



March 9, 2020

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

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

Dear Sir/Madam:

The American Pharmacists Association (APhA) appreciates the opportunity to submit comments in response to the Food and Drug Administration's (FDA) proposed rule, "Importation of Prescription Drugs" (Proposed Rule).¹ Founded in 1852 as the American Pharmaceutical Association, APhA represents nearly 60,000 pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care. APhA members provide care in all practice settings, including community pharmacies, specialty pharmacies, hospitals, long-term care facilities, community health centers, physician offices, ambulatory clinics, managed care organizations, hospice settings, and the uniformed services.

APhA supports efforts to provide Americans access to quality, safe, effective, and affordable prescription drugs. Despite FDA's good intentions and the effort FDA took to attempt to address patient safety concerns, APhA is concerned the Proposed Rule will seriously jeopardize patient safety. In addition, the Proposed Rule undermines the ongoing implementation of the Drug Supply Chain Security Act² (DSCSA) and the protections it affords to our nation's drug supply. It also creates significant workflow challenges that will disrupt patient care and pharmacist-delivered patient care services. Finally, required onerous program operational and systematic measures will add to drug costs and not result in significant cost savings to consumers.³

Pharmacists are the gatekeeper between the supply chain and the patient. It is the pharmacist's obligation to ensure that patients are provided safe, effective, high quality, and authentic drugs. Pharmacists' confidence in the safety and integrity of the drugs they dispense stems from the

¹ 84 Federal Register 70796 (December 23, 2019).

² P.L. 113-54, Title II of the Drug Quality and Security Act of 2013, (November 27, 2013).

³ "...we lack information to estimate such savings." FDA. "Importation of Prescription Drugs -- Preliminary Regulatory Impact Analysis. Docket No. FDA-2019-N-5711," at page 3. August 29, 2019. <https://www.fda.gov/media/133553/download> (accessed March 1, 2020).

protections afforded in the United States (U.S.) by the closed drug distribution system, combined with FDA's expertise and experience assuring that drugs meet the high U.S. approval standards. Any FDA drug importation program CANNOT compromise pharmacists' confidence in the drugs they dispense to patients. The program outlined in the Proposed Rule would significantly undermine pharmacists' confidence in the drugs they dispense, compromise patient confidence, and ultimately jeopardize patient safety, clinical outcomes, and medication adherence.

APhA strongly urges FDA not to finalize this Proposed Rule as written as it fails to meet the criteria set forth in Section 804(I)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (Section 804),⁴ which must be met for the Secretary of Health and Human Services (HHS) to certify implementation of Section 804. The Secretary will not be able to certify that implementation of Section 804 will pose no additional risk to the public's health and safety and result in a significant reduction in the cost of covered products to the American consumer.

APhA supports, agrees with, and incorporates by reference the comments submitted by the Pharmaceutical Distribution Security Alliance (PDSA), particularly the concerns related to DSCSA. Accordingly, many of the concerns raised in the PDSA comments are not repeated in this letter.

Additionally, APhA notes that we also submitted comments to this docket jointly with seven major national pharmacy organizations raising significant patient safety and cost concerns, and we incorporate those comments by reference as well.⁵

Below, APhA further describes in general comments why the Proposed Rule should not be finalized and provides feedback on the questions posed in the preamble of the Proposed Rule. Although we urge FDA to withdraw this Proposed Rule, throughout this letter APhA offers recommendations to include if FDA chooses to finalize the Proposed Rule despite the significant safety and cost concerns raised by APhA and hundreds of other comments submitted to this Docket.

I. GENERAL COMMENTS

a. FDA's proposed importation program jeopardizes patient safety.

Decades of federal and state laws have created patient safety and drug supply chain protections to ensure that the drugs that we dispense to patients are safe. The proposed program would bypass these protections and create supply chain vulnerabilities. Counterfeit or unsafe drugs could be introduced in these gaps in the supply chain, putting patients at an increased risk.

⁴ 21 U.S.C. § 384.

⁵ See Submission to Docket No. FDA-2019-N-5711 by American Pharmacists Association, American Society of Health-System Pharmacists, Academy of Managed Care Pharmacy, National Community Pharmacy Association, National Alliance of State Pharmacy Associations, American Society of Consulting Pharmacists, College of Psychiatric and Neurologic Pharmacists.

In an APhA Pulse on Pharmacy Survey⁶ (APhA Pulse Survey) conducted in February 2020, our members were asked questions related to FDA’s proposed drug importation program. Of the pharmacist members who responded, there was an overwhelming concern about FDA’s Proposed Rule. Over three-quarters of the respondents were concerned that the Proposed Rule would compromise the security of our drug supply chain. Nearly the same percentage stated they believe their patients are concerned about where their drugs come from.

1) Introduces gaps in the supply chain

Over the decades, federal and state laws and regulations have been established and implemented to create a tight, closed drug distribution system in the U.S. that provides transparency and accountability for participants and products involved in drug distribution. This was not an easy lift. The DCSCA created the building blocks for this closed system. Drug supply chain stakeholders have invested countless resources and hours designing and implementing systems, processes, standards, and more to further lock down the drug distribution system in the U.S.

Co-opting another country’s drug distribution system as part of the U.S. drug distribution system is wholly outside of the intent of DSCSA. DSCSA became law ten years *after* the Medicare Modernization Act,⁷ which codified Section 804, was promulgated. In passing DSCSA, Congress was fully aware of Section 804 and the program that was contemplated under that section, yet Congress codified a U.S. based program that excludes products and supply chain stakeholders who are not part of the closed system. Canadian drugs and supply chain stakeholders are not part of the closed system established by DSCSA. This creates supply chain gaps that jeopardize patient safety.

2) Leads to questionable drug product provenance

Although Canada has a well-established system of approval and oversight of their drug supply, at roughly 1/10th of the size of the U.S., Canada’s drug supply is wholly insufficient to supply the U.S. market. The U.S. demand dwarfs Canada’s supply. First, the numbers do not add up – Canada has 37.59 million people; the U.S. has 327.2 million people. Florida alone has 21.3 million residents. Canada’s drug supply could not possibly stretch to cover excess demand from Americans, unless Canada decided to substantially increase its purchases or imports from other countries to meet that demand. Should Canada decide to increase its purchases to meet new U.S. demand, it would likely only incentivize manufacturers to increase prices to offset the reduced demand in the U.S.

Second, the importation proposal assumes that Canada would be a willing partner to such an arrangement. Health Canada has said that they will protect their drug supply chain and access to drugs that Canadians rely on.⁸ It is expected that the Canadian government will take steps to cut

⁶ APhA conducted a pulse survey regarding drug importation on February 8-15, 2020. The survey was distributed via email to a random sample of 2,635 APhA members in a variety of practice settings. The survey yielded 114 responses for a 4% response rate.

⁷ P.L. 108-173 (December 8, 2003).

⁸ “Canada vows to ‘protect’ drug supplies after Trump proposes importing medication” (December 18, 2019), <https://globalnews.ca/news/6312986/us-drugs-canada-imports/> (accessed March 1, 2020).

off supply of Canadian drugs to Foreign Sellers. Additionally, Canadian pharmacists have objected to the FDA's plan, concerned that siphoning Canadian drugs into the U.S. market would result in shortages for their own patients.⁹ Thus, it appears likely that some of the foundational requirements for a workable Canadian importation proposal – sufficient supply and a willing partner country – are not guaranteed. If the Canadian government takes steps to block export of their drug supply, where will Foreign Sellers get their drugs for importation into the U.S.? FDA is well-aware of the mischief that occurs in the marketplace, such as data falsification in clinical trials, manufacturing, testing, and counterfeiting and diversion in the global marketplace. In order to fill the gap, Foreign Sellers will likely turn to the grey market or diverted drug from non-Canadian sources and falsify the provenance in order to participate in the Section 804 Importation Program (SIP). These countries do not have the same oversight and safeguards that the U.S. system has within DSCSA. The risk of patients receiving counterfeit or otherwise illegitimate drug products jeopardizes patient safety.

There are several fatal flaws that prevent operationalization of the SIP. One critical flaw is that Canadian manufacturers will not sell their drug products to Foreign Sellers if the product will be exported to the U.S. APhA has been told by several U.S. manufacturers that have operations in Canada that it is common practice that agreements with Canadian wholesalers contain clauses prohibiting the wholesaler from distributing the drug product for sale outside of Canada. If this is the case, where will Foreign Sellers get drug products for import into the U.S. under a SIP? Proposed § 251.13(a)(3) requires the Foreign Seller to buy the drug directly from the manufacturer. If the Canadian manufacturer will not sell to the Foreign Seller and the Foreign Seller must buy directly from the Canadian manufacturer, then ALL imported product must be considered suspect and will likely be found to be illegitimate upon investigation. This makes the Section 804 drug importation program a non-starter.

3) *SIP unable to verify FDA-approved is SAME AS Health-Canada approved*

Another fatal flaw in the basic premise of the proposed Section 804 drug importation program lies in the validation that the Health Products and Food Branch of Health Canada (HPFB)-approved drug “meets the conditions in an FDA-approved new drug application (NDA) or abbreviated new drug application (ANDA) for a drug that is currently marketed in the [U.S.], including those related to the drug substance, drug product, production process, quality controls, equipment, and facilities.”¹⁰ Proposed Sections 251.3 and 251.5 require submission by the SIP Sponsor of specific information about the HPFB-approved drug, including the establishment where the active ingredient for each drug is manufactured and the establishment where the finished dosage form for each drug is manufactured, if this information is available. FDA acknowledges that “this information is important for FDA to adequately assess whether the eligible prescription drug meets the conditions in an approved NDA or ANDA. If this information is not available to the SIP Sponsor at the time that the proposal is submitted, it would need to be provided later by the Importer in the Pre-Import Request.”¹¹

⁹ <https://www.reuters.com/article/us-canada-pharmaceuticals-exports-exclus/exclusive-canada-warns-us-against-drug-import-plans-citing-shortage-concerns-idUSKCN1UD2LN>

¹⁰ Proposed §251.2. Definition of Eligible Drug.

¹¹ 84 Fed. Reg. at 70806.

This is a fatal flaw in the Proposed Rule – because a manufacturer is presumably an unwilling partner in any importation program and this information is proprietary and confidential, it is highly unlikely that the manufacturer will provide the information to the SIP Sponsor or Importer. As noted earlier, the Canadian government has stated that they do not support any drug importation program that siphons drugs from Canadian citizens. It is also highly unlikely that the Canadian government will provide this information to the SIP Sponsor or FDA. Consequently, it is unclear how the SIP Sponsor or FDA will determine if the HPFB-approved drug is the SAME AS the FDA-approved version. Without this absolute validation, then it cannot be assumed that these products are interchangeable, thus jeopardizing patient safety. FDA cannot and should not trust any attestation from a SIP Sponsor unless the information is certified as originating directly from the manufacturer or HPFB. If this Proposed Rule is finalized, APhA urges FDA to determine how to overcome this significant shortcoming in the Proposed Rule in order to comply with Section 804 and certify safety.

4) *Recall procedures are inadequate*

APhA is concerned with the efficiency and robustness of the recall procedures outlined in proposed § 251.18(e). A key responsible party to effectuate recalls is the manufacturer. However, by design, in the proposed program, the manufacturer is not a party to the recall in the event that there is a problem with the HPFB-approved version that is imported into the U.S. If there is a serious problem with the marketed product, it is the responsibility under the Proposed Rule for the SIP Sponsor to monitor websites and track public announcements about drugs they import.¹² This is contrary to the way recalls are operationalized now in the U.S., where the manufacturer *actively initiates* steps for the supply chain recall in the event of a problem. The program set up under the Proposed Rule is *passive* and lacks robust notification and efficient response, particularly if the recall is so serious that it is down to the patient level. This could introduce delays in the conduct of recalls, thus jeopardizing patient safety.

Furthermore, there are instances where recalls of products vary across the global marketplace, causing confusion and chaos in the U.S. The recent series of nitrosamine-related recalls vividly illustrates the complexity of the global supply chain and the potential downstream risks to U.S. consumers.¹³ If the nitrosamine recalls occurred in relation to product imported under a Section 804 Program, it would have created significant chaos, confusion, and medication adherence concerns in the U.S.

5) *FDA admits inadequate resources for oversight*

In the preamble to the Proposed Rule, FDA acknowledges that “due to resource constraints that limit FDA’s ability to provide effective safety oversight, we considered placing a limit on the number of SIP Proposals that FDA would authorize and the number of SIPs that FDA would oversee.”¹⁴ Despite this admission, the preamble further discusses how FDA will not limit the

¹² Proposed § 251(e)(1). Drug Recalls.

¹³ See e.g., <https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine>

¹⁴ 84 Fed. Reg. at 70802.

number of SIP Proposals, Foreign Sellers, Importers, or products. It is unclear why FDA would put in place a program that it cannot adequately oversee, particularly since patient safety is at the core of the program. By FDA's own admission, the proposed importation program jeopardizes patient safety. If the Proposed Rule is finalized, APhA urges FDA to dedicate adequate resources for the active oversight and enforcement of all aspects of the Section 804 Program and seek additional funding from Congress before implementing the importation program if funds are not available.

b. FDA's proposed importation program undermines the DSCSA.

Pharmacists and other drug supply chain stakeholders have been working for years implementing DSCSA, which creates a closed supply chain to track and trace prescription drugs as they move from manufacturer to distributor to pharmacy. The Proposed Rule significantly deviates from the intent and purpose of DSCSA. Imported drugs will not be traced in a closed system from manufacturer to pharmacy. Safeguards like DSCSA do not exist in Canada. FDA's proposed rule creates a patchwork of interim supply chain measures that introduce gaps and loopholes in the supply chain as drugs are distributed from Canada into the U.S. Pharmacies have invested countless time and millions of dollars to put DSCSA systems in place. The Proposed Rule creates a disincentive for further investment and compliance. In fact, the Proposed Rule would effectively nullify much of that investment and place patients at risk.

FDA acknowledges in the Proposed Rule preamble that because DSCSA does not include an exemption for drugs imported under Section 804 of the FD&C Act, such drugs are subject to the requirements of Section 582 of the FD&C Act.¹⁵ However, FDA proposes to exempt from Section 582 certain transactions for drugs imported under a Section 804 program under the authority provided by Section 582(a)(3)(A)(iii) of the FD&C Act.¹⁶ This directly contradicts FDA's draft guidance for industry regarding "Waivers, Exceptions, and Exemptions" from the requirements of Section 582 of the FD&C Act.¹⁷ In this draft guidance, FDA states that it "intends to only establish exemptions under Section 582(a)(3)(A)(iii) on its own initiative where it determines that the exemption is appropriate to maintain public health or is otherwise appropriate. As with exceptions and exemptions that are granted pursuant to a request, before establishing exceptions or exemptions, FDA intends to consider how an exception or exemption might affect the security of the drug supply chain prior to establishing the exception or exemption on its own initiative."¹⁸ Although FDA did attempt to close the gap by proposing DSCSA-like interim requirements, the exemptions and lack of a track and trace system in Canada would indeed affect the security of the drug supply chain. FDA does not seem to be following its own draft guidance because substantial security gaps would exist as the product is distributed in Canada.

¹⁵ 74 Fed. Reg. at 70813.

¹⁶ *Id.*

¹⁷ FDA, Waivers, Exceptions, and Exemptions from the Requirements of Section 582 of the Federal Food, Drug, and Cosmetic Act Guidance for Industry (Draft) (May 2018). <https://www.fda.gov/media/113342/download> (accessed March 1, 2020).

¹⁸ *Id.* at page 6.

Furthermore, according to a recent report released by the U.S. Department of Health and Human Services Office of the Inspector General (HHS/OIG), FDA staff have stated that each time a drug product changes possession, there is a risk that the drug could be mishandled or stored improperly. If finalized, the Section 804 importation program would directly contradict concerns for patient safety expressed by FDA.¹⁹ This HHS/OIG Report identified an important current shortcoming of DSCSA that allows suspect and illegitimate products to enter the supply chain since physical movement of a drug is not documented. HHS/OIG recommended FDA should seek legislative authority to fill this gap and FDA agreed with the recommendation.²⁰ Consequently, a program that further complicates the supply chain, such as the one outlined in the Proposed Rule, would be contrary to HHS/OIG's and FDA's goal to further lock down the supply chain and the distribution path that drugs take in the U.S.

APhA identified the following non-exhaustive, non-prioritized, list of DSCSA-related security gaps that the Section 804 importation program creates.

- 1) *Security Gap: No transaction documentation is required to be passed from manufacturer to Foreign Seller. This is a key first-step in documenting the chain of ownership and essential as evidence for tracing in an investigation of suspect or illegitimate product.*
- 2) *Security Gap: Foreign Seller is not an authorized trading partner – not subject to same level of oversight as authorized trading partners in the U.S. DSCSA closed distribution system. The Foreign Seller is not held to the same rigorous standards for licensure as U.S. wholesale distributors.*
- 3) *Security Gap: No transaction statement is passed to Foreign Seller or to Importer, nullifying the validity of all subsequent transaction statements.*
- 4) *Security Gap: Relabeler/repackager vulnerabilities. When the SSI is placed on each package or case, it most likely will be performed by a relabeler or repackager in Canada. This creates an opportunity for mischief and misconduct and opens the door for falsification of the product or packaging. Additionally, there is no requirement for the relabeler/repackager to be registered with FDA or adhere to current good manufacturing practices when the SSI is applied.*
- 5) *Security Gap: Section 804 Serial Identifier (SSI) confusion upon association of SSI with DSCSA product identifier. For traceability, it is essential the SSI be correctly associated with the serialized DSCSA product identifier. This is a complex process that requires sophisticated systems and data validation and will be costly. Failure to*

¹⁹ See OIG. "Ownership – But Not Physical Movement – of Selected Drugs Can Be Traced Through the Supply Chain," at page 16, February 2020. <https://oig.hhs.gov/oei/reports/oei-05-17-00460.asp> (accessed March 4, 2020).

²⁰ *Id.* at 20.

implement adequate and appropriate systems or shortcuts will introduce product mix-ups, slow down drug distribution and availability, and frustrate product verification.

- 6) *Security Gap: Importer exemption from verifying product identifier makes downstream verification dubious at each subsequent transaction of the product. This is a critical step to ensure that the product is what it purports to be. Within the U.S. distribution system, such product would be considered suspect. If suspect product is given a free pass in this situation, it could lead trading partners to let their guard down on identifying and investigating other suspect product in the supply chain.*
- 7) *Security Gap: There are at least 3 product “touches” before DSCSA requirements apply. DSCSA is intended to be an END-TO-END traceability system. Starting the DSCSA supply chain protections halfway through the distribution of the product simply makes no sense and undercuts any subsequent safeguards for products imported under Section 804.*
- 8) *Security Gap: There is no DSCSA product identifier on dispensed product if the importer dispenses it directly, so the product would never be subject to DSCSA safeguards. This creates opportunities for suspect and illegitimate product to enter the supply chain.*
- 9) *Security Gap: No supply chain interoperability in Canada. Canada does not have a track and trace system in place. No transaction documentation is required to be passed so what is passed from one trading partner to another is not in any standardized format and is unlikely to be interoperable by DSCSA standards. This makes traceability in the event of an investigation for suspect or illegitimate product inefficient and ineffective. It also introduces opportunities for suspect and illegitimate product to be introduced into the supply chain if there is no interoperable transaction documentation to verify transaction history or product identifier.*
- 10) *Security Gap: There are greater interoperability concerns after the 2023 electronic system is implemented. It is expected that the 2023 DSCSA electronic interoperable system will rely on technologies and security features that will provide a higher level of confidence in the validity of the transaction documentation associated with distribution of the product and that the product is not suspect or illegitimate. This is premised on being able to trace the product identifier from the time the product is introduced into the distribution system by the manufacturer as it moves through the supply chain. Since Canada does not have a track and trace system and the product will not have a*

serialized product identifier from “birth,” it will bypass the protections of the sophisticated 2023 system, creating a greater security gap than exists currently.

11) Security Gap: The SIP is permitted to continue even if illegitimate product is found. Illegitimate foreign product or illegitimate product found in the supply chain is evidence of serious security breaches within the SIP. Such a finding should trigger revocation of the authorization of the SIP.

c. FDA’s proposed program would create pharmacy operation disruptions that could introduce barriers to access that may compromise patient safety.

The FDA-approved and the Canadian versions would be commingled in the marketplace. With already limited shelf space, and time spent on managing inventory, introducing these Section 804 products onto pharmacy shelves would interfere with pharmacy operations. Further, the proposed program would create product selection confusion with questionable interchangeability between products, and the pharmacist may not know which version of the drug to dispense to patients. Access to medication could be limited if a patient’s plan dictates dispensing one version and a pharmacy only has the other. It would also complicate insurance coverage and reimbursement at the pharmacy.

Identical products in the marketplace with different National Drug Code (NDC) numbers and different prices make product selection for patients at the pharmacy complicated and time-consuming. Because patients are on different insurance plans, their co-pay/co-insurance varies depending on their plan and the specific NDC of the dispensed product. Drug pricing in today’s marketplace is complex, non-transparent, inequitable, and not predictable. A specific product may be less expensive for one patient compared to another patient, regardless of whether it is an imported drug or not. Pharmacy benefit managers’ (PBM) practices (e.g., spread pricing, pharmacy claw-back fees, etc.) game the drug pricing system to maximize profits without necessarily reducing out-of-pocket expenses for the patient at the pharmacy counter.

In addition, due to manufacturer rebates and the lack of drug pricing transparency, a product with a higher list price may garner a higher manufacturer rebate, making it more profitable for the PBM, creating an incentive for the PBM to steer patients to receive the higher list price product. It is likely that there will not be a rebate for the Section 804 product, resulting in a higher out-of-pocket cost for the patient at the pharmacy counter for the imported drug. The Section 804 product, with a lower list price, may be preferable for patients who pay cash, such as those who have to meet a high deductible before coverage kicks in or for products that are not covered by insurance. Our members and their pharmacy staff will then have to sort out all of the confusion and, unless payers or patients are willing to cover these additional costs, the “ask” will once again be an unfunded mandate on pharmacists. A pharmacist will have to run both NDCs through the electronic claims system as separate claims and then reverse (cancel) the claim for the higher priced product. Checking both NDCs and reversing the higher priced NDC takes time and may raise audit red flags. There is also a fee to reverse a claim – adding an unnecessary expense. In addition, patients get frustrated and complain when they have additional wait time to

receive their prescription at the pharmacy due to administrative issues—adding to disruptions all around. All of this once again challenges pharmacists’ ability to spend time with patients on the real concerns around maintaining optimal drug therapy, and not just dispensing.

In order to accommodate the vast scope of patient plans and coverage, pharmacies would need to stock both the original FDA-approved and the Section 804 product. Shelf space in pharmacies is limited and they may not be able to stock both. If a pharmacy does not have the Section 804 product for the patient in stock, the patient will have to either wait until it is in stock or go to another pharmacy. This could create a disruption in patient care, potentially impacting medication adherence if the lack of availability leads the patient to miss a dose or doses or decide not to get the prescription filled at all.

FDA should expect supply disruptions as the marketplace adjusts to demand for one NDC over the other if the market cannot accommodate surges in demand. Therefore, APhA strongly recommends FDA monitor demand and supply issues closely in the marketplace to ensure uninterrupted patient care.

The APhA Pulse Survey demonstrates pharmacists’ overwhelming concerns. In the survey, pharmacists were told that “if the proposed drug importation program is implemented, a pharmacy may end up stocking the FDA-approved and Canadian versions, with different NDC numbers for different versions. Please indicate how concerned you would be about each of the following at your pharmacy.” Here are the results:

	n=	Very concerned	Somewhat concerned	Not too concerned	Not at all concerned	TOTAL CONCERNED	TOTAL NOT CONCERNED
Shelf space.	108	44%	31%	19%	6%	75%	25%
Storage issues (e.g., storing different versions together on your shelves).	104	42%	31%	20%	7%	73%	27%
Product selection for patients (e.g., which version would be dispensed for a particular patient).	107	46%	34%	16%	5%	80%	21%
Interchangeability of the FDA-approved and Canadian versions.	107	64%	19%	11%	6%	83%	17%
Reimbursement issues (e.g., dealing with insurance issues for patients who are eligible for imported drugs but prefer the FDA-approved version; determining which version is covered under different plans).	107	76%	19%	5%	1%	95%	6%

Pharmacists consistently rely upon FDA-approval as confirmation of a drug's safety and effectiveness. Proposals to allow prescription drug importation, although well-intended, devalues FDA's rigorous approval standards by permitting non-FDA approved medications to enter the supply chain. In the APhA Pulse Survey, 84% of the respondents said they prefer to dispense FDA-approved drugs to their patients. In addition, having FDA-approved and Canadian versions of the same medications could lead to an unintended consequence of discrimination, as individuals of lower socioeconomic or insurance coverage would only have access to the Canadian versions whose quality and safety is not assured like the FDA-approved products.

Official APhA policy²¹ affirms that pharmacists seek to dispense FDA-approved drugs and desire a safe, closed drug distribution system. Inserted directly below are the relevant APhA Policies:

Non-FDA Approved Drugs and Patient Safety

2009

1. The American Pharmacists Association calls for education and collaboration among health professional organizations, federal agencies, and other stakeholders to ensure that all manufacturer, distributor, and repackager marketed prescription drugs used in patient care have been FDA approved as safe and effective.
2. APhA supports initiatives aimed at closing regulatory and distribution system loopholes that facilitate market entry of new prescription drugs products without FDA approval.
3. APhA encourages health professionals to consider FDA approval status of prescription drug products when making decisions about prescribing, dispensing, substitution, purchasing, formulary development, and in the development of pharmacy/medical education programs and drug information compendia.

²¹ Official APhA policy is developed by the APhA House of Delegates. Comprised of delegates from state pharmacy associations, APhA membership academies, affiliated organizations, recognized pharmacy organizations, and ex-officio groups, the House of Delegates meet during the APhA Annual Meeting to debate and adopt policy proposals developed throughout the year. The APhA Online Policy Manual can be found at: <https://www.pharmacist.com/apha-house-delegates> (accessed March 1, 2020).

Protecting the Integrity of the Medication Supply

2004

1. APhA encourages pharmacists to enhance their role in protecting the integrity of the medication supply, including careful consideration of the source and distribution pathways of the medications they dispense.
2. APhA recommends that all individuals and entities of the pharmaceutical supply system, including manufacturers, wholesalers, pharmacies, pharmacists, and others, adopt appropriate technology, tracking mechanisms, business practices, and other initiatives to protect the integrity of the drug supply.
3. APhA supports public education about the risk of using medications whose production, distribution, or sale does not comply with U.S. federal and state laws and regulations.
4. APhA urges pharmacists and other health care professionals to report suspected counterfeit products to the Food and Drug Administration.

d. FDA’s proposed importation program fails to produce significant cost savings to American consumers.

As a result of additional steps in the supply chain, such as relabeling (twice) and laboratory testing requirements, it is highly unlikely that there will be a significant cost savings to consumers. The need for additional track and trace, recall, and adverse event reporting systems will further increase costs associated with the importation program. Also, most high-cost drugs are excluded from the program. The lack of clarity around unknown, unproven cost savings does not justify jeopardizing U.S. supply chain integrity and patient safety.

FDA does not provide an estimate of potential savings in the proposed rule,²² instead citing two older studies that indicate importation is unlikely to generate significant savings.²³ Similarly, two recent state analyses of potential savings - Vermont and Florida - do not project cost savings in amounts sufficient to justify risking the security of our national drug supply chain.

- The State of Vermont analysis suggests that, at best, an importation program would result in savings for \$1-5 million annually.²⁴ The analysis was completed before FDA’s proposal was published, so it may not have included high-cost drugs that would be excluded from SIPs. However, even if the full savings were realized, when extrapolated across Vermont’s population, the savings would amount to about \$4 per person – about the price

²² 84 Fed. Reg. at 70823. “We are unable estimate the cost savings from this proposed rule, as we lack information about the likely size and scope of SIP programs and about the specific drug products that may become eligible for importation, the degree to which imported drugs would be less expensive than non-imported drugs available in the United States, and which SIP eligible products are produced by U.S. drug manufacturers.”

²³ *Id.* at 70825 (References).

²⁴ See “Vermont’s Canadian Wholesale Importation Program for Prescription Drugs,” October 2019. <https://nashp.org/wp-content/uploads/2019/12/vt-submittal-to-omb-12-3-2019.pdf> (accessed March 1, 2020).

of a cup of coffee. This amount seems insufficient to meet the “significant reduction” test laid out in Section 804 of the FD&C Act and certainly does not rise to a level that justifies compromising patient safety.

- The State of Florida’s “concept paper” estimates a cost savings of \$150 million, based on a 45% markup to the Canadian drug price to cover the costs of relabeling, repackaging, testing, etc.²⁵ However, they acknowledge that given the “uncertainty of negotiations,” the importation costs could deviate substantially. Florida’s concept paper is also very data light – while there is a table showing savings for a sample of drugs, there are no numbers to back up the 45% markup figure or to justify their extrapolation of \$150 million in annual cost savings, or to determine who would benefit from a 45% markup. This type of back-of-a-napkin cost analysis lacks the rigor necessary to validate meaningful cost savings that would support importation. Florida does provide savings estimate for a subset of HIV/AIDS drugs, but that table indicates savings (using the 45% markup for importation costs) of approximately \$20 million – less than \$1 per Florida resident. Again, despite our desire to see reduced drug costs, we do not believe that such minimal amounts justify short-circuiting the safety requirements that protect the American drug supply.

We urge the agency not to approve any SIP Program without a thorough cost analysis, including hard data supporting markup estimates and cost savings estimates.

II. SPECIFIC REQUESTS FOR COMMENTS

The Preamble of the Proposed Rule contains specific questions and requests for comment. Below are APhA responses to some of the issues posed, specifically those that raise patient safety issues.

a. Should group purchasing orgs (GPO), pharmacy benefit managers (PBM), or union health/welfare benefit plans be co-sponsors of a SIP?²⁶

No, SIP sponsors or co-sponsors should be limited to government entities and wholesalers and pharmacists. Including wholesalers or pharmacists enables their expertise to be provided in the design and execution of the SIP. Having a government entity as the sponsor provides a level of oversight and accountability. However, opening the door to allow other non-governmental entities that have no experience or expertise as a sole supply chain stakeholder introduces vulnerabilities that may allow counterfeit and substandard drugs into the U.S. supply chain. Decisions related to drug product selection should focus on the clinical needs of patients, and first and foremost on product quality and safety, not profit.

²⁵ See “Florida’s Canadian Prescription Drug Importation Concept Paper,” Aug. 20, 2019. https://ahca.myflorida.com/executive/communications/requested_documents/Florida_Canadian_Prescription_Drug_Importation_Concept_Paper.pdf (accessed March 1, 2020).

²⁶ 84 Fed. Reg. at 70801.

b. Option 1/Option 2: Should pharmacists be a SIP Sponsor without a state or other non-governmental entity?²⁷

Having a state or other governmental entity as a SIP-cosponsor provides a layer of oversight, accountability, and enforcement that is not available if the pharmacist was the SIP sponsor and importer.

c. Should a SIP proposal be required to describe the SIP Sponsor's plan for ensuring that the FDA-approved patient labeling is dispensed to patients with the drug imported under section 804 of the FD&C?²⁸

Yes. The SIP proposal should describe the SIP Sponsor's plan to ensure that FDA-approved patient labeling is dispensed to patients with the imported drug. If FDA-approved patient labeling is required to be dispensed with a product, the manufacturer of that product would have identified and provided the means for the patient labeling to be dispensed with the product. However, Section 804 imported products will be relabeled and the relabeler may not be aware that such labeling is required to accompany the product so it is available at the point of dispensing. FDA-approved patient labeling contains important information for the safe and effective use of the product. Failure to ensure that it will be dispensed to patients with Section 804 product puts patient safety in jeopardy.

d. What factors should be considered in determining whether a reduction in the cost of covered products is significant? What measures would be relevant and available to SIP Sponsors during proposal development to compare pricing? What mechanisms could be put in place to ensure cost savings impact the American consumer?²⁹

Section 804(l)(1) of the FD&C Act requires the HHS Secretary to certify that the importation will “result in a significant reduction in the cost of covered products **to the American consumer.**”³⁰ SIP Proposals must contain the details necessary to demonstrate the imported drug will be significantly less out of pocket cost to the American consumer. This analysis cannot be a simple comparison of the difference in acquisition costs for the Canadian drug versus the FDA-approved drug. There are significant operational and systematic costs that attach to the drug in order to comply with the SIP program as it is distributed from the Foreign Seller to the American consumer. These cannot be underestimated and will increase the ultimate cost of the drug at the pharmacy. This includes relabeling (twice), testing, serialization of packages and cases, implementation of verification systems and processes, databases and data management, establishment and running of adverse event reporting mechanism, recall

²⁷ *Id.*

²⁸ *Id.* at 70806.

²⁹ *Id.* at 70807.

³⁰ 21 U.S.C. § 384(l)(1).

management system, compliance management, inventory management, and more. In addition, the supplemental costs for dispensing and product management to the patient needs to be included into the calculations.

Additionally, APhA urges FDA to make the SIP proposals, including the justification describing how patient safety will be assured and how the significant cost savings to the American consumer was calculated, publicly available. As described in our comments and by hundreds of comments in the docket, the associated cost savings and patient safety are dubious and must be available for public scrutiny in order to provide public assurances for these drugs that will be commingled in our nation's drug supply.

e. Is 2 years the appropriate initial period of time for a SIP, are 2-year reauthorization periods appropriate, and should there be a limit on the number of re-authorization periods?³¹

FDA should not authorize a renewal period unless and until the SIP Sponsor demonstrates that there is no additional risk to patients and results in a significant reduction in cost of the covered product to the American consumer. As stated throughout our comments, there are inherent safety risks associated with this type of importation and drug importation is not a solution to high drug prices. It is our hope that the private and public sectors will work towards addressing skyrocketing and unaffordable drug prices, ending once and for all the quest for drug importation as a panacea.

f. What elements should be included in a SIP's compliance plan, and what, if any, additional elements would be necessary to include if a SIP is co-sponsored?³²

APhA agrees with FDA's recommendations for what should be included in a SIP's compliance plan, including requiring: (1) A description of the division of responsibilities between co-sponsors, if any, (2) the creation of written compliance policies, procedures, and protocols; (3) the provision of education and training to ensure that Foreign Sellers, Importers, qualifying laboratories, and their employees understand their compliance-related obligations; (4) the creation and maintenance of effective lines of communication, including a process to protect the anonymity of complainants and to protect whistleblowers; and/or (5) the adoption of processes and procedures for uncovering and addressing noncompliance or misconduct.

All SIP parties, including co-sponsors should be included in the compliance plan. Additionally, the SIP should be routinely audited by a third party or inspected by FDA to ensure continued compliance given the significant gaps and opportunities for suspect and illegitimate product to enter the supply chain.

³¹ 84 Fed. Reg. at 70811.

³² *Id.*

g. What additional standards should be imposed, or qualifications required of Foreign Sellers?³³

Vetting, oversight, and accountability of the Foreign Seller is critically lax as proposed. Given the key role that the Foreign Seller plays in introducing the foreign drug product into the closed U.S. drug distribution system, FDA should add additional oversight if this Proposed Rule is finalized. For example, the Foreign Seller should be inspected by FDA prior to acceptance of the SIP Proposal. The inspection standards should be based on U.S. wholesale distributor licensing standards. Because of the significant gaps and opportunities for suspect and illegitimate product to enter the supply chain via the Foreign Seller, FDA should conduct unannounced inspections of the Foreign Seller's operation on a routine basis, at least every 6 months.

FDA should also routinely request records from the Foreign Seller to review and verify the supply chain for the SIP drug products.

h. Are there safeguards that can be put in place to enable FDA to authorize a SIP with multiple Foreign Sellers in a single supply chain in Canada? Provide specific details regarding additional safeguards and how they would provide the same level of protection to the supply chain.³⁴

APhA and other commenters have raised legitimate, significant public health and safety concerns with the Section 804 importation program. FDA took great effort to minimize the supply chain vulnerabilities by maintaining a seemingly shorter supply chain. Our concerns are amplified several-fold if SIPs are permitted to have more than one Foreign Seller in the program. Lengthening the supply chain and providing more opportunity for mischief and misconduct would greatly jeopardize patient safety. APhA urges FDA not to permit multiple Foreign Sellers in a SIP.

i. Seeking comment on whether proposed rule contains sufficient safeguards to ensure that the proposed importation poses no additional risk to health or safety.³⁵

As stated earlier in this comment letter, APhA has significant concerns about the Section 804 drug importation program in the Proposed Rule and firmly believes there are insufficient safeguards proposed or that can be put in place to mitigate the patient safety concerns.

³³ *Id.* at 70812.

³⁴ *Id.* at 70813.

³⁵ *Id.* at 70814

- j. Seek comment on the scope of their Foreign Seller’s proposed verification requirements and the extent to which Foreign Sellers currently or in the future may have systems or processes in place to meet such requirements.³⁶**

As stated earlier in this comment letter, APhA has significant concerns about the DSCSA-like provisions and their inability to ensure safe and secure closed drug distribution from manufacturer to dispenser. Furthermore, it is not clear how a Foreign Seller could respond to a verification request since the foreign product will be relabeled in the U.S. with a DSCSA product identifier and the Foreign Seller would not have the information to verify this new identifier.

- k. Should additional exemptions be included from DSCSA requirements?**

As stated earlier in this comment letter, APhA has significant concerns about the DSCSA-like provisions and their inability to ensure safe and secure closed drug distribution from manufacturer to dispenser. NO ADDITIONAL exemptions should be included, or patient safety would be even further jeopardized.

- l. We seek comment on whether having multiple otherwise identical drugs in the marketplace with different NDCs will create any issues, such as with pharmacy dispensing or otherwise, and, if so, if there are steps that can be taken to mitigate such issues.³⁷**

Yes, having similar drugs in the marketplace with different NDCs will create significant issues. See, section I.c. above.

- m. Does the statement below need to include the name of the SIP, or is it sufficient to state the drug was imported under a SIP? “This drug was imported from Canada under the [Name of State or Other Governmental Entity and of Its Co-Sponsors, If Any] Section 804 Importation Program to reduce its cost to the American consumer.”³⁸**

Yes, the labeling statement should include the name of the SIP in the statement. According to the Proposed Rule, FDA may approve more than one SIP. As such, more than one SIP may import the same drug from Canada but use different Foreign Sellers and Importers. Greater differentiation and information related to these products in the marketplace helps inform pharmacists and others in their decision-making in whether to stock and use the product.

³⁶ *Id.*

³⁷ *Id.* at 70819.

³⁸ *Id.* at 70820.

III. CONCLUSION

APhA shares FDA's goal to ensure that patients receive quality, safe, and effective drugs. However, importing foreign unapproved drugs from Canada is not the solution to high drug prices at the risk of patient safety. Although the comments above suggest ways to mitigate the safety concerns, even with these changes to the Proposed Rule significant safety concerns remain. APhA urges FDA not to finalize the Proposed Rule. As outlined above, the HHS Secretary will not be able to certify that importation under this, or any Section 804 drug importation program, poses no addition risk to public health and safety and will result in significant cost savings to the American consumer. APhA stands ready to work with FDA to develop innovative, yet safe, programs and initiatives to provide greater access to affordable drugs. We look forward to continuing to work with FDA on the implications of drug importation policies on patients and pharmacists and thank you in advance for considering our concerns. If you have any questions, or if we can be of any assistance, please do not hesitate to contact Michael Baxter, Director of Regulatory Affairs, at mbaxter@aphanet.org or by phone at (202) 429-7538.

Sincerely,

A handwritten signature in black ink that reads "Thomas E. Menighan". The signature is written in a cursive, flowing style.

Thomas E. Menighan, BSPharm, MBA, ScD (Hon), FAPhA
Executive Vice President and CEO