March 9, 2020
Division of Dockets Management (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,

On behalf of the Pharmaceutical Distribution Security Alliance (PDSA), I am pleased to submit these comments regarding the Food and Drug Administration's (FDA or Agency) Proposed Rule regarding the importation of prescription drugs (the Proposed Rule).

PDSA is a multi-stakeholder coalition with membership that spans the entire spectrum of the U.S. pharmaceutical distribution system, including manufacturers, repackagers, wholesale distributors, third-party logistics providers, and pharmacies. More than 30 companies are formal members of PDSA, while many other external stakeholders provide additional policy and technical support through industry trade associations. Our primary goal is ensuring patients have uninterrupted access to safe, authentic, FDA-approved medicine.

We recognize the multitude of pressures faced by both public- and private-sector stakeholders to address public concerns regarding the price of pharmaceuticals, but regulators have an even greater obligation to ensure that the supply of those products is safe, secure, and reliable. The United States pharmaceutical supply chain has invested incalculable time, energy, and resources over recent decades in order to establish the safest drug supply in the world, with the 2013 enactment of the Drug Supply Chain Security Act (DSCSA) being a critical element. PDSA has significant concerns that the Proposed Rule will undermine the safety and security of the United States' drug supply and put patients at risk. Accordingly, we urge the Agency not to finalize the Proposed Rule. We have identified numerous concerns that could lead to negative impacts on public health and safety through implementation of the Proposed Rule or similar drug importation programs. As such, we do not believe HHS can make the required statutory certification that the Proposed Rule implementation of Section 804 of the Federal Food, Drug and Cosmetic Act (FD&C Act) would "pose no additional risk to the public's health and safety."

We outline these public health concerns below. And while we do suggest changes to the Proposed Rule essential to protect public health, implementation of all of the protections proposed within these comments would still not sufficiently reduce the added risk that the proposed construct poses to public health, supply chain security, product quality, and patient safety. Accordingly, we believe the Proposed Rule should be withdrawn.

I. The Proposed Rule, and any similar drug importation construct, poses significant risk to the public's health and safety.

As the Agency notes, its authority to implement a drug importation program such as the one outlined in the Proposed Rule derives from 21 U.S.C. § 384. Section 384 only becomes effective if the Secretary certifies that implementation both "(A) pose[s] no additional risk to the public's health and safety; and (B) result[s] in a significant reduction in the cost of covered products to the American consumer." As a collective alliance of many of the nation's leading experts who have worked tirelessly for years implementing systems and processes to ensure the safety and security of the nation's drug supply chain, we simply do not believe the Proposed Rule, or any similar drug importation program, could be implemented without adding unacceptable risk to the public's health and safety. Though our expertise relates to supply chain security, and our comments accordingly focus on public health and safety, we also believe that the Proposed Rule cannot—if all costs required to address supply chain security are accounted for—produce a reduction in the cost of prescription drugs to American consumers.

Over the course of several decades, industry, FDA, and others—both domestically and globally—have developed and implemented numerous protections that make the U.S. drug supply chain among the safest in the world. For example, the United States has extensive child-resistant (C-R) or "special" packaging requirements that reduce the risk of poisoning in children via the ingestion of potentially hazardous items including certain prescription and over-the-counter (OTC) medications.[1] Further, the U.S. has more restrictive and protective labeling requirements with regard to the medication guides required with the product package insert.[2] The most recent and most significant protections were added in 2013 as part of the Drug Supply Chain Security Act (DSCSA), which builds on numerous prior U.S. policies and protections to help ensure the safety, quality, and purity of the prescription drug supply chain. This progression of protections is evidence of an important and fundamental principle: *Fraudulent actors are continually evolving their tactics to exploit any gaps or weaknesses in the supply chain. There is no "magic bullet" that will guarantee absolute security of the supply chain; industry and regulators must continually innovate and iterate to maintain as robust of protections as possible.*[3] The Proposed Rule, which waives numerous DSCSA protections, would instead be a step backward in protections.

The DSCSA is a critical example of the Agency's and industry's efforts to stay ahead of risks to the supply chain and public health. The DSCSA was enacted by Congress without a single vote in opposition; support for the critical protections of the DSCSA, which the Proposed Rule would waive, was sweeping. That support was built upon the DSCSA's recognition of the complexity and interrelated nature of supply chain security protections. Chief among those protections are:

[1] https://www.cpsc.gov/Business--Manufacturing/Business-Education/Business-Guidance/PPPA
[2] https://www.fda.gov/drugs/drug-safety-and-availability/medication-guides
[3] We agree with FDA's own acknowledgement of this reality in the preamble to the Proposed Rule. As it stated, *"The current system of drug regulation in the U.S. has been very effective in protecting public safety, but is facing new threats. It should be modified only with great care to ensure continued high standards of safety and effectiveness of the U.S. drug supply."*

1. *Authorized Trading Partner (ATP) and licensure protections to limit the supply chain to only those trading partners that have demonstrated their legitimacy and effective implementation of controls to maintain the quality and security of the supply chain.*

   The DSCSA requires that every trading partner only purchase prescription drugs from, and sell prescription drugs to, other trading partners that are duly registered or licensed by FDA or by State regulators in accordance with Federal standards The FD&C Act § 582(b)(3), (c)(3), (d)(3), (e)(3). This provision is a critical protection that closes the supply chain to substandard and fraudulent actors and ensures every trading partner has appropriate controls in place to ensure the quality and security of the supply chain. This also means that in addition to requirements restricting trading of product to ATPs, the DSCSA restricts verification and product tracing inquiries (and the related data access) to ATPs as a measure to maintain the security of serialization information. Protection of serialization information and algorithms is critical to applications that leverage this information for patient safety processes such as verification and tracing.

   Relatedly, the DSCSA also established a single, rigorous, uniform standard for licensure of wholesale distributors and third-party logistics providers. When paired with FDA requirements for registration of drug manufacturers and state licensure of pharmacies, these standards help to ensure that *every* trading partner is appropriately safeguarding the quality and security of the supply chain. These important protections not only help to prevent counterfeit and adulterated drugs from entering the supply chain, but also help ensure every trading partner that handles and distributes prescription drugs has appropriate controls to maintain the quality of those drugs, such as temperature and humidity controls, recall response procedures, etc. According to the requirements of the FD&C Act, failure to follow any of these processes would "cast doubt on the drug's safety, identity, strength, quality, and purity," thereby rendering such product non-saleable and *unfit for distribution* according to FDA.[4]

2. *Serialization requirements to uniquely identify every package of prescription drug that is legitimately in the supply chain.*

   As the complexity of the supply chain has increased, so have the strategies necessary to deter bad actors seeking to penetrate it. A key to that protection is the adoption of systems and processes at an increasingly granular level. Drugs were historically identified at the lot or batch level, and systems and processes to protect the supply chain generally leveraged that lot level identification. A fundamental objective of the DSCSA is to move toward salable unit-level (i.e., each individual package of drug, of which there may be tens or hundreds of thousands in a batch or lot) controls. As of 2018, every individual package of prescription drug introduced into the U.S. supply chain is uniquely identified by serial number.[5] This level of granularity dramatically raises the bar that bad actors must overcome to penetrate the supply chain.

[4] "Definitions of Suspect Product and Illegitimate Product for Verification Obligations Under the Drug Supply Chain Security Act" draft guidance for industry, Food and Drug Administration, March 2018.

[5] Serialization and traceability are rapidly becoming the global standard for supply chain security, with more than 50 countries having implemented such systems or announced their intent to do so. This trend is a reflection of the principle noted above that the supply chain must continue to evolve if it is to remain secure. Despite this global

3. *Complex data sharing and interoperability requirements to ensure that the legitimacy of each package of prescription drugs can be verified by its manufacturer and to trace its path through the supply chain.*

   Finally, the DSCSA requires multiple controls that leverage the unique serial number affixed to each individual package of prescription drug. First, DSCSA requires industry to implement interoperable electronic systems by which the manufacturer can verify the legitimacy of the data for each drug package. Second, industry must also implement interoperable secure electronic systems that enable all trading partners (of which there are more than 200,000) to trace the distribution path of a particular drug package. This will aid in the identification of suspect and illegitimate drugs and any gaps through which they may have entered the supply chain. Finally, these systems will be leveraged to improve the efficiency and accuracy of recalls by ensuring that product unfit for distribution is quickly identified and removed from the supply chain.

The Proposed Rule expressly waives all of these DSCSA protections for products imported through a SIP, § 251.14(d)(6), and in doing so, severely undermines the benefit of these protections within the traditional domestic supply chain. Concluding that a distribution model that lacks DSCSA protections (even if only for certain transactions) is not higher risk than the *status quo* effectively requires one to suppose that the DSCSA does nothing to improve the quality or security of the U.S. supply chain today. Such a conclusion would be entirely inaccurate and contradict Congress's clear intent. Further, under DSCSA and FDA guidance, imported product would, of its very nature, be considered suspect product under current DSCSA guidance from FDA.[6] Opening trade to products that are otherwise considered suspect complicates security and expands the level of vigilance needed across all trading partners. The following are specific examples of how the Proposed Rule undermines the benefit of DSCSA supply chain and patient safety protections:

1. *"Attaching" the U.S. supply chain to another non-U.S.-regulated supply chain undermines the entire DSCSA construct.*

   The core objective of the DSCSA is to fully secure the supply chain from manufacturer to dispenser. The ATP requirements discussed above are central to achieving this objective. Absent an effective ATP requirement, there is no way to ensure that every trading partner involved in the distribution of a drug has the necessary processes and controls in place to protect the quality and security of the supply chain. The Proposed Rule (and similar constructs) undermines the ATP requirement and the ability to close the supply chain in two ways, creating gaps that can be exploited. First, the Proposed Rule would essentially impose

trend, Canada does not require, nor have current plans to require, serialization. Waiving the DSCSA requirements, as recommended in the Proposed Rule, would set the U.S. back and leave us lagging behind dozens of global markets.

[6] According to "Definitions of Suspect Product and Illegitimate Product for Verification Obligations Under the Drug Supply Chain Security Act" draft guidance for industry, "FDA interprets the term *diverted* to refer to a…product that is labeled for sale in a non-U.S. market and that is introduced into the U.S. prescription drug distribution system to an authorized trading partner." According to "Identification of Suspect Product and Notification" December, 2016, draft guidance, FDA provides scenarios around the appearance of the product in which the trading partner should question whether the product is suspect due to missing NDC, whether it contains foreign identification features, and whether it is missing security and anti-counterfeiting features normally featured on FDA-approved product.

a supply chain unregulated by the U.S. onto the U.S. supply chain. As the adage goes, a chain is only as strong as its weakest link, and this holds true with supply chains. The DSCSA was designed to ensure that every link in the complex chain is up to a minimum standard of quality and security. Attaching links to the U.S. chain that are not duly registered or licensed with FDA or state authorities eliminates any ability to ensure the full end-to-end U.S. supply chain is appropriately authorized. This impacts not only the SIP distribution chain, but also the integrity and perception of the U.S. supply chain as a whole.

Second, even if there were a requirement within the SIP context for every trading partner to confirm the quality and validity of the trading partners they are buying from and selling to, an importation model like the one proposed eliminates the common basis or standard for assessing the quality and validity of trading partners in the U.S. supply chain. As noted above, the DSCSA established a framework for uniform licensing standards in order to provide assurance of the "strength" of each link in the chain. The Proposed Rule adds two additional links to the chain:1) a manufacturer that is not directly regulated by FDA through the SIP, and 2) a Foreign Seller with minimal FDA registration obligations that do not approach the detailed standards to which U.S. distributors are held.

For these reasons, the Proposed Rule is a step backward, undermines the closed supply chain specifically established by the DSCSA, and accordingly increases the risk to public health and safety.

2. *Even if similar types of data are shared within a SIP, the Proposed Rule will undermine interoperability and protections of verification and traceability.*

Section 251.14(c)(6) of the Proposed Rule and other related provisions impose obligations on the Foreign Seller and the Importer for the exchange of certain information, presumably in an attempt to mirror the requirements of the DSCSA. Even where that information is required to be provided, it will not be in an interoperable format for a number of reasons. First, DSCSA data requirements are constructed around the DSCSA product identifier, which is affixed to a drug product in a standardized format. Drugs imported through a SIP will lack a DSCSA product identifier, at least at the time of import, § 251.14(d)(6)(ii), and this identifier "key" is critical to data interoperability.

Second, the level at which units of trade are identified under the SIP will create incongruencies in data. The Proposed Rule appears to require a Section 804 Serial Identifier § 251.2 to be applied to the unit of trade that is imported, which is most often a case or pallet. This identifier would be, at a minimum, distinct from the package level serial number that forms the basis of the unit-level verification and tracing required by the DSCSA and, if a case is imported, would result in multiple case serial numbers in the event that a DSCSA product identifier is later added. We therefore ask the Agency to clarify the need to apply SSI to the individual unit-level packages. Further, the Rule proposes requiring the U.S. Importer to maintain records for six years associating the product identifier the repackager affixes to the product with the serial number that the Foreign Seller assigned as well as to the product's Canadian DIN. FDA notes that this requirement is analogous to the record retention requirement in § 582(e)(2)(A)(iv) for a repackager that associates a product identifier with a manufacturer-affixed product identifier, 84 Fed. Reg. at 70816, and we strongly support

inclusion of this requirement. However, the complexity and cost of associating these data should not be underestimated.

Third, the Proposed Rule will create significant confusion as to the identity of the various trading partners in the supply chain. For example, who is considered the manufacturer (for DSCSA purposes) in the SIP context? If it is the actual marketing authorization holder for the product, then they will fall outside of the data obligations in the Proposed Rule and their data cannot be incorporated into the interoperable DSCSA systems and processes. If it is someone other than the marketing authorization holder, then someone not actually engaged in the manufacturing activity will be treated as the manufacturer under the DSCSA, creating confusion and incongruencies with regard to their data and identification.

Fourth, tracing data for drugs imported through a SIP will be incomplete. Without data back to the original manufacturer, only partial tracing will be possible.

These issues are complex and technical, but the key point is this: Data related to drugs imported through a SIP cannot be interoperably integrated into DSCSA systems and processes. As a result, the imported drug packages cannot be electronically verified and traced in a prompt manner to ensure supply chain security, as required by the DSCSA. This lack of capacity to interoperably verify and trace imported product creates public health risks greater than those currently present in today's U.S. supply chain.

3. *Integrating SIPs into interoperable DSCSA systems and processes will create significant data integrity risks.*

FDA has placed increasing emphasis on data integrity and the risks that can result from a lack of data integrity in recent years. Consistent with the principles of data integrity, one of the key components of the DSCSA is a requirement for uniform transaction information (TI) that accompanies both inbound (*i.e.*, purchase of the drug) and outbound (*i.e.*, sale of the drug) transactions. Specifically, each trading partner is required, under the DSCSA, to receive inbound TI from the prior seller and to provide outbound TI to the subsequent owner. This chain of data creates the ability to reconcile inbound data against outbound data and prevent or deter any tampering with TI data, which could be used to facilitate the entry of counterfeit or adulterated drugs into the supply chain. TI required after importation—or even TI-like information required under § 251.14(c)(6)—will necessarily start *mid-supply chain* and will not have the benefit of reconcilable inbound and outbound TI required under the DSCSA. This missing control could be exploited by a fraudulent actor to introduce illegitimate product into the supply chain and even create documentation making that introduction more difficult to identify or detect. Such activity would be a significant risk to public health and safety.

4. *Drugs imported through a SIP and dispensed or administered without further sale will remain wholly outside of DSCSA protections.*

Beyond the challenges and risks associated with the negative impact the Proposed Rule would have on interoperability, as noted above, it is our understanding that some drugs imported under a SIP would remain wholly outside of DSCSA requirements. *(See page 70815)*. Specifically, it is our understanding based on the Proposed Rule that prescription

drugs imported under a SIP and dispensed or administered directly to patients without further supply chain transactions (i.e., further distributed) would not be subject to any DSCSA requirements. To suggest that the lack of DSCSA protections does not pose additional risk to the public's health and safety is wholly contrary to the realities of the supply chain's method of operation and Congress's clear intent when it enacted the DSCSA. We therefore suggest that a dispenser importing product should not be exempted from affixing identifiers to imported product, and that the imported product should state on the label that it is imported product.

For the reasons outlined above, we do not believe the Proposed Rule, or any importation program similar to the one outlined in the Proposed Rule, can be implemented without imposing additional risk on the public's health and safety, as required by 21 U.S.C. § 384. Accordingly, we urge the Agency not to finalize the Proposed Rule.

In the event that the Proposed Rule advances to finalization, there are numerous additional protections PDSA believes would be essential, but not sufficient, to protect the supply chain. Even with these additional protections, the Proposed Rule would still increase risk to the public's health and safety and would fail to meet the certification requirements under the statute.

II. Specific Risks and Essential Mitigations

We have critically examined the Rule and have identified public health risks relating to supply chain security throughout. DSCSA was created by Congress to ensure critical protections for a safe supply chain, securing patient health. The complex and intertwined provisions of the law require a sophisticated connection for all points of the production and consumption channel. The Proposed Rule would undermine ten years of critical work from all stakeholders including Congress and FDA, creating a dangerous environment.

The risks identified below highlight gaps in the oversight of Foreign Sellers, SIPs, and all parties engaged in prescription drug importation through Canada. While Canada currently enjoys a strong, reliable, and relatively safe supply chain, no law exists on the level of DSCSA for serialization and protection of pharmaceuticals in Canada. However, even if FDA addressed all these concepts, danger would persist. Additional protections would be necessary to elevate the security of the Proposed Rule, but even these mitigations would increase the risk to the public health above the level that the U.S. supply chain will have under the DSCSA, and would therefore preclude certification. Thus, we respectfully request that the Proposed Rule be withdrawn.

1. *SIP products that have a high risk of illegitimacy are not required to be promptly reported to FDA.*

   The DSCSA requires any trading partner in possession or control of an illegitimate product to report that instance to the FDA. For manufacturers, this reporting obligation also extends to instances in which the manufacturer believes there is a high risk of illegitimacy. The Proposed Rule (§§ 251.14(c)(1)(i)(C) and (c)(2)(i)) establishes some reporting requirements for illegitimate product. Absent the requirement to report instances of high risk of

illegitimacy, the reporting obligations (and the opportunity for regulatory response) under the Proposed Rule are *less than* under the DSCSA. The danger that there will be illegitimate product under the Proposed Rule is amplified by inadequate reporting requirements, creating greater risk to patients.

Requiring any entity that possesses or controls product under a SIP which is determined to be *suspect or illegitimate* to report to FDA within 24 hours would enhance the ability to respond to the increased risk of there being illegitimate product under a SIP. As explained throughout these comments, opportunities for introduction of illegitimate product abound under the SIP construct, and it is therefore essential that all such risks be promptly reported to FDA for evaluation. Absence of these DSCSA protections in reporting will increase the ability of criminals to manipulate vulnerabilities in the FDA proposal. Additionally, we strongly question the ability and expertise of SIPs and others to sufficiently and promptly investigate suspect or illegitimate products. A state health department, for example, would require additional staff with specific skills to appropriately investigate since this is not a typical function for state health agencies. This function is generally done with the coordination of multiple skilled groups to include law enforcement, FDA, and industry.

2. *The Proposed Rule does not provide for revocation of a SIP upon identification of illegitimate SIP product.*

Section 251.7(c) of the Proposed Rule sets forth grounds for revocation of a SIP authorization. Though that list includes consideration of whether continued implementation is likely to pose additional risk to public health and safety, noticeably absent is any express reference to the most significant risk associated with the Proposed Rule, namely the introduction of illegitimate product into the U.S. supply chain. It does not appear possible to address this risk explicitly in the Rule. If the identification of illegitimate product introduced through a SIP were to cause the automatic revocation of the SIP authorization, trading partners working closely with the SIP would be less inclined to identify and report the illegitimate product. Yet if a SIP were permitted to continue to operate and supply drugs to the U.S. market after having demonstrated inability to prevent the distribution of illegitimate product, patients would be put at serious risk. Indeed, the gravest risks associated with the Proposed Rule would not be appropriately addressed.

3. *Requirements for registration of Foreign Sellers are inadequate.*

Section 251.9 of the Proposed Rule establishes registration requirements for a Foreign Seller before FDA will authorize a SIP proposal. The minimal requirements outlined in the Proposed Rule do not allow appropriate oversight by FDA. This standard for participation in the U.S. distribution chain is significantly lower than the standards imposed on domestic distributors under the DSCSA licensure provisions (FD&C Act §§ 583, 584), creating additional public health risk. As explained above, the supply chain is only as strong as its weakest link, and the registration requirements for Foreign Sellers create the risk of significantly weaker links in what would ultimately become the U.S. supply chain under a

SIP. Further, U.S. supply chain partners known to each other over years of a trading relationship and subject to DSCSA and other product quality and safety requirements have established a community of trust and understanding that gives end users confidence in the authenticity of the product being dispensed or administered. Inadequate vetting of Foreign Sellers forces pharmacists and physicians to accept and dispense/administer product that comes from outside of this community of trust. Under FDA guidance, foreign product labels in and of themselves are cause for concern for downstream entities. In fact, FDA has expressly noted that foreign product labels, including a label referencing the product name for a foreign version of a drug, should be considered suspect product.[7] Adding additional doubt as to a product's origin only serves to further reduce confidence in supply chain integrity, data security, and product authenticity.

FDA could take additional steps to ensure that Foreign Sellers maintain robust controls and obtain and validate additional information concerning compliance and business history, including:

- Inspecting all Foreign Seller facilities against U.S. inspection standards for wholesalers in advance of any SIP transactions.
- Requiring submission of and review of Standard Operating Procedures (SOPs) and other policies prior to authorization to ensure quality and security of products owned by the Foreign Seller.
- Requiring review of the disciplinary history of the Foreign Seller.
- Complying with all national standards for wholesale licensure once promulgated and publicly providing license holder information.

That the Foreign Seller is outside the United States will create challenges for the FDA as compared to domestic distributors under the DSCSA, and it will be a challenge to maintain the level of ongoing oversight necessary to assure supply chain safety comparable to what will be achieved under the DSCSA.

4. *The disclosure of disciplinary history for Foreign Sellers is not sufficiently broad for FDA to assess their status.*

Sections 251.3(d)(2) and (3) of the Proposed Rule establish requirements for disclosure of past misconduct and discipline of the Foreign Seller or U.S. Importer. This critical information provides some detail for FDA, but PDSA believes the information is too limited to provide a complete picture of past criminal or prohibited acts. As noted in Subsection C., it is essential that FDA ensure Foreign Sellers are as strong of a link in the supply chain as possible. Specifically, FDA needs to broaden the disclosure requirements in order to more fully assess participants in the importation supply chain. Examples of such additional information requirements could include all members of the board, senior management of the company, and senior management of any facility involved in a SIP Proposal for the previous 10 years prior to submission of the SIP Proposal.

[7] "Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification," Guidance for Industry, FDA, December 2016.

5. *A DSCSA identifier is not required to be affixed to every package of prescription drug imported through a SIP.*

The preamble explains that "if the Importer intends to directly administer the product to patients, as may be the case if the Importer intends to dispense the drug as a pharmacist, a product identifier would never be required to be affixed or imprinted on each package and homogenous case of the eligible prescription drug." PDSA is concerned that allowing product transactions without a DSCSA identifier would further open the supply chain to suspect and illegitimate products. In addition, for reasons articulated above, the lack of an identifier will either cause certain products to be wholly outside of DSCSA requirements or create significant interoperability challenges, both of which add significant risk to the public health and safety. Although the addition of a DSCSA identifier will not fully remediate those additional risks, it would provide some level of added protection.

6. *Information akin to Transaction Information (TI) is not required for the purchase by the Foreign Seller.*

Section 251.14(c)(6) requires the Foreign Seller to provide the U.S. Importer with a series of data points akin to transaction information (TI). A Foreign Seller must provide (251.14(c)(6):

> (i) A statement that the Foreign Seller received the product from an FDA-registered manufacturer;
> (ii) The proprietary or established name of the product;
> (iii) The strength and dosage form of the product;
> (iv) The container size;
> (v) The number of containers;
> (vi) The lot number of the product;
> (vii) The date of the transaction;
> (viii) The date of the shipment, if more than 24 hours after the date of the transaction;
> (ix) The business name and address of the person associated with the Foreign Seller from
> whom ownership is being transferred;
> (x) The business name and address of the person associated with the Importer to whom
> ownership is being transferred;
> (xi) The SSI for each package and homogenous case of product; and
> (xii) The Canadian DIN for each product transferred.

As explained above, exchange of TI is the heart of DSCSA and must be consistent for products placed into the hands of U.S. patients through this Proposed Rule. Under the DSCSA there is confidence in the accuracy and legitimacy of any TI because there is both outbound and inbound TI that can be reconciled. Under the Proposed Rule, however, Foreign Sellers are not required to capture this data on inbound transactions. For the reasons

explained above, that gap creates significant risk and jeopardizes data integrity. Such additional data would create greater assurance of supply chain security, but not close the gap created by the Proposed Rule.

7. *The recall process proposed in the Proposed Rule is incomplete*.

PDSA agrees that if the original manufacturer of a SIP product issues a recall, the Importer must have appropriate procedures in place to recall any of the drugs they imported and to which they applied a new NDC. However, we believe the Proposed Rule does not adequately address the importance of coordination with the original product manufacturer in the event that the SIP Sponsor issues a recall. The Proposed Rule includes a series of steps that the Importer must follow in the event of a recall by the SIP sponsor, but coordination of activities with the original manufacturer is not one of them. While transportation, storage, or other issues may have precipitated the need for the recall, excluding the original manufacturer from the process is not in the best interest of the patients who have received other batches of the product. Some level of investigation and coordination with the original manufacturer is essential. Therefore, we propose that the Rule include a requirement that the SIP sponsor and importer notify the manufacturer in the event of a recall and provide their findings that led to the recall so that the manufacturer can determine whether the issues that prompted the recall are limited to actions by the importer, or whether the recall should be expanded to other product distributed by the manufacturer.

8. *Adverse Event reporting under the Proposed Rule could lead to significant delays, which would threaten patient safety*.

Under the Proposed Rule, the Importer is given 15-day and 90-day notification periods for reporting unexpected and expected adverse events to the original manufacturer. If a manufacturer's product is being imported under many SIPs, and receiving many NDC values, the time period to collate adverse event data will be extended by months. This additional delay as a manufacturer waits for information from the importer could mean the difference between executing an efficient, effective recall and threatening patient safety. If the determination that a recall was warranted were delayed by 3 months, many patients would be placed significantly at risk. PDSA believes that the recall process for imported product should mirror the requirements for non-imported product and should specifically include swift coordination with the product manufacturer.

9. *The Proposed Rule waives the requirement of trading partners to provide a transaction statement, which limits FDA's ability to enforce compliance with supply chain security requirements*.

The Proposed Rule waives the provision of the DSCSA requiring trading partners to provide a transaction statement (TS) pursuant to a product transaction. The TS is an important statement of compliance which serves as the legal "hook" by which FDA can take certain enforcement actions against trading partners that deviate DSCSA's strict requirements. Without TS, the ability of the FDA to enforce compliance with supply chain security requirements is significantly hampered, which undermines deterrence to bad actors seeking to exploit gaps in a SIP.

PDSA does not believe that the FDA can close the security gaps created through FDA's proposal. If the FDA finalizes the Rule in spite of these gaps, we urge the FDA to reconsider the Proposed Rule's lax oversight of Foreign Sellers, SIPs, and all parties engaged in prescription drug importation through Canada, as compared to the strong FDA regulatory scheme that exists today in our country and protects American patients. For example, the DSCSA requires any trading partner in possession or control of an illegitimate product to report that instance to the FDA. For manufacturers, this reporting obligation also extends to instances in which the manufacturer believes there is a high risk of illegitimacy. While the Proposed Rule (§§ 251.14(c)(1)(i)(C) and (c)(2)(i)) and (c)(2)9I) establishes some reporting requirements for illegitimate product, it reduces the protections provided under the DSCSA. The risk mitigation strategies discussed above will not close the security gaps created through FDA's proposal; however, they will improve the Proposed Rule.

III. Full Assessment of Supply Chain Costs

As explained above, the Agency's statutory authority to establish an importation model is limited by both public health and savings. The latter specifically requires that any importation plan "result in a significant reduction in the cost of covered products to the American consumer." PDSA's expertise is in supply chain security, and we do not offer comprehensive comments on this cost-saving component. We do, however, believe it is essential that the assessment of any SIP proposal fully and accurately consider *all* costs associated with the SIP, including the extensive costs associated with supply chain security. This includes the full cost of the systems, processes, and infrastructure for supply chain security and DSCSA compliance.

To date, PDSA member companies have invested over a decade of time and capital, beginning with state requirements and working to federal requirements, to enhance supply chain security and to implement the requirements of the DSCSA (i.e., interoperable data exchange, interoperable unit-level verification, interoperable tracing). In doing so, our members have acquired a unique understanding of the immensity of DSCSA implementation and the cost of compliance with what, as was noted above, are bipartisan, industry-supported measures to protect U.S. patients. As proposed, the importation program will undermine years of industry improvements to patient safety.

This experience has provided us with great insights into the true and full costs of protecting the supply chain. Building on that experience, we believe it is essential that the assessment of any proposed SIP account for all of the following supply chain cost components:

1. *Systems for serialization of units, cases, and logistical units.*

   Wholly new serialization systems would need to be constructed by SIPs. The cost of constructing a serialization system includes not just the baseline cost of new mechanical equipment for serialization, but also the cost of acquiring software licenses, developing printing systems, and establishing online data storage for serialization information. In addition, the Proposed Rule would permit the Importer within a SIP to affix (rather than print

on the package) the product identifier via a sticker. To the degree that stickers are used, there would be an additional per-unit cost associated with application of the serial number/product identifier. Regardless of the serialization media choice, the serialization data itself would need to be stored in a repository where it could be used to provide verification responses and requests for information to trace saleable units. These data should be retained for at least six years following associated transactions. These repositories would either contain or link to transaction information and attestation of that information, which would be necessary to comply with a product trace.

2. Verification systems and processes.

In addition to developing new systems for serialization, printing, and application of the product identifier, systems for verification would need to be constructed. Specifically, there are concrete costs associated with responding to verification requests, but also many additional costs associated with the procedures for appropriately responding to a negative verification response (*i.e.*, investigating and documenting suspect product). Following a negative verification request, trading partners within the SIP would need to have the ability to conduct a suspect product investigation, to submit a Form 3911 to FDA as required under the DSCSA, and to have locations, processes, and procedures for quarantining product as needed.

3. Relabeling, repackaging.

The Proposed Rule requires relabeling by the Importer as well as repackaging needed to allow for relabeling. The costs incurred would include changes to the package artwork (detailed below), labor costs, and the physical cost of the label.

4. Package artwork.

The proposed importation plan would require a complete overhaul and redesign of package artwork (*i.e.*, labeling and barcodes). The redesigning of artwork could potentially impact the size of product packaging, which could subsequently impact logistical design. Any such change would include costs associated with system and personnel management to execute the changes. Further, there would be substantial waste of the initial product packaging following the redesign and overhaul of package artwork.

5. Data integration.

Costs would be incurred during the integration of serialization data with trading partners and existing systems. More specifically, when integrating data with existing trading partners, system enhancements, configurations, and platform/software costs would inevitably be incurred. Also included with integration are the costs associated with contracting new vendors to perform parts of the overall compliance to DSCSA requirements. Subsequent overhead costs would be incurred as new vendors would call for incremental project staff and adjusted processes and project flows.

6. Call centers.

For any new system or process, as a SIP would be initiating, there will need to be staff on call to handle product questions, emergencies, and requests for product verification. As such, the implementation of the proposed importation plan would trigger the need for new call

centers to become operational. The costs of a new call center would include additional staff and personnel training, security staff and the implementation of security protocols, and data access costs.

7. Recalls.

The recall process is complex, and in the traditional supply chain trading partners incur a number of costs to provide efficient and effective recalls. A SIP would incur the cost of new processes for effectuating and documenting recalls. These processes would include data entry, adverse event reporting, trading partner notification of quality issues, and FDA notification (*i.e.*, submission of 3911 forms).

8. Inventory management.

SIP participants would need to ensure separate stock pools for products intended for the U.S. market via the SIP or product intended for the Canadian market.

9. Enforcement.

Given the unique nature of the SIP supply chain, the SIP would also incur enforcement costs specific to the process of importation. These include training for regulators and enforcement agents as well as the costs of any enforcement procedures at the border (*e.g.*, space to hold product).

10. Quality assurance.

SIP product would incur the costs of laboratory testing, quarantine, and release, as well as other quality assurance procedures.

In addition to the costs noted above, PDSA would also like to emphasize the true complexity of assessing costs to patients. Calculations may be based on a number of potential price points (e.g., the U.S. list price, the Canadian list price, the best price, the contracted price), which could drastically impact the assessment of SIP cost. We also note that depending on the product path, many of the costs described above (e.g., relabeling) will be incurred multiple times. It is critical that FDA assess all supply chain costs across all transactions as a product moves through the SIP pathway to a U.S.-based patient.

IV. Direct Responses to Feedback Requested by the Agency

In the preamble to the Proposed Rule, FDA raises several specific questions for stakeholders to consider. PDSA believes that several of these questions, detailed below, are directly relevant to the impact that importation plan under the Proposed Rule would have on patient safety and the security of the supply chain, particularly as it relates to the additional safeguards provided by the DSCSA.

1. *What additional standards should be imposed, or qualifications required of Foreign Sellers? (See p. 70812).*

The Proposed Rule does not provide adequate safeguards for Foreign Sellers. Although the following additional standards should be imposed, they will still not be adequate to protect the public:

(1) **Licensure and Registration**. As proposed, Foreign Sellers are licensed by Health Canada and registered with the provincial pharmacy authority. While these measures are important, they do not permit FDA to assess, investigate, or audit the Foreign Seller, which leaves all security in the hands of a foreign government. As noted above, to appropriately perform their regulatory and oversight functions, FDA needs additional information from Foreign Sellers, including compliance and business history.

(2) **Relabeling**. As proposed, the Foreign Seller would be responsible for relabeling drug product to affix or imprint the SSI on each package and homogenous case of eligible prescription drugs. PDSA therefore proposes that Foreign Sellers be subject to the requirements of repackagers, which includes the record retention requirement in § 582(e)(2)(A)(iv) for a repackager that associates a product identifier with a manufacturer-affixed product identifier. We also propose that Foreign Sellers be subject to cGMP and all other requirements of relabelers.

(3) **Disclosures**. As noted above, FDA needs to broaden the disclosure requirements in order to more fully assess participants in the importation supply chain. Examples of such additional information requirements could include all members of the board, senior management of the company, and senior management of any facility involved in a SIP Proposal for the previous 10 years prior to submission of the SIP Proposal.

(4) **TI-like Information**. As discussed above, exchange of TI is the heart of DSCSA and must be consistent for products placed into the hands of U.S. patients through the Proposed Rule. Under the DSCSA there is confidence in the accuracy and legitimacy of any TI because there is both outbound and inbound TI that can be reconciled. Under the Proposed Rule, however, Foreign Sellers are not required to capture information akin to TI data on inbound transactions. That gap creates significant risk and jeopardizes data integrity. Such additional data should be required to be captured and maintained so as to create greater assurance of supply chain security, with the recognition that these data will not fully close the gap created by the Proposed Rule.

(5) **TS-like Information**. As discussed above, the Proposed Rule waives the provision of the DSCSA requiring trading partners to provide a transaction statement (TS) pursuant to a product transaction. The TS is an important statement of compliance which serves as the legal "hook" by which FDA can take certain enforcement actions against trading partners that deviate DSCSA's strict requirements. Without TS, the ability of the FDA to enforce compliance with supply chain security requirements is significantly hampered, which undermines deterrence to bad actors seeking to exploit gaps in a SIP.

2. *Is it feasible and sufficient for the screening to include the following: (1) examination of the Canadian labeling from a sample in each shipment of section 804 drugs to verify that the labeling is consistent with that of an HPFB-approved drug, and (2) examination that the drugs have been serialized as prescribed? What additional or alternative screenings could the Importer do to ensure that imported eligible prescription drugs are not adulterated, counterfeit, damaged, tampered with, or expired? (See p. 70812).*

Visual examination of packaging is an important component of product authentication. Through guidance, FDA has detailed specific examples of scenarios that could significantly increase the risk of a suspect product entering the drug supply chain and should therefore result in increased vigilance by trading partners.[8] SIPs should be subject to all product inspection requirements and considerations, which include consideration of trading partners and product sourcing; the supply, demand, history, and value of the product; and the appearance of the product.

3. *Does this Proposed Rule contain sufficient safeguards to ensure that the proposed importation poses no additional risk to health or safety? (See p. 70814).*

No; as described in Section I of this letter, 21 U.S.C. § 384 expressly prohibits the implementation of a drug importation program unless the Secretary certifies that such program both "(A) pose[s] no additional risk to the public's health and safety; and (B) result[s] in a significant reduction in the cost of covered products to the American consumer." As a collective alliance of many of the nation's leading experts who have worked tirelessly for years implementing systems and processes to ensure the safety and security of the nation's drug supply chain, we simply do not believe the Proposed Rule, or any similar drug importation program, could be implemented without adding unacceptable risk to the public's health and safety. In large part, this additional risk is a result of waiving specific protections imposed by the DSCSA, namely:

(1) Authorized Trading Partner (ATP) and licensure protections to close the supply chain to only those trading partners that have demonstrated their legitimacy and effective implementation of controls to maintain the quality and security of the supply chain.
(2) Serialization requirements to uniquely identify every package of prescription drug that is legitimately in the supply chain.
(3) Complex data sharing and interoperability requirements to ensure the legitimacy of each package of prescription drugs can be verified by its manufacturer and trace its path through the supply chain.

We do not believe the Proposed Rule, or any importation program similar to the one outlined in the Proposed Rule, can be implemented without imposing additional risk on the public's health and safety, as required by 21 U.S.C. § 384. Accordingly, we urge the Agency not to finalize the Proposed Rule.

[8] "Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification," Guidance for Industry, FDA, December 2016.

4. *Does a manufacturer provide sufficient information to the Importer about the imported drug's movements in the pre-U.S. supply chain if (1) the manufacturer is required to provide the Importer all relevant documentation about the transaction to the Foreign Seller upon its transfer of ownership of the product for the Canadian market, and (2) the Importer is required to use the information obtained from manufacturers under section 804(e) of the FD&C Act to help determine whether the supply chain was intact? Are different or additional safeguards necessary to ensure the integrity of the supply chain with respect to drugs imported under section 804 of the FD&C Act? (See pp. 70816-17).*

No, as noted earlier in this letter, the lack of an exchange of interoperable transaction data between the manufacturer and the Importer is a significant gap under the Proposed Rule. Under the DSCSA, each trading partner is required to receive inbound TI from the seller and to provide outbound TI to the subsequent owner. This chain of data creates the ability to reconcile inbound data against outbound data and to prevent or deter any tampering with TI data, which could be used to facilitate the entry of counterfeit or adulterated drugs into the supply chain. TI required after importation—or even TI-like information required under § 251.14(c)(6)—will necessarily start *mid-supply chain* and will not have the benefit of reconcilable inbound and outbound TI for every transaction back to the manufacturer, as required under the DSCSA. This missing control could be exploited by a fraudulent actor to introduce illegitimate product into the supply chain and even create documentation making that introduction more difficult to identify or detect. Such activity would be a significant risk to public health and safety.

Further, as was also discussed above, even where that information is required to be provided, it will not be in an interoperable format for a number of reasons. First, DSCSA data requirements are constructed around the DSCSA product identifier affixed to a drug product in a standardized format. Drugs imported through a SIP will lack a DSCSA product identifier, at least at the time of import, § 251.14(d)(6)(ii), and this identifier "key" is critical to data interoperability. Second, although the Proposed Rule requires a Section 804 Serial Identifier § 251.2, that identifier will be applied to the unit of trade that is imported, which is most often a case or pallet. This is, at a minimum, distinct from the package level serial number that forms the basis of the unit-level verification and tracing required by the DSCSA and, if a case is imported, will result in multiple case serial numbers if a DSCSA product identifier is later added. Third, the Proposed Rule will create significant confusion as to the identity of the various trading partners in the supply chain. Without data back to the original manufacturer, only partial tracing will be possible.

5. *In reporting cost savings, is it enough for SIPs to report their total cost savings to consumers as well as the methodology used to calculate this measure? In calculating cost savings, should the following factors be considered: based on savings to the American consumer, prices paid by the intended consumer population, and account for factors that may influence cost savings over time? What other factors are relevant to reporting cost savings? (See p. 70821).*

No, reporting total cost savings to consumers is not sufficient to calculate the full cost of an SIP. Please refer to section III of this letter for further details.

As a coalition dedicated to ensuring patients have uninterrupted access to safe, authentic, FDA-approved medicine, we do not believe HHS can make the required statutory certification that the Proposed Rule implementation of Section 804 of the Federal Food, Drug and Cosmetic Act (FD&C Act) would "pose no additional risk to the public's health and safety." The Proposed Rule expressly waives all of these DSCSA protections for products imported through a SIP, § 251.14(d)(6), and in doing so severely undermines the benefit of these protections within the traditional domestic supply chain. We have identified numerous concerns that could lead to negative impacts on public health and safety through implementation of the Proposed Rule or similar drug importation programs. As such, we urge the Agency not to finalize the Proposed Rule.

To the extent that it is useful to the Agency, PDSA offers our experience and expertise as a resource and welcomes the opportunity for further discussion.

Sincerely,

The Pharmaceutical Distribution Security Alliance (PDSA)[9]:

Manufacturers:

Association for Accessible Medicines (AAM)

Pharmaceutical Research and Manufacturers of America (PhRMA)

abbvie

Allergan

Apotex

AstraZeneca

Bayer

Bristol-Meyers Squibb

Fresenius Kabi

Genentech

[9] Members are listed according to their primary supply chain sector, but many operate business units across multiple sectors.

GlaxoSmithKline

Johnson & Johnson

Merck

Mylan

Novartis

Pfizer

Upsher-Smith Laboratories

Wholesale Distributors:

Healthcare Distribution Alliance (HDA)

AmerisourceBergen

CardinalHealth

Medline Industries

Third-Party Logistics Providers:

International Warehouse Logistics Association (IWLA)

Inmar

UPS

Dispensers:

American Pharmacists Association (APhA)

American Society of Health-System Pharmacists (ASHP)

National Association of Chain Drug Stores (NACDS)

CVSHealth