March 6, 2020

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2019-N-5711: Importation of Prescription Drugs; Proposed Rule

Dear Sir or Madam,

Innovative Medicines Canada (IMC) is pleased to submit comments on the notice of proposed rulemaking ("NPRM" or "proposed rule") titled "Importation of Prescription Drugs" published by the U.S. Food and Drug Administration (FDA) of the Department of Health and Human Services (HHS) in the Federal Register of December 23, 2019.

IMC represents Canada's research and development pharmaceutical industry. Our 40 member companies range from established organizations to fledgling startups, all of whom are dedicated to improving healthcare through the discovery and development of new medicines and vaccines. Our mission is to ensure that Canadians have access to the innovative treatments they need.

As a representative of manufacturers of medications vital to the health of Canadians, IMC is sympathetic to concerns regarding patient affordability for medicines in the United States. However, it has not been demonstrated, as required by U.S. law, that importation of prescription drugs from Canada to the United States will provide American consumers with more affordable choices.

Bulk importation under the proposed rule would result in drug shortages in Canada that would deprive Canadian patients of necessary medicines and strain international relations between Canada and the United States.

FDA's proposed importation program also poses significant safety risks to U.S. patients and does not demonstrate that it would significantly reduce costs for U.S. citizens. Given the global realities of the supply chain and the practical limits of both Canadian law and FDA's enforcement abilities, neither the Canadian regulatory system nor the proposed rule can ensure the safety of drugs imported to the United States under the proposed program. In addition, in light of Canada's legal framework for drug pricing, the proposed rule's contingencies, and the policy options available to Canadian lawmakers to address drug shortages, importation is unlikely to achieve any savings for U.S. consumers.

In light of these significant issues, IMC questions whether the HHS can or should certify that section 804 poses no additional risk to the U.S. public's health and safety and will result in a significant reduction in cost of prescription drugs to American citizens, and FDA should withdraw the proposed rule. We summarize our concerns with the proposed rule below:

- Bulk drug importation will cause drug shortages in Canada that will deprive Canadian patients of necessary medicines.
- Gaps in the regulation of imported drugs between the Canadian and U.S. systems will increase risks to public health and safety.

- It has not been demonstrated that importation of drugs from Canada will achieve significant cost savings for U.S. citizens.
- Drug importation will likely threaten Canada's trade relations with other nations.
- HHS should not certify Section 804 and the FDA should not finalize the proposed rule, and the FDA should not approve a Section 804 Importation Program (SIP) proposal without the input of Canadian stakeholders.

I. The Proposed Rule Would Result in Significant Drug Shortages for Canadian Patients.

IMC is concerned that the proposed rule would result in drug shortages for Canadian patients.[1] Canada's drug supply system is designed to serve its population of 37.8 million people,[2] not the 329 million residents of the United States.[3] Canada's drug supply system is particularly inadequate to serve the needs of Americans given that Americans use prescription drugs at higher rates than Canadians.[4] A recent study estimated that, if Canada supplies 20 percent of Americans' brand name prescription drug needs, Canada's drug supply as well as pharmacy safety reserves would be exhausted in nine and a half months.[5] In order for the importation program to have any meaningful impact on the U.S. drug market, it would necessarily decimate Canada's prescription drug supply, leaving Canadian residents without access to medically-necessary treatments. As a result, it is reasonably foreseeable that Canada's government would act quickly to prevent any material diversion of drugs intended for Canadian patients.

Drug shortages force healthcare providers to choose among reducing doses, turning patients away, or substituting less effective and often costlier alternatives.[6] Providers have expressed fear that shortages will drive Canadian patients to attempt to procure medicines outside the normal supply chain.[7] This could potentially fuel the growth of illegal online pharmacies and introduce counterfeit and substandard drugs into Canada's drug supply.[8] Given Canada's proximity to the U.S., this would also contribute to the potential for counterfeit and substandard drugs to make their way into the U.S. drug supply.

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[1] FDA's Preliminary Regulatory Impact Analysis for the proposed rule acknowledged that "the proposed rule may risk creating or exacerbating drug shortages in Canada." FDA Preliminary Regulatory Impact Analysis at 14.

[2] Statistics Canada, Quarterly Population Estimate (October 2019), available at https://www150.statcan.gc.ca/n1/daily-quotidien/191219/dq191219c-eng.htm?HPA=1&indid=4098-1&indgeo=0.

[3] U.S. Census Bureau, U.S. Population (Feb. 5, 2019), available at: https://www.census.gov/popclock/.

[4] *See* Centers for Disease Control and Prevention, Prescription Drug Use Among Adults Aged 40–79 in the United States and Canada (August 2019), available at: https://www.cdc.gov/nchs/products/databriefs/db347.htm?deliveryName=USCDC_171-DM6888

[5] Marv Shepherd, New pathways for U.S. importation threaten Canadian prescription drug supply, Canadian Health Policy (Sept. 2019).

[6] *See* Hanan Shaban, et al., Impact of Drug Shortages on Patient Safety and Pharmacy Operation Costs, 35 Fed. Pract. 24, 24 (2018).

[7] *See* Letter from Canadian Healthcare Providers to Minister Ginette Petitpas Taylor (July 25, 2019), available at: https://buysaferx.pharmacy/wp-content/uploads/2019/07/Health-Canada-Stakeholder-Letter_Importation.Minister.FINAL072519.pdf.

[8] *Id.*

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As a coalition of Canadian pharmacists and healthcare providers noted in a recent letter to Canada's Minister of Health, "[h]ospital and community pharmacies in Canada are resourced to serve the Canadian public. They are not equipped to support to the needs of a country 10 times its size without creating important access or quality issues."[9] FDA's preliminary regulatory impact analysis for the proposed rule also acknowledged the harm to Canadians when it concluded that "costs imposed on Canadian consumers may be larger on an individual basis than corresponding benefits received by U.S. consumers, due to the comparative magnitudes of U.S. demand and Canadian supply with respect to most, if not all, drugs."[10]

Several organizations that would be integral to any importation program have expressed an unwillingness to participate based on the danger of drugs shortages. Two of Canada's major drug distributors, which were listed in Florida's importation proposal,[11] have stated that they will not sell into the U.S. as part of an importation program because of the need to serve the Canadian market first.[12] In addition, the Canadian Association for Pharmacy Distribution Management has stated that none of its members will participate, noting that these members had not been contacted before being included in any state importation plans.[13]

The proposed rule also harms IMC members by creating considerable uncertainty in terms of manufacturing demand for particular products. Our members depend upon long-term contracts with suppliers and manufacturers to meet patients' needs. Diverting a portion of the Canadian supply to the U.S. would interrupt existing supply arrangements. Our member companies and their contracting partners likely would not have the capacity to ramp up production to meet the increased volume of drug products needed under the proposed importation plan. However, any attempt to compensate for increased demand is frustrated by the fact that our member companies would not be able to predict which particular drugs would experience shortages.

While the NPRM is certain to result in drug shortages, it leaves the selection of particular medications to be imported to the discretion of SIPs. Once SIP plans are released, it is impossible for manufacturers to predict which of the proposed SIP plans will be approved by FDA. Even after approval, manufacturers have no basis on which to estimate the amount that any given SIP plan will increase demand for a particular product. Thus, the proposed rule puts IMC's members in a position in which increased demand will result in a serious shortage of our products for the Canadian market, yet they would lack the necessary information to predict the details of and prepare for the shortage.

II. Drug Importation under Section 804 Poses Safety Risks to U.S. Patients

The proposed importation plan places the safety of the U.S. drug supply at risk. As HHS has previously acknowledged, Canada has not assumed responsibility for the safety of drugs sold into Canada for export to the United States. In addition, the NPRM ignores the risk associated with imposing "manufacturer"

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[9] *Id.*

[10] FDA Preliminary Regulatory Impact Analysis at 14.

[11] State of Florida, Canadian Prescription Drug Importation Concept Paper, Ex. B.

[12] Allison Martell, Canadian drug distributors say no to Trump import plan, Reuters (Dec. 20, 2019), available at: https://www.reuters.com/article/us-usa-healthcare-canada/canadian-drug-distributors-say-no-to-trump-import-plan-idUSKBN1YO24O.

[13] *Id.*

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obligations on the various entities that participate in global manufacturing. Moreover, the NPRM does not attempt to address questions regarding FDA's own jurisdictional reach and how those questions may hinder its ability to safeguard the U.S. drug supply chain. In light of these regulatory gaps, HHS cannot make the necessary safety certification under Section 804 and implementation of FDA's proposed rule would put U.S. patients at risk of receiving counterfeit, diverted, or adulterated drugs.

A. Canada's Lower Level of Regulatory Scrutiny of Drugs Intended for Export Poses Safety Risks to U.S. Patients

Health Canada, Canada's national drug safety regulator, has a different and lower standard with respect to drugs for export outside of Canada. These products are specifically exempted from the regulatory approval process applied to drugs for use in Canada.[14] As noted in the HHS 2004 Task Force Report, "Health Canada does not assure that products being sold to U.S. citizens are safe, effective, and of high quality, and does not intend to do so in the future."[15] This is because "foreign governments give priority to ensuring the safety of drugs used by their citizens. Foreign governments have little incentive and limited resources to ensure the safety of drugs exported from their countries, particularly when those drugs are transshipped or are not intended for import."[16] As a result, "most countries impose a lesser level of regulation on products intended for export to other countries, such as the U.S."[17]

Nothing in the NPRM guarantees that Canada will assume the responsibility for ensuring the safety of the drugs that the Foreign Seller would sell to the United States. For example, the NPRM does not outline a specific strategy regarding how the two governments would collaborate on the effective oversight of section 804 importation. Moreover, Canadian law has not had to address how Health Canada will regulate drugs for commercial use that are imported for sale in Canada, but subsequently become drugs for export. Health Canada's priority is to ensure the safety of drugs used by Canadians. It has limited resources to ensure the safety of drugs intended for export. Consequently, Health Canada is likely to adopt only a limited level of regulation for products destined for American patients.

B. Imposing Obligations on "Manufacturers" that No One Entity Can Necessarily Meet Endangers U.S. Patient Safety

HHS's ability to certify that drug importation will not pose any additional risk to the U.S. public's health and safety depends on compliance of entities with the conditions of the proposed rule, including requirements imposed on manufacturers for statutory testing, attestations, and labeling. As FDA explained, "[t]he Secretary's certification will be conditioned on each authorized SIP meeting the requirement of section 804 of the FD&C Act and this rule."[18] The proposed rule, however, fails to contemplate and account for the realities of global manufacturing that will make ensuring compliance exceedingly difficult. In a variety of scenarios, no one entity will have access to vital categories of information the proposed rule requires "manufacturers" to provide. Imposing "manufacturer" obligations on multiple entities, at times with distinct

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[14] *Food and Drugs Act*, R.S.C. 1985, s. 37.

[15] HHS 2004 Task Force Report at 60–61

[16] *Id*.

[17] *Id.* at 62.

[18] 84 Fed. Reg. at 70803.

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and disparate functions, makes the importation process complex and uncoordinated, which carries the risk that the conditions of the proposed rule will not be met, and U.S. patients may be exposed to unsafe drugs.

"Manufacturer" is defined broadly to include "an applicant," as defined in 21 CFR 314.3, or a person "who owns or operates an establishment that manufactures an eligible prescription drug" or "a holder of a drug master file containing information necessary to authenticate an eligible prescription drug."[19] As the definition of "manufacturer" reflects, the applicant, the manufacturer of the drug (e.g., a contract manufacturer), and the drug master file holder may be three different entities. In addition, the entity that manufactures a given drug for the U.S. market is not always the same entity that manufactures that same drug for the Canadian market. Further, the entity that holds the drug master file for the NDA is not always the same company as the one which holds the master file for Canada.

The proposed rule places many significant regulatory obligations on the "manufacturer." For example:

- The manufacturer must either perform statutory testing or "provide the Importer with formulation information about the HPFB-approved drug and FDA approved drug and any testing methodologies and protocols that the manufacturer has developed that the Importer needs to conduct statutory testing."[20]
- Manufacturers must provide an attestation to the Importer or to FDA establishing that "but for the fact that it bore the HPFB-approved labeling, the drug that the manufacturer sold to the Foreign Seller in fact met the condition in FDA-approved NDA or ANDA."[21]
- The attestation requires manufacturers to confirm that "the HPFB-approved drug conforms to the specifications in FDA-approved drug's NDA or ANDA regarding the quality of the drug substance, drug product, intermediates, raw materials, reagents, components, in-process materials, container closure systems, and other materials used in production of the drug."[22]
- The attestation requires manufacturers to specify that the drugs were manufactured in accordance with CGMP requirements.[23]
- Manufacturers must provide executed certificates of analysis for a recently-manufactured batch of both the Canadian and American versions of the drugs.[24]
- Manufacturers must provide the Importer with authorization to use the drug's approved labeling at no cost.[25]

Given global manufacturing realities, no single entity that falls within the definition of manufacturer will be able to comply with the "manufacturer" obligations in the proposed rule. If the manufacturer of the Canadian drug does not also manufacture the U.S. drug, the Canadian manufacturer who sold the drug to the Foreign Seller would not have access to the specifications and processes used to produce the U.S.

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[19] *Id.* at 70828.

[20] *Id.* at 70818.

[21] *Id.*

[22] *Id.*

[23] *Id.*

[24] *Id.*

[25] *Id.* at 70819.

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product, which would be needed to perform statutory testing and to support the required attestation. Likewise, if the Canadian master file holder is a different company from the NDA holder, this manufacturer also would not be privy to the information needed for the testing or attestation. Neither of these entities would have the ability to grant permission for the Importer to use the U.S.-approved labeling. Thus, full compliance with the "manufacturer" obligations under the proposed rule may be impossible for a single entity.

Having multiple global entities carry out the "manufacturer" obligations under the proposed rule complicates an already complex importation process. It also runs the risk that the information supplied by the various entities will not be coordinated and complementary.

C. FDA's Lack of Clear Authority Over "Manufacturers" Without a U.S. Nexus Compromises Drug Safety for U.S. Patients

The uncertainty regarding FDA's ability to enforce the provisions of the proposed rule will pose additional risks to the public's health and safety. The proposed rule's definition of "manufacturer" encompasses entities without a nexus to the United States. For example, contract manufacturers for the Canadian market and pharmaceutical companies marketing the Canadian version of a drug pursuant to a license agreement with the NDA holder may have no connection to the United States and therefore do not fall squarely within FDA's jurisdiction. FDA may struggle to summon a company with no nexus to the U.S. market to a U.S. court to enforce the provisions of the rule.

The lack of clarity regarding FDA's jurisdiction could compromise drug safety at several stages in the importation process. FDA may be challenged over its authority to require all entities in the supply chain to comply with the requirements posed by the proposed rule. FDA would also be challenged in its ability to address serious safety issues that result in patient harm. For example, if a drug produced by an international manufacturer that is arguably outside of FDA's jurisdiction caused adverse health effects in the United States, FDA could struggle to compel that company to cooperate in an investigation or correct safety issues. Because companies involved in section 804 importation may fall outside FDA's regulatory ambit, FDA cannot be confident in its ability to ensure compliance or to fully investigate and redress violations.

The proposed rule attempts a partial but insufficient workaround of these jurisdictional issues. The NPRM provides that, in the event a manufacturer fails to provide the required information for statutory testing, attestation, or labeling, FDA may itself provide the information or, in the case of permission to use the label, deem the authorization to have been given.[26] While FDA may have access to labeling information and specifications for U.S. manufacturing, FDA would not have access to the complete body of information needed to ensure the safety and authenticity of the drug product. For example, FDA may not have the information needed to compare the manufacturing processes for the Canadian drug with the specifications in the NDA, or other information required by the proposed rule, such as the date of manufacture or the details of the manufacturer's transaction with the Foreign Seller.[27] As such, these provisions cannot fully account for the gaps created by the international nature of manufacturing.

[26] *Id*. at 70819.

[27] *Id*. at 70818.

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III. It Has Not Been Demonstrated that Importation of Drugs From Canada Will Achieve Significant Cost Savings for American Citizens

The proposed importation plan does not demonstrate that there will be significant cost savings for American citizens. Obstacles such as inapplicability of Canadian price controls to sales by distributors, increased costs of a longer supply chain, and likely Canadian government policy responses will erode any potential savings. FDA has not addressed how these factors would affect cost savings for American citizens. Given the multitude of possibilities that could eliminate any meaningful savings and FDA's inability to address these possibilities, it is not clear how the proposed rule would "result in a significant reduction in the cost of covered products to the American consumer."[28]

First the primary driver of lower costs for branded prescription drugs in Canada are price controls that would not apply to drugs exported to the United States. Canada's Patented Medicine Prices Review Board (PMPRB) has statutory authority to set maximum prices. Under section 83 of the Patent Act:

> Where the Board finds that a patentee of an invention pertaining to a medicine is selling the medicine **in any market in Canada** at a price that, in the Board's opinion, is excessive, the Board may, by order, direct the patentee to cause the maximum price at which the patentee sells the medicine in that market to be reduced to such level as the Board considers not to be excessive and as is specified in the order.[29] (emphasis added)

The PMPRB has no jurisdiction to regulate prices of patented medicines sold outside of Canada. As a result, a Foreign Seller's sale to a U.S. Importer would not be subject to the same price ceiling controls that contribute to lower branded drug prices in Canada, allowing them to charge higher prices and eliminate cost savings.

Second, any potential cost savings will be eroded by the need for Importers to make a profit.[30] As acknowledged in FDA's preliminary regulatory impact analysis,

> By contracting with SIP sponsors, importers and private intermediaries would face costs to implement SIPs and use markups to cover these costs and profit. Existing prices may provide a limited basis for forecasting savings to consumers without information on the likely markups applied at each stage in the supply chain.[31]

When FDA considers these markups by each entity in the supply chain, the savings for American citizens would be even further diminished.

Finally, the Canadian government's options for responding to concerns about drug shortages may prevent importation completely or reduce savings for U.S. consumers. The Canadian government has stated on several occasions that it will protect Canada's drug supply in the event of potential shortages caused by

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[28] *See* FDCA § 804(l)(1)(B).

[29] Patent Act, R.S.C. 1985, c. P-4, s. 83 (emphasis added).

[30] FDA Preliminary Regulatory Impact Analysis at 14.

[31] *Id.* at 9.

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importation.[32] The most direct policy option available to Canadian lawmakers to address any shortage caused by the proposed rule would be to ban prescription drug exports, which would, in practice, nullify the proposed rule.[33] Another policy option would be to impose a tariff on exported drugs, which would further increase prices in the United States. Given the multitude of avenues by which cost savings could be eliminated or reduced, it does not appear that the proposed rule would significantly reduce costs for the American consumer.[34]

IV. The Proposed Rule Could Strain International Relations

Moving forward with a policy that places the health of Canada's residents at risk has potential to strain trade relations between the United States and Canada. Canada is the United States' second largest trading partner, with more than $718 billion in goods and services exchanged in 2018.[35] Canada's ambassador to the United States has already expressed public opposition to an importation program, citing concerns about the drug supply.[36] Global Affairs Canada has prepared its officials to oppose the importation plan based on the consequences of importation for Canada's drug supply and to implore U.S. officials to seek alternate solutions.[37] When an importation program was proposed in the past, legislation was tabled in the Canadian Parliament to restrict exports to the United States.[38] Any action by the U.S. government that places Canadians' health at risk would become a significant strain on good relations between the two countries.

Furthermore, the proposed rule could call into question the United States' compliance with its obligations under international trade agreements, for example, the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). TRIPS requires its member countries to maintain a legal structure to provide for intellectual property protection of imported products.[39] Because the statute and proposed rule require manufacturers to provide authorization for Importers to use their U.S.-approved labeling without compensation, implementation would be inconsistent with the United States' obligations to provide intellectual property protection under TRIPS.[40] Any provision that violates trade agreements like TRIPS could undermine trading partners' confidence in the United States' commitment to its trade agreements and make it more difficult for the United States to enforce these obligations with other trading partners.

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[32] *See e.g.*: https://nationalpost.com/news/pm-pledges-access-to-medication-as-pharmacists-patient-groups-fear-shortage

[33] *See id.* at 14.

[34] *See* FDCA § 804(l)(1)(B)

[35] U.S. Trade Representative, U.S. Canada Trade Facts, available at: https://ustr.gov/countries-regions/americas/canada.

[36] Allison Martell, "Canadian ambassador says drug imports would not lower U.S. prices," Reuters (Nov. 1, 2019), available at: https://www.reuters.com/article/us-canada-health-supplies/canadian-ambassador-says-drug-imports-would-not-lower-u-s-prices-idUSKBN1XB55E.

[37] Allison Martell, "Exclusive: Canada warns U.S. against drug import plans, citing shortage concern," Reuters (July 18, 2019), available at: https://www.reuters.com/article/us-canada-pharmaceuticals-exports-exclus/exclusive-canada-warns-us-against-drug-import-plans-citing-shortage-concerns-idUSKCN1UD2LN.

[38] *See, e.g.*, Bill C-387, House of Commons of Canada, Second Session, 39th Parliament.

[39] *See* Trade-Related Aspects of Intellectual Property Rights, World Trade Organization, available at: https://www.wto.org/english/tratop_e/trips_e/trips_e.htm.

[40] *See* 2004 HHS Task Force Report at 94.

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V. Canadian Stakeholders Should Have, At Minimum, The Opportunity to Comment on Section 804 Certification, a Re-Proposed Rule, and SIP Proposals

The health and safety certifications required by Section 804(l) are impossible to make without soliciting input from Canadian stakeholders, including governments, pharmaceutical manufacturers, distributors, pharmacies and others. As noted above, legislative or regulatory responses by the Canadian government and decisions made by private entities such as distributors may decrease or eliminate any potential savings to the American consumer. Manufacturers must also have an opportunity to advise on whether increased production for a particular drug is feasible. Likewise, Canadian stakeholders should be consulted concerning Canada's legal provisions for pharmaceuticals, including customs and export provisions, to determine whether FDA can properly conclude that the program "will pose no additional risk to the public's health and safety".

Canadian stakeholders should have the opportunity to comment on any safety and cost findings underlying section 804 certification, as well as a proposed rule that includes a more robust significant international impact analysis under Executive Order 13609. Executive Order 13609 encourages "international regulatory cooperation" in service of "meeting shared challenges involving health [and] safety[.]"[41] The preliminary regulatory impact assessment provided for the proposed rule acknowledged the adverse effects on manufacturers selling drugs in Canada and on Canadian patients, but failed to provide actual safety and cost estimates of these impacts, depriving interested Canadians stakeholders of a meaningful opportunity to comment. Canadian stakeholders should have the opportunity to comment on a rule that provides a comprehensive picture of its international effects. In addition, SIP proposals should be subject to public notice and comment so that the Canadian stakeholders have the opportunity to provide input on individual SIP proposals before FDA makes a determination regarding a particular SIP plan.

IMC greatly appreciates the opportunity to comment on the proposed rule and looks forward to further opportunities to provide input to FDA as it seeks to advance policies that meet the needs of American citizens without deleteriously affecting Canadian patients, posing additional risks to the U.S. drug supply, or harming Canada's relationship with the United States. Please do not hesitate to contact IMC with respect to any questions or comments related to our submission.

[41] Exec. Order. 13609 at §1.

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