer that seeks approval of labeling that omits a patent-protected method of use (e.g., through a "section viii statement") is not required to provide notice. Article 20.F.16.1(b) requires "adequate time and sufficient opportunity" for a patent holder/owner to seek available remedies. Hatch-Waxman provides various time periods to initiate litigation and a 30-month stay on ANDA approval for patents listed in the Orange Book before an ANDA is submitted. It is unclear, however, whether or not this would be viewed as "adequate time and sufficient opportunity" under this article. Further, both Article 20.F.16.1(a) and (b) should be revised to strike the "prior to the marketing" limitations for both the notice and remedies provisions. While Hatch-Waxman provides for notice to the patent holder of paragraph IV certifications, nothing in Hatch-Waxman requires ANDA or 505(b)(2) applicants to provide notice of marketing, which this language could be interpreted to require.

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([48] For greater certainty, for the purposes of this Article, a Party may provide that a "patent holder" includes a patent licensee or the authorized holder of marketing approval.)	(I) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on— (aa) the date on which the court enters judgment reflecting the decision; or (bb) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed; (II) if before the expiration of such period the district court decides that the patent has been infringed— (aa) if the judgment of the district court is appealed, the approval shall be made effective on— (AA) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or (BB) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or (bb) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the	

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	district court in a court order under section 271(e)(4)(A) of title 35, United States Code; (III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in subclause (I); or (IV) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in subclause (II). In such an action, each of the parties shall reasonably cooperate in expediting the action.	