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4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 1 and 251

[Docket No. FDA-2019-N-5711]

RIN 0910-AI45

Importation of Prescription Drugs

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Secretary of Health and Human Services (Secretary) is issuing a final rule to implement a provision of the Federal Food, Drug, and Cosmetic Act (FD&C Act) to allow importation of certain prescription drugs from Canada. Under this final rule, States and Indian Tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the Food and Drug Administration (FDA, the Agency, or we) for review and authorization. An importation program may be cosponsored by a State, Indian Tribe, pharmacist, or wholesaler. The final rule contains all requirements necessary for a sponsor to demonstrate that their importation program will pose no additional risk to the public's health and safety. In addition, the final rule requires that the sponsor explain how they will ensure their program will result in a significant reduction in the cost of covered products to the American consumer.

DATES: This final rule is effective [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: For access to the docket to read background documents or comments received, go to <https://www.regulations.gov> and insert the docket number found in brackets in the heading of this final rule into the “Search” box and follow the prompts, and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: *With regard to the final rule:* Lyndsay Hennessey, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993, 301-796-7605.

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I. Executive Summary

A. *Purpose of the Final Rule*

The Secretary is issuing this rule to implement section 804(b) through (h) of the FD&C Act (21 U.S.C. 384(b) through (h)) to allow importation of certain prescription drugs shipped

from Canada. The purpose of the final rule is to achieve a significant reduction in the cost of covered products to the American consumer while posing no additional risk to the public's health and safety.

B. Summary of the Major Provisions of the Final Rule

Under the final rule, section 804 of the FD&C Act will be implemented through time-limited Section 804 Importation Programs (SIPs), which will be authorized by FDA and managed by States or Indian Tribes, or in certain circumstances by pharmacists or wholesale distributors (SIP Sponsors). A SIP can be cosponsored by a State, Indian Tribe, pharmacist, or wholesale distributor.

The final rule requires that a SIP Sponsor specify the eligible prescription drugs that will be included in the SIP. To be eligible under the final rule, a drug needs to be approved by the Government of Canada's Health Canada's Health Products and Food Branch (HPFB) and, but for the fact it bears the HPFB-approved labeling when marketed in Canada, needs to otherwise meet the conditions in an FDA-approved new drug application (NDA) or abbreviated new drug application (ANDA). Essentially, eligible prescription drugs are those that could be sold legally on either the Canadian market or the American market with appropriate labeling.

The final rule also requires that the SIP Proposal identify the Foreign Seller in Canada that will purchase the eligible prescription drug directly from its manufacturer, and the Importer in the United States that will buy the drug directly from the Foreign Seller. Although the initial SIP Proposal will identify just one Foreign Seller and one Importer, if a SIP can show that it has consistently imported eligible prescription drug(s) in accordance with section 804 of the FD&C Act and the rule, the SIP Sponsor will be able to submit a supplemental proposal to add Foreign

Sellers or Importers. Each supply chain under a SIP must be limited to three entities, i.e., one manufacturer, one Foreign Seller, and one Importer.

The final rule requires that the Foreign Seller be licensed to wholesale drugs by Health Canada and registered with FDA as a Foreign Seller, and that the Importer be a wholesale distributor or pharmacist licensed to operate in the United States. Both the Foreign Seller and the Importer will be subject to the supply chain security requirements set forth in this rulemaking and under the FD&C Act. Among other things, the Foreign Seller has to ensure that a section 804 serial identifier (SSI), which is an alphanumeric serial number unique to each package or homogenous case, is affixed to or imprinted on each package and homogenous case of the drugs. The Importer has to ensure that a product identifier meeting the requirements of section 582 of the FD&C Act (21 U.S.C. 360eee-1) (i.e., a product identifier that includes a National Drug Code, unique alphanumeric serial number of up to 20 characters, lot number, and expiration date, in both human- and machine-readable format) is affixed to or imprinted on each package and homogenous case of eligible prescription drugs received from the Foreign Seller. The final rule clarifies that the lot number that is included as part of the product identifier is the number that was assigned by the manufacturer of the eligible prescription drug; separately, section 804(d)(1)(H) of the FD&C Act requires that the Importer shall submit it to the Secretary. The Importer also has to maintain records linking the product identifier affixed to or imprinted on a package and homogenous case to the SSI that the Foreign Seller assigned. The Foreign Seller must maintain records associating the SSI with the drug identification number (DIN) from the HPFB and all the records the Foreign Seller received from the manufacturer upon receipt of the original shipment intended for the Canadian market.

After FDA has authorized a SIP Proposal, the Importer must submit a Pre-Import Request to FDA at least 30 calendar days before the scheduled date of arrival or entry for consumption of a shipment containing an eligible prescription drug covered by the SIP, whichever is earlier.

“Entered for consumption,” as defined in 19 CFR 141.0a(f), is the most common entry type for FDA-regulated products and is used when products are imported for use in the United States and go directly into United States commerce without any restrictions of time or use placed on them. Once the shipment arrives or is entered at a port of entry, it may be examined by a government agency.

Entry and arrival of a shipment containing an eligible prescription drug is limited under the final rule to the U.S. Customs and Border Protection (CBP) port of entry authorized by FDA. The Importer or its authorized customs broker is required to electronically file an entry for consumption in the Automated Commercial Environment (ACE) or other electronic data interchange system authorized by CBP for each eligible prescription drug imported or offered for import into the United States. These entries must be filed as formal entries. If an eligible prescription drug that is imported or offered for import does not comply with section 804 of the FD&C Act and the provisions of this final rule, that drug will be subject to refusal under section 801 of the FD&C Act (21 U.S.C. 381).

In accordance with section 804(e)(1) of the FD&C Act, the final rule requires the manufacturer or the Importer to conduct testing of the eligible prescription drugs for authenticity, degradation, and to ensure that the eligible prescription drugs are in compliance with established specifications and standards (Statutory Testing). If the manufacturer does not perform the Statutory Testing required under section 804 of the FD&C Act, the Importer must arrange for Statutory Testing by a qualifying laboratory in the United States and must also ensure that the

drug complies with all labeling requirements under the FD&C Act. If such testing is performed by the Importer, section 804(e)(2) requires that the manufacturer of the eligible prescription drug supply the information the Importer needs to authenticate the drug and to confirm that its labeling complies with all labeling requirements under the FD&C Act. In the final rule, FDA requires that the manufacturer provide the Importer with, among other things, protocols to support required testing, including a validated stability-indicating assay so the drug can be tested for degradation.

Under the final rule, the Importer can choose to admit the drug or drugs specified in the section 804 Pre-Import Request to an authorized foreign trade zone and then conduct the required Statutory Testing and relabeling; or alternatively, the Importer can file an entry for consumption and request to recondition the drug or drugs, which would include the required testing and relabeling. Under the final rule, the results of this testing will be subject to review and acceptance by FDA, and subsequently, the drug has to be relabeled to be consistent with the FDA-approved labeling before the drug can be distributed in the United States.

Pursuant to section 804(c)(3) of the FD&C Act, the final rule also sets forth post-importation requirements. Each SIP Sponsor is required to provide FDA with data and information about its SIP, including the SIP's cost savings to the American consumer. An Importer is required to submit adverse event, field alert, and other reports to a drug's manufacturer and to FDA. If FDA or any participant in a SIP determines that a recall is warranted, the SIP Sponsor is responsible for effectuating the recall. The final rule requires that each SIP have a written recall plan that describes the procedures to perform a recall of the product and specifies who will be responsible for performing those procedures.

A SIP is eligible for extension by FDA before the end of its authorization period. A SIP may also be terminated by FDA at any time for the reasons outlined in this final rule.

C. Legal Authority

Section 804(l)(1) of the FD&C Act provides that section 804 becomes effective only if the Secretary certifies to Congress that the implementation of this section will pose no additional risk to the public's health and safety, and will result in a significant reduction in the cost of covered products to the American consumer. The Secretary is making this certification with regard to section 804(b) through (h) to Congress concurrent with the issuance of this final rule. The Secretary is issuing this final rule regarding importation of prescription drugs under section 804(b) through (h) of the FD&C Act. The final rule is also being issued pursuant to the Secretary's authorities related to adulterated and misbranded drugs under sections 501 and 502 of the FD&C Act (21 U.S.C. 351 and 352); the Secretary's authorities with regard to wholesale distribution under section 503(e) of the FD&C Act (21 U.S.C. 353(e)); the Secretary's authority related to new drugs under section 505 of the FD&C Act (21 U.S.C. 355); the Secretary's authorities related to pharmaceutical supply chain security in sections 581 and 582 of the FD&C Act (21 U.S.C. 360eee and 360eee-1); the Secretary's authority related to inspection under section 704 of the FD&C Act (21 U.S.C. 374); and the Secretary's authority related to rulemaking under section 701(a) of the FD&C Act (21 U.S.C. 371(a)).

D. Costs and Benefits

The final rule allows commercial importation of certain prescription drugs from Canada through time-limited programs sponsored by a State or Indian Tribe, or in certain future circumstances by a pharmacist or wholesale distributor, with possible cosponsorship by a State, Indian Tribe, pharmacist, or wholesale distributor. If such programs are authorized and

implemented, allowing Importers to leverage drug price differences between the United States and Canada for the eligible prescription drugs identified in the SIP, these programs will result in cost savings for the American consumer.

Costs of the final rule may accrue to the Federal Government, SIP Sponsors, Importers, and manufacturers of imported drugs. The Federal Government will incur costs to implement the final rule and conduct oversight of authorized programs. SIP Sponsors will face costs to prepare proposals, implement authorized programs, and produce records and program reports. Drug manufacturers will have to provide certain information to Importers if their drugs are imported into the United States from Canada by a SIP. SIPs may offer cost savings to patients, as well as participating States, Indian Tribes, wholesale distributors, pharmacies, hospitals, and third-party payers. As SIP Sponsors and Importers realize savings in acquiring eligible prescription drugs and pass some of these savings on to consumers, it is possible that U.S.-based drug manufacturers may experience a transfer in U.S. sales revenues to these parties.

We are unable to estimate the cost savings from this final rule because we lack information about the likely size and scope of SIPs, the specific eligible prescription drugs that may be imported, the degree to which these imported drugs will be less expensive than non-imported drugs available in the United States, and which eligible prescription drugs are produced by U.S.-based drug manufacturers.

II. Table of Abbreviations/Commonly Used Acronyms in This Document

Abbreviation	What it Means
ACE	Automated Commercial Environment or any Other Electronic Data Interchange System authorized by U.S. Customs and Border Protection
ANDA	Abbreviated New Drug Application
ANSI	American National Standards Institute
APA	Administrative Procedure Act
API	Active Pharmaceutical Ingredient

Abbreviation	What it Means
BLA	Biologics License Application
BPCI Act	Biologics Price Competition and Innovation Act of 2009
CBP	U.S. Customs and Border Protection
CDER	Center for Drug Evaluation and Research
CGMP	Current Good Manufacturing Practice
DIN	Drug Identification Number
DSCSA	Drug Supply Chain Security Act
ESG	Electronic Submissions Gateway
FDA	Food and Drug Administration
FD&C Act	Federal Food, Drug, and Cosmetic Act
HHS	Health and Human Services
HPFB	Health Canada Health Products and Food Branch
ICSR	Individual Case Safety Reports
MMA	Medicare Prescription Drug, Improvement, and Modernization Act of 2003
NDA	New Drug Application
NDC	National Drug Code
NPRM	Notice of Proposed Rulemaking
OMB	Office of Management and Budget
PHS Act	Public Health Service Act
REMS	Risk Evaluation and Mitigation Strategies
RWD	Real-World Data
RWE	Real-World Evidence
SIP	Section 804 Importation Program
SSI	Section 804 Serial Identifier
TRIPS	Trade-Related Aspects of Intellectual Property Rights
USP	United States Pharmacopeia

III. Background

A. *Need for the Regulation/History of the Rulemaking*

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) (Pub. L. 108-173) was signed into law on December 8, 2003. Section 1121 of the MMA amended section 804 of the FD&C Act to its current version, which, among other things, authorizes the Secretary, after consultation with the U.S. Trade Representative and the Commissioner of Customs, to issue regulations permitting pharmacists and wholesalers to import

certain prescription drugs from Canada under certain conditions and limitations. Since the passage of the MMA, the Commissioner of Customs is now known as the Commissioner of CBP. For section 804 of the FD&C Act to become effective, the Secretary must certify that its implementation will pose no additional risk to the public's health and safety, and that it will result in a significant reduction in the cost of covered products to the American consumer.

As described in the notice of proposed rulemaking (NPRM), there has been interest for many years in allowing the importation of less expensive drugs from Canada to help American consumers benefit from these lower prices. However, no prior Health and Human Services (HHS) Secretary has made the certification required under section 804(l)(1) to begin implementing any part of section 804 of the FD&C Act.

In the *Federal Register* of December 23, 2019 (84 FR 70796), FDA published a proposed rule to implement section 804(b) through (h) of the FD&C Act to allow importation of certain prescription drugs from Canada.

Executive Order 13938 of July 24, 2020 (85 FR 45757), directs the Secretary, as appropriate and consistent with applicable law, to take action to expand safe access to lower-cost imported prescription drugs by, among other things, completing the rulemaking process regarding the proposed rule to implement section 804(b) through (h) of the FD&C Act to allow importation of certain prescription drugs from Canada.

B. Summary of Comments to the Proposed Rule

We received over 1,200 comment letters on the proposed rule by the close of the comment period. We received comments from consumers, consumer groups, trade organizations, industry, public health organizations, public advocacy groups, States, Canadian

entities (including governmental agencies), and others. These comments addressed nearly every aspect of the proposed rule and a number responded to specific FDA requests for comment.

IV. Legal Authority

Section 804(l)(1) of the FD&C Act provides that section 804 becomes effective only if the Secretary certifies to Congress that the implementation of this section will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of covered products to the American consumer. The Secretary is making this certification with regard to section 804(b) through (h) to Congress concurrent with the issuance of this final rule. The Secretary is issuing this final rule under the Secretary's rulemaking authority regarding importation of prescription drugs under section 804(b) through (h) of the FD&C Act. The final rule is also being issued pursuant to the Secretary's authorities related to adulterated and misbranded drugs under sections 501 and 502 of the FD&C Act; the Secretary's authorities with regard to wholesale distribution under section 503(e) of the FD&C Act; the Secretary's authority related to new drugs under section 505 of the FD&C Act; the Secretary's authorities related to pharmaceutical supply chain security in sections 581 and 582 of the FD&C Act; the Secretary's authority related to inspection under section 704 of the FD&C Act; and the Secretary's authority related to rulemaking under section 701(a) of the FD&C Act (21 U.S.C. 371(a)).

V. Comments on the Proposed Rule and FDA Response

A. Introduction

We describe and respond to comments on the proposed rule in sections V.B through L. We have numbered each comment to help distinguish between different comments. We have grouped similar comments together under the same number, and, in some cases, we have separated different issues discussed in the same comment and designated them as distinct

comments for purposes of our responses. The number assigned to each comment or comment topic is purely for organizational purposes and does not signify the comment's value or importance or the order in which comments were received. The Agency also received a number of comments that were outside the scope of the proposed rule and therefore were not considered in its final development and are not discussed here.

B. Description of General Comments and FDA Response

Many comments made general remarks supporting or opposing the proposed rule without focusing on a particular proposed provision. In the following paragraphs, we discuss and respond to such general comments.

(Comment 1) Several comments assert that limitations on the volume of eligible prescription drugs that could be imported, due to the geographic restriction to Canada and supply of prescription drug products in Canada, could limit the overall program's effectiveness in reducing U.S. prescription drug costs.

(Response 1) The final rule affords significant flexibility to SIPs to choose which eligible prescription drugs to import and in what quantities. This flexibility could allow SIPs to make adjustments in response to the supply of eligible prescription drugs available for importation. In addition, several potential SIP Sponsors have indicated in comments that they believe they can implement a SIP that, if authorized by FDA, will achieve a significant reduction in the cost of covered products to the American consumer with no additional risk to the public's health and safety.

(Comment 2) Several comments ask FDA to expand the proposed rule to implement section 804(j) of the FD&C Act to allow personal importation of certain prescription drugs.

Several comments support FDA's decision not to address in this rulemaking personal importation under section 804(j).

(Response 2) We are not implementing the personal importation provisions in section 804(j) of the FD&C Act through this rulemaking. We note that Executive Order 13938 of July 24, 2020, directs the Secretary, as appropriate and consistent with applicable law, to take action to expand safe access to lower-cost imported prescription drugs by, among other things, facilitating grants to individuals of waivers of the prohibition of importation of prescription drugs, provided such importation poses no additional risk to public safety and results in lower costs to American patients, pursuant to section 804(j)(2) of the FD&C Act.

C. Comments on General Provisions

(Comment 3) Several comments recommend expanding the definition of "eligible prescription drug," in particular to include biological products.

(Response 3) Section 804(a)(3) of the FD&C Act excludes several categories of drug products from the definition of "prescription drug" that can potentially be imported from Canada pursuant to section 804 of the FD&C Act, including controlled substances, biological products (as defined in section 351 of the Public Health Service Act (PHS Act) (42 U.S.C. 262)), infused drugs (including a peritoneal dialysis solution), intravenously injected drugs, and drugs that are inhaled during surgery.

(Comment 4) Several comments suggest that some risk evaluation and mitigation strategies (REMS) could be implemented effectively under a SIP with no additional risk, so drugs that are subject to REMS should not be excluded from the definition of "eligible prescription drug."

(Response 4) As discussed in the NPRM (84 FR 70796 at 70804), REMS drugs are high-risk products with known safety issues. REMS programs are mandated by FDA but implemented by manufacturers. In order to implement and assess a REMS, a manufacturer needs to have control over the drug that is the subject of the REMS. For example, for REMS that require tight controls on distribution of a drug in order to mitigate risks, use of Foreign Sellers will make it much more difficult to maintain those controls and could introduce gaps that have a significant impact on the safety of the drug.

(Comment 5) Several comments recommend excluding certain other types of drug products from the definition of “eligible prescription drug.” One comment suggests that the definition of “eligible prescription drug” should be limited to sole-source drugs and exclude drugs with remaining patents or exclusivities, drugs subject to post-marketing commitments or requirements, and drugs considered biologics in Canada. In addition, several comments request clarification regarding criteria FDA may use in determining whether a particular drug product can be imported safely in the context of a specific SIP Proposal.

(Response 5) At this time, FDA is not excluding additional categories from the final rule. For products not excluded by the final rule, FDA will determine whether the product can be imported safely in the context of a specific SIP Proposal on a product-by-product basis, including, for example, sterile drugs; drugs requiring special storage conditions such as temperature controls; or drugs intended to be used solely with a specific, separately distributed delivery system (such as may be the case for drug constituent parts of cross-labeled combination products, see 21 CFR 3.2(e)(3), (4)). A SIP Sponsor would need to explain in its SIP Proposal how it will address any concerns arising from the manufacture, storage, and transport of each

eligible prescription drug, including concerns related to controlling contamination, preserving sterility, and ensuring stability.

(Comment 6) Several comments raise concerns about SIPs potentially turning to online pharmacies as Foreign Sellers.

(Response 6) We are not changing the rule based on these comments, as the final rule includes provisions to safeguard against a SIP turning to rogue online pharmacies as Foreign Sellers. As discussed in the NPRM, while there are pharmacy websites that operate legally and offer convenience, privacy, and safeguards for purchasing medicines, we agree that there are many rogue online pharmacies that sell medicines at deeply discounted prices, often without requiring a prescription or adhering to other safeguards followed by pharmacies licensed by a State in the United States (Refs. 1 and 2). The final rule defines “Foreign Seller” to mean an establishment within Canada engaged in the distribution of an eligible prescription drug that is imported or offered for importation into the United States. The final rule further provides that a Foreign Seller must have an active drug establishment license to wholesale drugs by Health Canada and must be registered with provincial regulatory authorities to distribute HPFB-approved drugs. The final rule also requires that a Foreign Seller cannot be licensed by a provincial regulatory authority with an international pharmacy license that allows it to distribute drugs that are approved by countries other than Canada and that are not HPFB-approved for distribution in Canada. A Foreign Seller must also be registered with FDA under section 804 of the FD&C Act. The final rule also includes a number of supply chain requirements for Foreign Sellers. Moreover, FDA retains the authority not to approve a SIP, or to discontinue a SIP, absent a continued demonstration that the Foreign Seller meets all the relevant safety criteria.

(Comment 7) One comment proposes that FDA revise the definition of the term “manufacturer” to include only an applicant, as defined in § 314.3 (21 CFR 314.3), who owns an approved NDA or ANDA for an eligible prescription drug.

(Response 7) As described in the NPRM, under the rule the term “manufacturer” includes an applicant, as defined in § 314.3, who owns an approved NDA or ANDA for an eligible prescription drug, or a person who owns or operates an establishment that manufactures an eligible prescription drug. “Manufacturer” also means a holder of a drug master file containing information necessary to conduct the Statutory Testing, prepare the manufacturer’s attestation and information statement, or otherwise comply with section 804 of the FD&C Act or this part. We decline to change this definition because we continue to believe that a person that owns or operates an establishment that manufactures an eligible prescription drug or a holder of a drug master file containing information necessary to conduct the Statutory Testing or prepare the manufacturer’s attestation and information statement may have information about eligible prescription drugs that will be needed to ensure that the drugs comply with the FD&C Act and the requirements in this final rule. An Importer will determine which manufacturer, as defined in the rule, has the information needed, in particular for the Pre-Import Request, and will send a request for information to the appropriate manufacturer, which might not be the applicant. For example, the Importer may send a request for batch and stability testing records to the facility that manufactured the eligible prescription drug and that entity would be required to provide those records if the records are in the facility’s possession or control.

(Comment 8) Several comments request that the definition of “SIP Sponsor” include a State agency that a State has authorized to submit a SIP Proposal even if the State agency does not otherwise oversee pharmacies and wholesaler distributors.

(Response 8) FDA has revised the definition of the term “SIP Sponsor” to clarify that the term means a State or Indian Tribe that regulates wholesale drug distribution or the practice of pharmacy, submits a proposal to FDA that describes a program to facilitate the importation of prescription drugs from Canada under section 804 of the FD&C Act, and is responsible for oversight of the implementation of the program. Under section 201 of the FD&C Act (21 U.S.C. 321), the term “State” generally means any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico. In certain circumstances, a pharmacist or wholesale distributor may be a SIP Sponsor. FDA has also added a separate definition for the term “SIP Co-Sponsor,” which means any other State, Indian Tribe, pharmacist, or wholesale distributor that, with the SIP Sponsor, signs a SIP Proposal. A State agency that a State has authorized to submit a SIP Proposal may submit a SIP Proposal on behalf of the State, even if the State agency does not otherwise oversee pharmacists and wholesale distributors. We note that a SIP Proposal must, among other things, explain how the SIP Sponsor will ensure that all the participants in the SIP comply with the requirements of section 804 and this rule and describe the procedures the SIP Sponsor will use to ensure that requirements are met.

(Comment 9) Several comments suggest that the rule be changed to allow pharmacists or wholesalers to be SIP Sponsors without a State or Indian Tribe as a cosponsor. Some of these comments assert, for example, that pharmacists and wholesalers operate under robust regulatory requirements and that oversight by a State or Tribe would be redundant and could lead to an increase in administrative costs that would decrease the savings to American consumers under the program. Some comments assert that State sponsorship could result in individual SIP differences that will complicate the distribution and tracking of drugs. Other comments oppose allowing pharmacists or wholesalers to be SIP Sponsors without a State or Indian Tribe as a

cosponsor. Those comments suggest, for example, that pharmacists and wholesalers would not have adequate resources or authority to manage oversight functions effectively, and that involvement of a State or Indian Tribe is critical to facilitate a prompt response in the case of a recall or other event that requires a quick, coordinated response from practitioners, pharmacies, wholesalers, or other entities to protect the public health.

(Response 9) In the NPRM, FDA sought comment on whether it could be possible for a pharmacist or wholesaler to be a SIP Sponsor without a State or Indian Tribe as a sponsor, while posing no additional risk to the public's health and safety. We believe oversight by a State or Indian Tribe is an important safeguard because these entities, which oversee pharmacies and wholesale distribution and have tools to protect public health, are uniquely positioned to provide independent oversight of importation activities. Although we could not foresee how this approach could be adopted without posing additional risk to the public's health and safety, we stated that if we received information that demonstrates how a proposal that does not include a State or Indian Tribe as a sponsor would provide the same level of assurance of safety as a proposal with such a sponsor, we would consider having the final rule allow for this possibility. We provided an alternative codified provision that appeared under "Option 2" in proposed § 251.2 (21 CFR 251.2). FDA declines to adopt the alternative codified provision. However, we are open to the possibility that a pharmacist or wholesaler, after actively participating in a SIP, may be able to demonstrate that their proposal that does not include a State or Indian Tribe as the SIP sponsor could provide the same level of assurance of safety. Further, we recognize that Agency experience with this novel program is necessary to determine how to appropriately evaluate whether a pharmacist or wholesaler has adequately supported such a demonstration. Accordingly, we have revised the rule to provide that, after an initial 2-year period beginning on

the date of the first import entry under any SIP authorized under this rule, the Secretary may determine, based on experience under the program, that there is a sufficient likelihood that a proposal that does not include a State or Indian Tribe as the SIP sponsor could provide the same level of assurance of safety as a proposal that does include such a sponsor, such that FDA may begin receiving, reviewing, and potentially authorizing applications for SIPs without such a sponsor. After the Secretary makes such a determination, a pharmacist or wholesaler may propose a SIP that does not include a State or Indian Tribe as a sponsor, and FDA may authorize such a SIP if the sponsor demonstrates that the SIP meets the criteria for authorization with the same level of assurance of safety as a proposal that includes a State or Indian Tribe as the SIP sponsor, which FDA shall evaluate consistent with any considerations described in the Secretary's determination, including by evaluating whether the application demonstrates that the proposed sponsor has sufficient relevant experience, such as participating in a SIP and demonstrating compliance with the requirements of the FD&C Act and the rule.

(Comment 10) Several comments suggest that a pharmacist or wholesaler should not be allowed to be both a SIP cosponsor and an Importer in the same SIP, because it could remove a key layer of oversight and result in conflicts of interest. One comment suggests that entities and individuals receiving imported drugs should fall within the jurisdiction of the State sponsoring each SIP.

(Response 10) We are not changing the final rule in response to these comments. We continue to believe, as discussed in the NPRM (84 FR 70796 at 70801), that cosponsorship could introduce valuable flexibility (for example, multiple States could cosponsor a plan with a wholesale distributor) and allow SIPs to benefit from the experience of pharmacists and wholesale distributors, while generally preserving the advantages that accrue from sponsorship

by at least one State or Indian Tribe. SIP Sponsors need to explain in their SIP Proposals how they will address conflicts of interest and ensure that there is sufficient oversight of the SIP participants. We have clarified in the rule that FDA may decide not to authorize a SIP Proposal or supplemental proposal because of, among other reasons, the potential for conflicts of interest. Likewise, if a SIP Sponsor chooses to allow for the distribution of the eligible prescription drugs it imports to entities or individuals outside of the State's jurisdiction, it should explain in the SIP Proposal how it will address any issues that might arise from this distribution.

(Comment 11) Several comments suggest that non-governmental entities other than pharmacists and wholesalers, such as group purchasing organizations and pharmacy benefit managers, should be permitted to cosponsor SIPs. One comment, for example, says the inclusion of pharmacy benefit managers would allow SIP Sponsors to more adequately trace the origins and disposition of imported products. Several comments oppose such a change, referencing, for example, a lack of accountability and transparency and a negative effect that the business practices of pharmacy benefit managers have on patients' ability to access medications. In addition, some comments oppose cosponsorship by any non-governmental entity.

(Response 11) As noted above, FDA continues to believe that cosponsorship could introduce valuable flexibility and allow SIPs to benefit from the experience of pharmacists and wholesale distributors, while generally preserving the advantages that accrue from sponsorship by at least one State or Indian Tribe. We decline to change the final rule, at this time, to expand or limit this provision. Section 804 of the FD&C Act specifically provides for the participation of a pharmacist or wholesaler, but not any other non-government entity. If a non-government entity is a licensed pharmacist or wholesaler and meets the requirements of this rule, the entity can cosponsor a SIP.

D. Comments on SIP Proposals and Pre-Import Requests

(Comment 12) Several comments request that FDA amend the proposed rule to allow submission of SIP Proposals without identifying or providing certain information about participating entities or persons and provide for “conditional approval” of SIPs before those specific participating entities or persons are identified, followed by “final approval” when participation agreements are in place. According to these comments, entities or persons such as a potential Foreign Seller or Importer may be unwilling to commit to participating in a SIP until they are assured that a prospective SIP Sponsor has received FDA authorization. The comments also assert that a SIP Sponsor would need sufficient time to determine and finalize contracts or other arrangements with the entities or persons that will be participating in a SIP.

(Response 12) In response to these comments and related concerns, in particular about finding a Foreign Seller to obtain the eligible prescriptions drugs identified in the SIP Proposal, we are revising the final rule to provide that FDA may use a phased review process to review a SIP Proposal that does not identify a Foreign Seller in an initial submission but otherwise meets the requirements of this part. Importers, relabelers, and repackagers still need to be identified and the required information regarding these participating persons must be included in the initial submission of the SIP Proposal. A Foreign Seller must be identified within 6 months of the initial submission date of the SIP Proposal. This change to allow for phased review reflects the importance of finding a well-qualified Foreign Seller for a short supply chain. The 6-month period helps ensure that the information provided in the SIP Proposal to FDA for consideration is current and FDA is able to better handle the workload of reviewing SIP proposals. A Foreign Seller will still need to be identified and registered with FDA, and FDA will still review information about the Foreign Seller, before FDA will authorize a SIP.

(Comment 13) Several comments recommend that the proposed rule be changed to allow an initial SIP Proposal to identify more than one Foreign Seller and more than one Importer. Several comments also support allowing a longer supply chain, to include multiple Foreign Sellers. These comments assert, for example, that a short supply chain would allow drug manufacturers to discriminate against a Foreign Seller specified in a SIP, preventing the SIP from demonstrating to FDA that the SIP can consistently and successfully import eligible prescription drugs. Other comments express support for the rule as proposed, noting among other things that more complex supply chains may be less secure.

(Response 13) As described in the NPRM (84 FR 70796 at 70797), the rule provides that a SIP Proposal needs to identify the Foreign Seller in Canada that will purchase the eligible prescription drug directly from its manufacturer, and identify the Importer in the United States that will buy the drug directly from the Foreign Seller before FDA will authorize the SIP. We have revised the rule to clarify that each supply chain under a SIP must still be limited to one manufacturer, one Foreign Seller, and one Importer. Although the initial SIP Proposal would be authorized to allow just one Foreign Seller and one Importer, if the SIP can show that it has consistently imported eligible prescription drugs in accordance with section 804 of the FD&C Act and the rule, the SIP Sponsor can submit a supplemental proposal to add supply chains, which would each consist of one or more eligible prescription drugs, one Foreign Seller, and one Importer. We believe that because SIPs are new and unique programs which may be challenging to implement at first, they should begin with a single importer and single foreign seller. Based on FDA's experience with drug importation and implementation of new programs, we believe that an increase in the number of entities a SIP must oversee and, potentially, a corresponding increase in the volume of product, could multiply the opportunity for supply chain security

problems. Absent a demonstrated track record of oversight capability and compliance, initially limiting a SIP to one Foreign Seller and one Importer is an important safeguard. With regard to the concern raised in some comments that a manufacturer could refuse to deal with participating Foreign Sellers, we do not intend to publicly disclose information from the SIP Proposal or authorization that is confidential business information where such disclosure is restricted by law, potentially including information about Foreign Sellers or the eligible prescription drugs that might be imported. Generally, information about suppliers and proposed business plans is confidential business information unless that information is made public by the information owner. However, this information might become public in other ways, such as through state open records laws. Even under such circumstances, the relationship between a manufacturer and a Foreign Seller will be subject to complex market dynamics, with many variables including relative market power, and it is difficult to predict what transactions might or might not occur.

(Comment 14) One comment recommends that SIP Proposals describe a plan for ensuring that FDA-approved patient labeling is dispensed to patients. One comment asks that the FDA-approved patient labeling include additional information pertaining to importation under a SIP generally or under a particular SIP. For those eligible prescription drugs that do not have FDA-approved patient labeling, the comment asks that FDA require that they have patient labeling that is not specific to a particular product that includes information pertaining to importation under a SIP generally or under a particular SIP. The comment asks that this patient labeling include the labeling statement described in § 251.13.

(Response 14) We are not making changes to the final rule with regard to this comment. The final rule provides that Importers are responsible for, among other things, ensuring that eligible prescription drugs are relabeled with the required U.S. labeling, including patient

labeling such as Medication Guides, Instruction for Use documents, and patient package inserts.

As described in the NPRM, a SIP Proposal must identify the FDA-registered repackager or relabeler in the United States that will relabel the imported drugs with the required U.S. labeling, including the carton and container labeling, Prescribing Information, and any patient labeling, such as Medication Guides, Instruction for Use documents, and patient package inserts. The final rule requires that the SIP Proposal explain how the SIP Sponsor will educate pharmacists, healthcare providers, pharmacy benefit managers, health insurance issuers and plans, as appropriate, and patients about the eligible prescription drugs imported under its SIP. We do not believe it is necessary to add a requirement to provide patient labeling that is not specific to a particular product and that includes information pertaining to importation under a SIP generally or under a particular SIP.

(Comment 15) Several comments address issues related to identification in a SIP Proposal of drugs that may meet program requirements, if some information about potentially eligible prescription drugs is not available to the SIP Sponsor at the time it submits a SIP Proposal. One comment suggests that manufacturers should not be required to disclose manufacturing information before SIP authorization.

(Response 15) We decline to make changes in response to these comments. As noted in the NPRM (84 FR 70796 at 70807), we recognize that at the time of submission of a SIP Proposal the SIP Sponsor may not know whether a drug meets the conditions in an FDA-approved NDA or ANDA. FDA intends to review, among other things, the information that the SIP Sponsor is able to provide about each of the drugs that the SIP Sponsor seeks to import to confirm that each is approved by both HPFB and FDA, that each FDA-approved drug is currently marketed in the United States, and that none of the drugs falls into any of the

exclusions from the definition of eligible prescription drug. Under the final rule, § 251.3(d)(5)-(6), (e)(5) and (7), manufacturers are not required to disclose information before a SIP is authorized.

(Comment 16) One comment claims that the rule would, if finalized as proposed, increase risks to the public health by assigning pharmacovigilance and recall responsibilities to States and other entities with little to no experience in conducting, or capability to conduct, these complex activities.

(Response 16) The rule requires a SIP Sponsor to demonstrate that post-importation pharmacovigilance and other requirements of the FD&C Act and this final rule are met. As discussed in the NPRM, for example, States provide the primary oversight of wholesale distributors' storage, handling, and distribution practices to ensure the quality of drugs is maintained. States also ensure that pharmacies and pharmacists comply with statutes and regulations governing the practice of pharmacy, which includes dispensing of drugs to patients. States have the authority to inspect pharmacies and wholesale distributors, and, in some cases, other pharmaceutical supply chain participants the States license, and to take disciplinary action if warranted. States also have tools that they can use to respond rapidly should activities under their SIP adversely affect the public health. In addition, under the final rule, Importers will submit adverse event, field alert, and other reports to both FDA and the manufacturer. The reports will aid the manufacturer in its pharmacovigilance efforts and will provide FDA with information that may be relevant to its review of SIP Proposals and Pre-Import Requests, as well as to its oversight of drugs imported under section 804 of the FD&C Act and of section 804 in general. The SIP Proposal must include a written recall plan that will be reviewed for completeness and effectiveness by the Agency before the SIP is authorized. In addition, FDA

assists firms with carrying out their recall responsibilities to protect the public health from distributed products in violation of the FD&C Act and other laws administered by FDA.

(Comment 17) Several comments suggest that before FDA authorizes a SIP Proposal submitted by a State agency, a potential SIP Sponsor should need to show that the SIP and any necessary funding have been approved by the State's legislature and executive.

(Response 17) We decline to make these changes in the final rule because it may not be feasible for a State to make a final funding determination for a SIP before FDA evaluates the SIP Proposal. Instead, the final rule requires that a SIP Proposal include, among other things, an explanation of how the SIP Sponsor will ensure that all the participants in the SIP comply with the requirements of section 804 of the FD&C Act and the rule, as well as a description of the procedures the SIP Sponsor will use to ensure that these requirements are met. In addition, the final rule provides that, among other reasons, FDA may decide not to authorize a SIP Proposal because of potential safety concerns with the SIP, because there exists a degree of uncertainty that the SIP Proposal would adequately ensure the protection of public health, because of the relative likelihood that the SIP Proposal would not result in significant cost savings, or in order to limit the number of authorized SIPs so FDA can effectively and efficiently carry out its responsibilities under section 804 of the FD&C Act in light of the amount of resources allocated to carrying out such responsibilities.

(Comment 18) Several comments suggest that various entities or persons participating in a SIP, including Foreign Sellers, Importers, repackagers, relabelers, and laboratories, should be inspected by FDA before the SIP could be authorized. One comment suggests that FDA should conduct periodic audits of shipments of eligible prescription drugs being imported.

(Response 18) FDA is not making these changes because we believe the Agency's other mechanisms for oversight are sufficient. Although we decline to add a pre-authorization inspection requirement, we note, as discussed in the NPRM, that we retain our right to conduct inspections under section 704 of the FD&C Act. Inspections may occur before authorization or as part of FDA's risk-based inspection program. In addition, the final rule requires SIP Sponsors and other SIP participants to agree to submit to audits of their books and records and inspections of their facilities as a condition of participation in a SIP. If a SIP Sponsor, manufacturer, Foreign Seller, Importer, qualifying laboratory, or other participant in the supply chain that is subject to inspection, delays, denies, or limits that inspection, or refuses to permit entry or inspection of its facility or its records, any drug held by that entity would be deemed to be adulterated (see section 501(j) of the FD&C Act). In those circumstances, FDA could also suspend the SIP, in whole or in part, immediately. We also decline to add a provision for periodic audits of shipments of eligible prescription drugs. All shipments are subject to Statutory Testing and, under this rule, FDA will be provided with three sets of the samples of each imported drug to enable FDA to also conduct the Statutory Testing as FDA deems warranted. In addition, FDA already has the authority to collect samples of shipments under 21 CFR 1.90.

(Comment 19) One comment proposes that SIP Proposals should be required to include background information for all entities or persons that are downstream of the SIP, in addition to the entities or persons in the SIP, if the SIP does not distribute drugs directly to patients.

(Response 19) FDA declines to make this change. The final rule requires that SIP Proposals include, among other things, certain background information about Importers and Foreign Sellers. In the NPRM, we requested comment on whether the rule should require additional or alternative background information and on whether the background information

requirement should cover additional or alternative individuals or entities. At this time, we do not believe that additional background information about downstream supply chain entities or persons is necessary to assure the security of the SIP supply chain or to assure that the requirements of the FD&C Act and this rule will be met because these entities and persons need to be in compliance with licensure and other Federal and State requirements.

(Comment 20) Several comments discuss the important role a Foreign Seller would play in a SIP. One comment recommends that FDA take additional steps to ensure Foreign Sellers maintain robust controls and that FDA obtain additional information regarding compliance and business history, including through inspections. The comment also recommends that the Foreign Seller or the Importer be required to disclose any civil judgments against or settlements entered into by the Foreign Seller or Importer related to liability for violations of State, Federal, or Canadian laws regarding drugs or devices or the sale or distribution of drugs or devices. One comment suggests that FDA require SIP Proposals to include disciplinary actions imposed against the Foreign Seller or the Importer beyond just United States and Canadian borders. Several comments reference potential difficulties in vetting and regulating Foreign Sellers.

(Response 20) FDA declines to make changes in response to these comments because we believe the final rule includes sufficient controls without these requirements. Under the final rule, Foreign Sellers must, among other things, be licensed by Health Canada as drug wholesalers and be registered with a provincial regulatory authority to distribute HPFB-approved drugs. The final rule also requires that the SIP Sponsor's importation plan include, among other things, a list of all disciplinary actions imposed against the Foreign Seller or the Importer by State, Federal, or Canadian regulatory bodies, including any such actions against the principals,

owners, directors, officers, or any facility manager or designated representative of such manager for the previous 7 years before submission of the SIP Proposal.

(Comment 21) Several comments suggest ways a SIP Proposal might account for costs and benefits associated with the SIP and determine whether the SIP would significantly reduce costs for American consumers. Several comments suggest that FDA should limit the ways in which a SIP Proposal should be able to meet this requirement. Several comments asked about how section 804 drugs will be treated under government programs, including Medicaid and the 340B Drug Pricing Program. One comment suggests that FDA should identify a threshold for whether a reduction in cost is significant.

(Response 21) We decline to make any changes to the rule in response to these comments. As discussed in the NPRM, FDA intends to determine whether a reduction in cost is significant in the context of considering a specific proposal. The information needed to demonstrate anticipated cost savings to the American consumer will be dependent on the specific mechanisms which the SIP Proposal is using to reduce costs for American consumers. The SIP proposal should clearly articulate the mechanism by which the proposal will reduce costs to consumers and provide relevant information given that context. To demonstrate expected cost savings, a SIP Sponsor could compare anticipated acquisition costs or consumer prices per unit of each eligible prescription drug that the SIP Sponsor is seeking to import. A SIP Sponsor could also compare the current retail cash price of the drugs. If the cost savings do not go to consumers directly, because, for example, they accrue to a healthcare provider or payor, the SIP Proposal would need to show that the SIP will result in a significant reduction in the cost of covered products to the American consumer. We anticipate that some SIP Sponsors may seek to import drugs to be used by patients in State-run programs in which consumers do not directly

pay the cost of drugs. In such cases, a SIP Sponsor could submit information about whether cost-sharing expenses are reduced for the participants, or whether the program will result in cost savings that are passed on to consumers in other ways, such as increasing the number of people covered by a State program, or increasing the availability of drugs covered by the program. A SIP proposal cannot demonstrate cost savings in connection with a government program if the eligible prescription drugs to be imported under the SIP do not meet the program's requirements. This rule is not intended to address how agencies other than FDA, such as those that administer Medicaid or other government programs, may apply their authorities to drugs imported under a SIP. HHS may issue further guidance or rulemaking as appropriate. HHS guidance, including the relevant Medicaid guidance for drugs imported under a SIP, can be found at <https://www.hhs.gov/guidance/>.

(Comment 22) One comment recommends that SIP Sponsors be required to demonstrate to FDA that participants in the SIP, including Importers and Foreign Sellers, are capable of meeting program requirements, such as for serialization and monitoring for counterfeit drugs. Several comments express concern that entities or persons involved in the SIP might lack capacity, experience, and resources to demonstrate that they could meet all the requirements under the proposed rule.

(Response 22) We are not making changes based on these comments because we believe the final rule includes sufficient mechanisms for FDA to evaluate participants in a SIP. The final rule requires a SIP Sponsor, in its proposal, to explain how the SIP Sponsor will ensure that all the participants in the SIP comply with the requirements of section 804 of the FD&C Act and the rule, and describe the procedures the SIP Sponsor will use to ensure requirements are met, including steps regarding storage, handling, and distribution practices; supply chain security; and

screening eligible prescription drugs for evidence that they are adulterated, counterfeit, damaged, tampered with, expired, suspect foreign product, or illegitimate foreign product. Under the final rule, a Foreign Seller is responsible for relabeling drug products to affix the SSI to or imprint the SSI on each package and homogenous case of the eligible prescription drug(s). In addition, the Foreign Seller must maintain records associating the SSI with the DIN from the HPFB and all the records it received from the manufacturer upon receipt of the original shipment intended for the Canadian market. The Importer is also responsible for ensuring compliance with requirements for serialization and identifying suspect or illegitimate product when the drugs arrive in the United States.

(Comment 23) Several comments asked whether eligible prescription drugs imported under a SIP could be returned, and how those returns would be handled.

(Response 23) We have revised the rule to provide that a SIP Sponsor's importation plan must include the SIP's return plan, including an explanation of how the SIP Sponsor will ensure that a product that is returned after being in U.S. distribution is properly dispositioned in the United States if it is a non-saleable return in order to protect U.S. patients from expired or unsafe drugs. We are requiring that returned products be dispositioned in the United States, as appropriate, to prevent these products, which have been in U.S. distribution with the FDA-approved labeling prior to their return, from possible distribution in Canada with the U.S. labeling or from being re-imported into the U.S. as a non-SIP drug. In addition, it is unclear whether such products, which will have been relabeled to comply with U.S. requirements, could be returned to the Foreign Seller under Canadian law. Therefore, as an additional safeguard under section 804(c)(3) of the FD&C Act and to reduce opportunities for diversion and other forms of fraud, the return plan must explain how the SIP Sponsor will ensure that returned

eligible prescription drugs, which have been relabeled for the U.S. market, are not exported from the United States. If the SIP Sponsor anticipates that its program will have returned product that may be considered as saleable and therefore re-distributed in the United States, the return plan should address how returned eligible prescription drugs will be determined to be saleable and how those products will be handled.

(Comment 24) One comment proposes several additional elements to be included in a SIP compliance plan, which must be submitted as part of the SIP Proposal. The comment suggests that a SIP compliance plan should include: (1) a compliance committee, (2) a program for internal monitoring and auditing, and (3) well-established processes for disciplinary actions for noncompliance. The comment also suggests that SIPs have promotion compliance programs that address interactions with healthcare professionals, patient advocacy organizations, and others. The comment further recommends that FDA adopt certain submission requirements for promotional materials.

(Response 24) As discussed in the NPRM (84 FR 70796 at 70811), SIP Sponsors need to develop a compliance plan and describe it in detail in their SIP Proposal for FDA's review and authorization. We have revised the rule to provide that a SIP Sponsor's importation plan must include the SIP's compliance plan, including: (1) a description of the division of responsibilities among cosponsors, if any, which includes a plan for timely communication of any compliance issues to the SIP sponsor; (2) identification of responsible individual(s) and a description of the respective area(s) of compliance that will be monitored by each responsible individual; (3) the creation of written compliance policies, procedures, and protocols; (4) the provision of education and training to ensure that Foreign Sellers, Importers, qualifying laboratories, and their employees understand their compliance-related obligations; (5) the creation and maintenance of

effective lines of communication, including a process to protect the anonymity of complainants and to protect whistleblowers; and (6) the adoption of processes and procedures for uncovering and addressing noncompliance or misconduct. At this time, we decline to require that every SIP compliance plan include each element proposed in the comment. In recognition of the SIP Sponsors' and cosponsors' responsibilities, we have also revised the SIP Proposal provisions to require the signature of the SIP Sponsor and cosponsors, if any, or an authorized representative. In addition to the compliance plan, a SIP sponsor's importation plan must explain how the SIP Sponsor will ensure that all the participants in the SIP comply with the requirements of section 804 of the FD&C Act and the rule. In addition, the final rule requires the SIP Sponsor to describe the procedures it will use to ensure that, among other things: (1) the storage, handling, and distribution practices of supply chain participants, including transportation providers, meet certain requirements and do not affect the quality or impinge on the security of the eligible prescription drugs; (2) the supply chain is secure; (3) the Importer screens the eligible prescription drugs it imports for evidence that they are adulterated, counterfeit, damaged, tampered with, expired, suspect foreign product, or illegitimate foreign product; and (4) the Importer fulfills its responsibilities to submit adverse event, field alert, and other reports. The SIP Proposal must also explain how the SIP Sponsor will educate pharmacists, healthcare providers, pharmacy benefit managers, health insurance issuers and plans, as appropriate, and patients about the drugs imported under its SIP. With regard to requirements for promotional materials, under the FD&C Act and the final rule, imported eligible prescription drugs cannot be misbranded and must meet applicable labeling requirements. As with other aspects of compliance, the SIP Proposal and the compliance plan it contains must explain how the SIP will ensure that drugs are not misbranded.

(Comment 25) Several comments suggest that FDA should establish specific timeframes for reviewing and authorizing SIP Proposals. One comment recommends that SIP Proposals should be addressed on a first-come, first-served basis. One comment recommends that SIPs be limited at first to ensure FDA can effectively and efficiently carry out its responsibilities in connection with the SIP, there are no adverse impacts on Canada, and cost savings for consumers are achieved.

(Response 25) Because this program is novel, we do not have sufficient information to estimate a timeframe for the review of a SIP Proposal. Review times may depend on factors such as the quality and complexity of proposals and Agency resource constraints. FDA plans to establish internal processes for its review of SIPs, rather than specifying details, such as the order of its review, in this regulation.

(Comment 26) One comment proposes that each reauthorization of a SIP be accompanied by a new assessment of whether the SIP would “pose no additional risk to the public’s health and safety.”

(Response 26) We decline to change the rule in response to this comment. The final rule provides that FDA may deny a request for authorization, modification, or extension of a SIP including if a proposed SIP does not meet the standard for authorizing a SIP. The final rule further provides that if a SIP Proposal meets the requirements of the rule, FDA may nonetheless decide not to authorize the SIP Proposal. The final rule also provides that FDA may decide not to authorize a SIP Proposal because of potential safety concerns with the SIP or because of the degree of uncertainty that the SIP Proposal would adequately ensure the protection of public health.

(Comment 27) Several comments support requirements on Importers to provide certain manufacturing information, including the source of the imported product and active pharmaceutical ingredient (API) information, and to maintain records of transactions.

(Response 27) The final rule provides that a prescription drug may not be imported or offered for import under this part unless the Importer has filed a Pre-Import Request for that drug that has been granted by FDA. The Pre-Import Request must identify and include a description of the eligible prescription drug(s) covered by the Pre-Import Request, including among other things, the established and proprietary name of the drug, API information, and manufacturer information. Additionally, the final rule provides that Importers would need to maintain records, for not less than 6 years, that allow the Importer to associate the product identifier it affixed or imprinted to each package and homogenous case of product it received from the Foreign Seller, with the SSI that had been assigned by the Foreign Seller, and the Canadian DIN that was on the package when the Foreign Seller received the product from the original manufacturer.

(Comment 28) Several comments assert that the final rule should rely as little as possible on requiring manufacturers to take certain actions and make certain disclosures. The comments say that because manufacturers may oppose those requirements, the final rule should primarily rely on other measures where possible to achieve the same aims. The comments assert that FDA must also be prepared to provide any necessary information that a manufacturer refuses to provide and to take any other action against the manufacturer as appropriate.

(Response 28) The obligations on manufacturers under section 804 and this rule are enforceable under section 301(aa) of the FD&C Act (21 U.S.C. 331(aa)), which provides that, among other things, a violation of the regulations implementing section 804 is a prohibited act. Furthermore, section 303(b)(6) of the FD&C Act (21 U.S.C. 333(b)(6)) provides for a prison

term of up to 10 years for manufacturers or Importers that knowingly fail to comply with a requirement of section 804(e) of the FD&C Act, including that: (1) the manufacturer or Importer conduct the Statutory Testing at a qualifying laboratory; (2) if the Importer conducts the testing, the manufacturer supply the information needed to authenticate the drug being tested and to confirm that the labeling is in compliance with the FD&C Act; and (3) if the manufacturer supplies this information to the Importer, the Importer keep it in strict confidence and only use it for testing and complying with the FD&C Act. Violators are also subject to fines under 18 U.S.C. 3571. Because of these provisions, we have determined that it is not necessary to include proposed § 251.16(i) in the final rule. That provision stated that “FDA may transmit information that the manufacturer is required to provide to an Importer under this section on the manufacturer’s behalf if the manufacturer has not transmitted such information to the Importer in a timely fashion and if such information is available to FDA in the NDA or ANDA.”

(Comment 29) One comment recommends that FDA shorten the pre-import notification period to give SIPs more flexibility to respond to emerging needs based on demand for certain products, and to avoid having to forecast demand far in advance of importation.

(Response 29) The NPRM provided that after FDA has authorized a SIP Proposal, the Importer would submit a Pre-Import Request to FDA at least 30 calendar days before the scheduled date of arrival or entry for consumption for a shipment containing an eligible prescription drug covered by the SIP, whichever is earlier. FDA declines to change this provision because the Agency will need sufficient time to review the Pre-Import Request and determine if the Importer will meet all the requirements for importation. FDA may consider expediting reviews of Pre-Import Requests, if appropriate, and depending on resources.

(Comment 30) Several comments recommend that the final rule require an Importer to file a separate Pre-Import Request for each shipment of eligible prescription drugs.

(Response 30) FDA is not making changes in response to these comments. As discussed in the NPRM, when a Pre-Import Request is granted by FDA, that Pre-Import Request covers subsequent shipments of the eligible prescription drug(s) identified in the Agency's grant of that Request, provided that all of the information contained in the Pre-Import Request, with the exception of the anticipated dates of shipment, is the same for each subsequent shipment covered by the Pre-Import Request when the shipment arrives in the United States. We believe that Importers should have the flexibility to decide how many shipments should be covered by a Pre-Import Request. An Importer could choose to send each eligible prescription drug covered by a Pre-Import Request in a separate shipment, for example. An Importer could also choose to send one eligible prescription drug covered by a Pre-Import Request in multiple shipments. Requiring an Importer to file a separate Pre-Import Request for each shipment would not facilitate the importation of eligible prescription drugs and would unnecessarily burden both the Importer and the Agency.

(Comment 31) One comment recommends that FDA clarify that a manufacturer is not required to provide an attestation unless it has received formal notification from FDA that an applicable SIP has been authorized. The comment further recommends that FDA clarify that a manufacturer may decline to provide an attestation if, in the manufacturer's opinion, the Canadian version of the drug fails to meet any of the conditions in the FDA-approved NDA or ANDA, including process-related and manufacturing specifications. The comment also asks FDA to clarify that the refusal or failure to provide an attestation under such circumstances is not a violation of section 804 of the FD&C Act or the final rule. The comment requests that FDA

clarify that a manufacturer has the initial option to conduct such testing and that the Importer may conduct it only if the manufacturer declines, because such testing requires the disclosure of sensitive information.

(Response 31) We decline to change the rule in the manner suggested. We intend to provide updates on SIP authorizations and do not believe it is necessary to provide additional, formal notification to manufacturers. We further believe that the rule is sufficiently clear that a manufacturer does not need to provide an attestation and information statement if the drug proposed for import does not, except for the fact that it bears the HPFB-approved labeling, meet the conditions in the FDA-approved NDA or ANDA, including any process-related or other requirements for which compliance cannot be established through laboratory testing. To facilitate importation, the final rule clarifies that the manufacturer must notify the Importer and FDA if it cannot provide the required attestation and information statement and articulate with specificity the reasons it cannot provide that attestation and information statement. We do not believe that it is necessary to revise the rule to clarify that a manufacturer has the initial option to conduct the Statutory Testing and that the Importer may conduct it only if the manufacturer declines to do so. Under the final rule, the manufacturer must notify the Importer and FDA of the manufacturer's intent to perform the Statutory Testing within 30 calendar days of receipt of a request from the Importer.

(Comment 32) The proposed rule provided that unless an extension is granted, authorization for a SIP automatically terminates after 2 years, or a shorter period of time if a shorter period of time is specified in the authorization for the SIP. Several comments assert that this limitation could discourage participation.

(Response 32) As discussed in the NPRM (84 FR 70796 at 70810), we believe that the initial 2-year period will provide sufficient time for SIP Sponsors to implement the authorized SIP. The 2-year authorization period for a SIP would begin when the Importer, or its authorized customs broker, files an electronic import entry for consumption for its first shipment of eligible prescription drugs under the SIP. We further believe, as we explained in the NPRM, that SIPs should terminate after 2 years unless re-authorized because importation under section 804 of the FD&C Act is novel and by the end of a 2-year period we can evaluate how the SIP performed, such as the extent to which it resulted in cost savings. The final rule provides that an authorized SIP Sponsor would be able to submit a proposal asking for authorization to extend the SIP for additional 2-year periods.

(Comment 33) One comment recommends that FDA clarify what kinds of changes warrant submission of an amendment to an authorized SIP. The comment also recommends that FDA allow the SIP to continue to operate while an amendment to the SIP is under consideration. The comment further recommends that FDA include a prompt and reasonable timeframe for responding to amendment requests.

(Response 33) A SIP Sponsor must not make any changes or permit any changes to be made to a SIP without first securing FDA's authorization of a supplemental proposal. For example, as described in the NPRM, if a SIP Sponsor wishes to amend the list of eligible prescription drugs it seeks to import or to work with a different Foreign Seller, Importer, or qualifying laboratory, the SIP Sponsor must submit a supplemental proposal. The final rule provides that a SIP Sponsor can propose to add Foreign Sellers or Importers to an authorized SIP once it has consistently imported eligible prescription drugs in accordance with section 804 of the FD&C Act and the final rule. The final rule also provides that a SIP Sponsor may request

that FDA extend the authorization period of an authorized SIP. Consistent with responses to comments above, we decline to set a timeframe given that this depends on, among other factors, the quality and complexity of submissions and Agency resource constraints. Moreover, because this program is novel, we do not have sufficient information to estimate a timeframe for these reviews.

E. Comments on Certain Requirements for Section 804 Importation Programs

(Comment 34) Several comments suggest that Importers' screening of eligible prescription drugs for evidence regarding whether they are adulterated, counterfeit, damaged, tampered with, or expired is not sufficient. One comment notes that visual inspection does not replace the need for Statutory Testing.

(Response 34) The final rule, like the proposed rule, sets out a number of steps, including Statutory Testing, that a SIP Sponsor and others would need to take to ensure that the supply chain is secure and importation will pose no additional risk to the public's health and safety. Visual inspection does not replace the need for Statutory Testing in accordance with the requirements of section 804 and the rule. Additionally, FDA reviews import entries to ensure that they do not contain articles that appear to violate the FD&C Act and takes samples of FDA-regulated products for examination when appropriate. Arrivals and entries of eligible prescription drugs under a SIP will be limited to a port authorized by FDA in order to facilitate our admissibility review of entries containing eligible prescription drugs.

(Comment 35) Several comments address whether the labeling for an eligible prescription drug needs to be the same as the manufacturer's FDA-approved labeling. For example, one comment suggests that because Canadian drug packaging and instructions are written in English already, relabeling is unnecessary. Another comment asserts that

differentiation between eligible prescription drugs and other drugs could inadvertently lead to the misperception that eligible prescription drugs are less safe. Several comments agree with conspicuous label requirements; some comments suggest additional ways to distinguish eligible prescription drugs. One comment says that under the FD&C Act, if a United States Pharmacopeia (USP) monograph exists for an eligible prescription drug, the labeling requirements in the monograph play a role in ensuring that the drug is labeled according to U.S. labeling requirements.

(Response 35) Pursuant to section 804(d)(1)(K)(ii) of the FD&C Act, this final rule requires that an eligible prescription drug imported in accordance with this rule meet all labeling requirements under the FD&C Act. Additionally, pursuant to section 804(c)(1) of the FD&C Act, this final rule requires that each eligible prescription drug imported under this rule comply with sections 501, 502, and 505 of the FD&C Act. Generally, even if there is a USP monograph, the labeling for an imported eligible prescription drug will be the same as the FDA-approved prescription drug labeling under the NDA or the ANDA, except the labeling will need to display a National Drug Code (NDC) and serial number that is unique to the eligible prescription drug, it will need to provide information about the Importer, and it will need to include the labeling statement required by this rule. If the SIP maintains a website, the labeling statement could also include the website address. As discussed below, we have revised the required labeling statement as follows: “[This drug was/These drugs were] imported from Canada without the authorization of [Name of Applicant] under the [Name of SIP Sponsor] Section 804 Importation Program.” We have also revised the rule to provide that NDC(s) must be included on the immediate container label and outside package. Also, as discussed in the NPRM, if an eligible prescription drug’s container is too small to fit the additional information required by this rule,

FDA would consider a supplemental proposal to modify the labeling of an eligible prescription drug.

(Comment 36) One comment requests that FDA amend the rule to not allow identification of the manufacturer on the labeling of a drug imported and distributed via a SIP unless the manufacturer consents to such identification.

(Response 36) We decline to make this change. In the NPRM, we proposed to require that if the FDA-approved labeling of a drug imported and distributed via a SIP did not include the name and place of business of the manufacturer, that the name and place of business of the manufacturer be added. We have decided that it is not necessary to add the name and place of business of the manufacturer if that information is not already included on the FDA-approved labeling. The labeling will include the name and place of business of the manufacturer, packer or distributor that appears on the FDA-approved labeling and it will also include the name and place of business of the Importer. This will ensure that those responsible for the product can be identified. We note that the final rule includes the addition of a phrase in the labeling statement explaining that the drug is imported without the manufacturer's authorization, which will help to prevent potential misperceptions regarding whether the manufacturer authorized the product to be imported.

(Comment 37) Comments ask that the proposed labeling statement that Importers are required to add to the labeling of a section 804 drug not include the phrase "to reduce its cost to the American consumer." A comment says that this statement would not be consistent with FDA regulations and the purpose of labeling, which the comment says is to provide safety and effectiveness and use information. Another comment notes that generic drugs typically are not permitted to be labeled with comparative cost information.

(Response 37) We have determined that it is not necessary to include the phrase “to reduce its costs to the American consumer” in the labeling statement that § 251.13(b)(4)(iv) requires Importers to add to the labeling of a section 804 drug. In the proposed rule, we explained that the purposes of the labeling statement are to help avoid potential confusion between products with the same name and to help pharmacists distinguish a section 804 product when selecting the product on the pharmacy shelf (84 FR 70796 at 70819). The labeling statement may also aid in pharmacovigilance (84 FR 70796 at 70820). The phrase “to reduce its costs to the American consumer” is not necessary to achieve these ends.

(Comment 38) One comment seeks clarification regarding whether, if a manufacturer updates the labeling or packaging of a product, the labeling for an eligible prescription drug would also need to be updated. The comment also requests clarification regarding whether paper labeling will be included in the package of the imported prescription drug. Another comment questions who would be responsible for ensuring that labeling of drugs imported under the rule reflects safety labeling updates.

(Response 38) As discussed in the NPRM, an Importer is responsible for relabeling a drug, or arranging for it to be relabeled, to meet the requirements of the final rule. The relabeling and associated limited repackaging activities must meet applicable requirements, including applicable current good manufacturing practice (CGMP) requirements under parts 210 and 211 (21 CFR parts 210 and 211). Consistent with the NPRM, we have clarified in the final rule that at the time an eligible prescription drug is sold or dispensed by the Importer, it has to have been relabeled to be consistent with the FDA-approved labeling, including the carton and container labeling, Prescribing Information, and patient labeling, such as Medication Guides, Instructions for Use, and patient package inserts. In addition, the eligible prescription drug needs

to have been assigned a product identifier in compliance with section 582 of the FD&C Act. The relabeled eligible prescription drug will be considered consistent with the FDA-approved labeling if it varies from the FDA-approved labeling, including carton and container labeling, Prescribing Information, and patient labeling, solely to the extent described in this final rule.

(Comment 39) One comment says that failure to relabel a container closure system, such as a blister pack, could lead to consumer confusion or medication errors, but relabeling could breach or otherwise damage the container system.

(Response 39) If it is not possible to relabel a product without affecting the container closure system, such as a blister pack, then the product cannot be imported under a SIP. Certain repackaging that is necessary to perform the relabeling described in the final rule is permissible under this rule, but the rule does not allow repackaging of drugs that breaches the container closure system, such as a blister pack, which would introduce unnecessary risk of adulteration, degradation, and fraud for drugs imported under a SIP.

(Comment 40) Several comments express concern about the availability of new NDC numbers.

(Response 40) FDA is considering options to address potential demand for new labeler codes for NDC numbers to ensure availability.

(Comment 41) Several comments recommend that FDA assign a Canadian NDC as a unique labeler code and maintain the U.S. NDC product code and package size code. One comment also recommends that the use and assignment of NDC labeler codes under this rule be aligned with FDA's draft guidance for industry titled "Importation of Certain FDA-Approved Human Prescription Drugs, Including Biological Products, under Section 801(d)(1)(B) of the Federal Food, Drug, and Cosmetic Act," available at

<https://www.fda.gov/media/133646/download>.¹ One comment suggests that different NDCs for imported drugs sharing the same proprietary name as FDA-approved drugs may help in accurately capturing reports on counterfeits or suspect products for the imported drug.

(Response 41) Generally, FDA does not mandate the use of particular NDC numbers.

The final rule provides that imported drugs sharing the same proprietary name as FDA-approved drugs will have different NDCs from their FDA-approved counterparts.

(Comment 42) Several comments express concerns that the rule, as proposed, would open the “closed” U.S. drug distribution system for prescription drugs and could increase the opportunity for counterfeit and other substandard drugs to enter the supply chain. Several comments also assert that the proposed rule would undermine developments in supply chain security in the United States. Several comments express concerns about law enforcement resources. One comment suggests that the HHS Task Force Report regarding importation of prescription drugs that was submitted to Congress in December 2004 (Ref. 3) is still relevant today because there is still no Canadian system in place to ensure the pedigree of a product originally intended for Canada that becomes intended for the United States, nor are there any new international authorities to address the pedigree of the imported product and international recalls. Several comments support the proposed supply chain security requirements.

(Response 42) As described in the NPRM, we believe that section 804 of the FD&C Act can be implemented in a manner consistent with the section 804(I)(1) certification criteria through programs, overseen by States or Indian Tribes, or in certain future circumstances by pharmacists or wholesale distributors, and their cosponsors, if any, that require authorization by and reporting to FDA. The final rule includes requirements relating to the types of drugs eligible

¹ When final, this guidance will represent FDA’s current thinking on this topic.

for importation, the distribution channels and methods used for product traceability, and the testing of eligible prescription drugs for authenticity and degradation. In addition, in accordance with section 804 of the FD&C Act, the final rule requires that drugs imported under section 804 meet the specifications of an FDA-approved NDA or ANDA. These programs must also demonstrate significant cost reductions to the American consumer. In addition, as described in the NPRM (84 FR 70796 at 70800), in the intervening years since the Task Force Report was issued in 2004, Canada has amended its regulations to strengthen its oversight of both pharmaceutical manufacturing practices (Ref. 4) and pharmaceutical supply chain participants (Ref. 5), and regulatory harmonization between Canada and the United States has increased. As noted elsewhere, the final rule does not open the closed U.S. distribution system; instead, it expands it. The SIP Sponsor must demonstrate, among other things, how it will ensure that the supply chain in the SIP is secure, as required by § 251.3(d)(11).

(Comment 43) Several comments express concern that some product tracing provisions of the FD&C Act could strengthen the rule's safety requirements, but those provisions will not be widely implemented for several years. Several comments recommend that the final rule should not be implemented before the development of national standards for wholesale distribution licensure and State adoption of those standards because those standards will be a key element of FDA and State oversight over wholesale drug distributors and pharmacists, in addition to manufacturers.

(Response 43) Key traceability requirements added by the DSCSA, including product tracing, product identification (which involves serialization), and verification for handling of suspect and illegitimate product, have been in effect for several years and have been implemented by trading partners in the U.S. pharmaceutical distribution system. FDA

acknowledges and agrees that there are other important DSCSA supply chain security requirements that will be phased-in over the next several years, including national standards for licensure of wholesale distributors and third-party logistics operators, that will be vital to further securing the pharmaceutical supply chain, once implemented. However, FDA believes the final rule includes sufficient provisions to secure the supply chain, including requirements on direct purchasing of drugs and recordkeeping.

With regard to the comments recommending that the final rule should not be implemented before the development of national standards for wholesale distribution licensure and State adoption of those standards, as described in the NPRM (84 FR 70796 at 70801), States provide the primary oversight of wholesale distributors' storage, handling, and distribution practices to ensure the quality of drugs is maintained. States also ensure that pharmacies and pharmacists comply with statutes and regulations governing the practice of pharmacy, which includes dispensing of drugs to patients. States have the authority to inspect pharmaceutical supply chain participants and to take disciplinary action against them if warranted. States also have tools that they can use to respond rapidly should activities under a SIP adversely affect the public health.

However, in considering these and other comments regarding licensure of wholesale distributors as discussed in the NPRM, we have modified the definition of "wholesaler" in the final rule. Section 804(a)(5) of the FD&C Act states that "wholesaler" means, in general, "a person licensed as a wholesaler or distributor of prescription drugs in the United States under section 503(e)(2)(A)." Several years after the addition of section 804(a)(5), the DSCSA amended section 503(e) of the FD&C Act such that section 503(e)(2)(A) no longer addressed the licensure of wholesalers or distributors (section 503(e)(2)(A) currently sets forth reporting

obligations for persons engaged in wholesale distribution). Accordingly, in the NPRM, FDA defined “wholesaler” as, in general, “a person licensed as a wholesaler or distributor of prescription drugs in the United States under section 503(e)(1) of the Federal Food, Drug, and Cosmetic Act.” Upon further consideration, and in light of comments received on wholesale distribution licensure, FDA has further modified the definition of “wholesaler” in the final rule to mean a licensed wholesale distributor, as the terms “licensed” and “wholesale distributor” are defined in sections 581(9)(A) and (29) of the FD&C Act, respectively, of the FD&C Act. This modification is consistent with section 804(a)(5) of the FD&C Act, which incorporates section 503(e)(2)(A) as it had applied prior to DSCSA. At the time it was incorporated into part 804, section 503(e)(2)(A) had required that, in accordance with FDA regulations that were later established in 21 CFR part 205, “no person may engage in the wholesale distribution in interstate commerce of drugs subject to [section 503(b)] in a State unless such person is licensed by the State.” (See Prescription Drug Marketing Act of 1987, P. L. 100-293, Sec. 6). The incorporation into this rule of definitions in sections 581(9)(A) and 581(29) added by DSCSA clarifies that even prior to Federal standards being effective, a wholesale distributor must have a license under either section 503(e) or section 582(a)(6), as applicable. Section 582(a)(6) provides that having a valid license under State law is sufficient for a wholesale distributor to be considered “licensed” or “authorized” for purposes of meeting the DSCSA requirements that this rule incorporates.

This clarifies our intent, as expressed in the NPRM, that wholesalers participating in a SIP as Importers are subject to all applicable DSCSA requirements in section 582 of the FD&C Act. This modification also ensures that such wholesale distributors are considered to be

“authorized” for purposes of DSCSA in advance of FDA’s establishment of national standards for wholesale distributor licensure, as prescribed in section 583 of the FD&C Act.

Finally, we also conclude that defining “wholesaler” through use of the term “wholesale distributor,” rather than “wholesaler or distributor” as stated in section 804, aligns with DSCSA, and, because it is more in line with current terminology and usage in the supply chain industry, adds clarity and consistency.

(Comment 44) Several comments say that it is not uncommon for prescription drugs to be purchased and imported directly into Canada in bulk by a manufacturer and then be repackaged and relabeled by a third party. The comments therefore recommend allowing the importation, repackaging, and relabeling of “bulk” eligible prescription drugs that lack finished packaging and labeling. One comment suggests that the final rule should allow importation of drugs that have not been approved in Canada. Other comments express concern about risks posed by transshipments and counterfeits from or through Canada.

(Response 44) We decline to make these changes in the final rule. The final rule provides that a SIP Sponsor must ensure that each drug imported under the SIP is HPFB-approved and labeled for sale in Canada from the point of manufacture until it reaches the Foreign Seller. To help ensure that drugs imported under a SIP are not transshipped through Canada and to reduce opportunities for counterfeiting or other forms of fraud, the final rule requires that each drug imported under the SIP and manufactured outside Canada must be authorized for import into Canada by the manufacturer, labeled by the manufacturer for the Canadian market, and imported into Canada before importation under the SIP. In addition, each drug imported under the SIP must be sold by the manufacturer directly to a Foreign Seller, which ships the drug directly to the Importer in the United States. The Importer(s) and Foreign

Seller(s) identified in the SIP must meet the applicable requirements of the final rule and section 582(c) and (d) of the FD&C Act.

(Comment 45) Several comments address whether imported eligible prescription drugs might be considered suspect. One comment asks what a Foreign Seller should do with suspect products. One comment suggests additional reporting requirements. One comment recommends adding a requirement for a Foreign Seller to report to FDA and trading partners any suspect product and any product that is at a high risk of illegitimacy. One comment supports adding provisions in the proposed rule requiring notification of illegitimate products based on requirements in the FD&C Act.

(Response 45) We decline to make changes in response to these comments. Section 581 of the FD&C Act defines various terms for purposes of meeting the requirements of the DSCSA. Although imported eligible prescription drugs, like other products that enter the U.S. drug supply chain, may be considered “suspect” or “illegitimate” for a variety of reasons per section 581(21) and (8), respectively, as noted in the NPRM (84 FR 70796 at 70816), the Agency would not consider the eligible prescription drugs imported in accordance with the requirements of this rule to be “diverted” for the purpose of meeting verification obligations under DSCSA, solely as a result of being imported under section 804 of the FD&C Act and this final rule. However, such a product could still be found to be “suspect” or “illegitimate” for having other characteristics listed in section 581(21) and (8) of the FD&C Act (e.g., counterfeit or stolen).

We also note that separate from the definitions of “suspect product” and “illegitimate product,” as those terms are used for the purposes of meeting verification requirements under the DSCSA, the NPRM introduced, and this rule establishes, the terms “suspect foreign product” and “illegitimate foreign product” with regard to obligations that the Foreign Seller must meet for the

drugs it receives from the manufacturer and intends to send to the Importer under a SIP. Under the final rule, a Foreign Seller must have systems in place to determine whether a drug in its possession or control that it intends to sell to the Importer under a SIP is a suspect foreign product. If the Foreign Seller determines that a drug in its possession or control is a suspect foreign product, or if the Foreign Seller receives a request for verification from FDA that the Foreign Seller has determined that a product within its possession or control is a suspect foreign product, a Foreign Seller must: (1) quarantine the product within its possession or control until the product is cleared or dispositioned; (2) promptly conduct an investigation, in coordination with the Importer and the manufacturer, as applicable, to determine whether the product is an illegitimate foreign product, and verify the product at the package level, including the SSI; and (3) if the Foreign Seller makes the determination that a suspect foreign product is not an illegitimate foreign product, promptly notify FDA of the determination for those products that FDA has requested verification (the product may be further distributed). The final rule requires steps for the Foreign Seller to quarantine and properly disposition illegitimate foreign product to ensure that the product is not further distributed, in addition to notifying FDA and the Importer of products determined to be illegitimate foreign products.

We also note that the definitions of “suspect foreign product” and “illegitimate foreign product” proposed in the NPRM, and finalized here, include the use of the term “diverted.” In investigating a potentially suspect foreign product or identifying an illegitimate foreign product, a Foreign Seller may conclude a drug it receives is “diverted,” which for the purposes of these obligations means that there was not a direct transaction of the drug from the manufacturer to the Foreign Seller as required under this rule. For example, a Foreign Seller may conclude that a drug it receives from the manufacturer is “diverted,” if the product left the Canadian

pharmaceutical supply chain and is reintroduced in Canada in a transaction with the manufacturer or other supply chain entity; or the product is labeled for sale in a non-Canadian and non-U.S. market and is introduced into the Canadian pharmaceutical distribution supply chain through a transaction with the manufacturer or other supply chain entity.

Finally, the requirement in the DSCSA that a covered drug that is at high risk of illegitimacy be reported to the FDA and immediate trading partners is an obligation limited to manufacturers who may have specific programs in place that could generate such information. We believe that the final rule includes sufficient additional provisions to secure the supply chain without a “high risk of illegitimacy” provision that is similar to that which pertains only to manufacturers under DSCSA.

(Comment 46) Several comments suggest that Foreign Sellers should be required to comply with all requirements for relabelers in the United States. Some of these comments highlight the importance of a short, secure supply chain. One comment proposes that Foreign Sellers be subject to the requirements of repackagers.

(Response 46) FDA declines to make changes in response to these comments, because we believe the final rule’s requirements (which include requirements to ensure a short, secure supply chain) are sufficient to maintain supply chain security. Specifically, under the final rule, a Foreign Seller is responsible for relabeling drug products solely to affix the SSI to or imprint the SSI on each package and homogenous case of the eligible prescription drug(s). The Foreign Seller is required to adhere to all applicable CGMP requirements in accordance with section 501(a)(2)(B) of the FD&C Act and part 211. In addition, as noted in the NPRM (84 FR 70796 at 70814), the Foreign Seller must maintain records associating the SSI with the DIN and all the

records it received from the manufacturer upon receipt of the original shipment intended for the Canadian market.

(Comment 47) Several comments address a Foreign Seller's responsibilities with regard to the SSI. One comment asserts that although the rule states that the SSI should be "unique," the SSI could be duplicated between Foreign Sellers. The comment further suggests that the SSI would not allow traceability back to a manufacturer because, unlike a product identifier, the SSI does not contain the serial number of the manufacturer. One comment seeks clarification about what information a Foreign Seller needs to maintain about products received from a manufacturer.

(Response 47) Although FDA acknowledges the possibility that SSIs could be duplicated between Foreign Sellers, we have revised the rule to require, as described in the NPRM (84 FR 70796 at 70814), that the Foreign Seller maintain records associating the SSI with the Canadian DIN and all the records it received from the manufacturer upon receipt of the original shipment intended for the Canadian market. Those records received from the manufacturer upon receipt of the original shipment are the same as those that the manufacturer is required to submit to the importer under § 251.14(b).

FDA also notes that while the SSI is required to be affixed by the Foreign Seller on the portion of drugs received from the manufacturer that it intends to place into U.S. commerce in a transaction with the Importer, this requirement is intended to work in complementary fashion to other safeguards in the rule, including a requirement for a direct purchase between the Foreign Seller and manufacturer, and requirements on the Importer to ensure that the records received from the Foreign Seller accord with those the manufacturer provided to the Foreign Seller upon

sale of the product for the Canadian market, to ensure that the product has come directly from the original manufacturer.

FDA believes that the SSI requirement is necessary as an additional safeguard in the rule to allow for Importers and Foreign Sellers to verify the product that they transacted at the package level; such a requirement helps foster the ability of Importers and Foreign Sellers to quickly identify potentially suspect or illegitimate foreign products.

(Comment 48) Several comments suggest that the rule should allow relabeling of drugs to occur in Canada.

(Response 48) FDA declines to make this change. The final rule requires that relabeling only take place after the Agency has accepted the results of the Statutory Testing, which takes place at a qualifying laboratory in the United States. This avoids the potential diversion that could occur if eligible prescription drugs are relabeled for the U.S. market prior to import, and then fail the testing requirements. If eligible prescription drugs were relabeled in Canada before they were tested in the United States, diversion could happen before or after export of the refused drugs to Canada. Eligible prescription drugs cannot be relabeled in Canada after they are tested in the United States, because, as explained later, sampling upon arrival in the United States helps ensure that the sample is selected from the actual shipment of drugs that arrives in the United States. In addition, if the drugs are counterfeit, they would be counterfeits of the Canadian drug. Relabeling the drugs in Canada would destroy the evidence of counterfeiting which is often found on the label. The Importer and FDA would, therefore, be impeded in our efforts to detect that a drug being imported under a SIP is a counterfeit.

(Comment 49) Several comments raise concerns about whether the product identifier that would be affixed or imprinted by an Importer, if the Importer intends to place the product into further transactions in commerce, provides sufficient information about the product's origin.

(Response 49) The final rule provides that once the Importer receives an eligible prescription drug from the Foreign Seller, relabeling would need to include affixing or imprinting a product identifier that is associated with the SSI that the Foreign Seller assigned to the product before sending it to the Importer. As noted in the NPRM (84 FR 70796 at 70815), a relabeler who contracts with the Importer to affix a product identifier on the Importer's behalf must, even if not engaged in a repackaging operation with respect to the eligible prescription drug, have systems and processes in place to meet applicable requirements of a "repackager" under section 582(e) of the FD&C Act for any transaction involving the eligible prescription drug.

As described in the NPRM (84 FR 70796 at 70815), per section 581(14) of the FD&C Act, the product identifier must include a "standardized numerical identifier" (SNI), as that term is defined in section 581(20) of the FD&C Act; the lot number assigned by the manufacturer; and expiration date of the product and be in human and machine-readable form encoded in a two-dimensional barcode. An SNI consists of an alphanumeric serial number and NDC under section 581(20) of the FD&C Act. With regard to the serial number component of the SNI, the Importer may elect to use the same serial number (i.e., the SSI) that the Foreign Seller had previously assigned to the product, or the Importer may elect to assign a new serial number. Under the final rule, the Importer would need to maintain records, for not less than 6 years, that allow the Importer to associate the product identifier it affixed or imprinted to each package and homogenous case of product it received from the Foreign Seller, with the SSI that had been

assigned by the Foreign Seller, and the Canadian DIN that was on the package when the Foreign Seller received the product from the original manufacturer. The Foreign Seller in turn is required to maintain records associating the SSI to the Canadian DIN. As noted in the NPRM (84 FR 70796 at 70816), this recordkeeping is analogous to the record retention requirement in section 582(e)(2)(A)(iv) of the FD&C Act for a repackager that associates a product identifier with a manufacturer-affixed product identifier. Furthermore, the final rule clarifies that the lot number that is included in the product identifier is that assigned by the manufacturer of the eligible prescription drug.

(Comment 50) Several comments urge FDA to require product identifiers to be affixed on all products imported pursuant to the final rule, including where an Importer intends to directly dispense the product to patients.

(Response 50) We agree with these comments and have accordingly modified the rule to clarify that the requirement to affix or imprint a product identifier applies to all eligible prescription drugs. The final rule provides that an Importer must facilitate affixation or imprinting of a product identifier on each package or homogenous case of an eligible prescription drug upon receiving it from the Foreign Seller. In the NPRM (84 FR 70796 at 707815), we had signaled that if an Importer is a pharmacist who directly dispenses the product to patients, a product identifier would not be required to be affixed or imprinted on each package and homogenous case of the eligible prescription drug. However, after consideration of comments, we agree that in the context of the section 804 program, all eligible prescription drugs (which must meet the definition of “product” under the DSCSA) warrant a product identifier that is affixed or imprinted by the Importer or by a relabeler that the Importer authorizes. Even in the instances of an Importer who is a pharmacist intending to dispense the product directly to

patients, the affixing or imprinting of a product identifier is needed in order to facilitate verification activities through the Importer's maintenance of records associating the product identifier at the package level with the SSI that had been placed by the Foreign Seller, thus enhancing supply chain security.

(Comment 51) Several comments oppose providing exemptions to Importers from certain DSCSA requirements, citing concerns about opening a path for counterfeit and unsafe drugs into the U.S. supply chain.

(Response 51) The final rule identifies specific exemptions from DSCSA requirements in section 582 of the FD&C Act, as permitted by section 582(a)(3)(iii), because they would be difficult or impossible to apply to eligible prescription drugs imported under a SIP. FDA understands and agrees with the importance of the underlying statutory requirements to supply chain security and considered potential effects on supply chain security in identifying such exemptions. To ensure the exemptions from section 582 of the FD&C Act do not compromise the security of the supply chain for drugs imported under section 804 of the FD&C Act, the final rule includes additional safeguards to protect the public health. For example, under the final rule, an Importer is exempt from the prohibition on receiving a product for which the previous owner did not provide the transaction history, transaction information, and transaction statement, under section 582(c)(1)(A) or (d)(1)(A) of the FD&C Act as applicable, provided the Importer receives from the Foreign Seller certain transaction-related information that is adequate to ensure no additional risk to supply chain security. These additional safeguards are authorized under section 804(c)(3) of the FD&C Act and are necessary for the Secretary to certify that implementation of section 804 of the FD&C Act would pose no additional risk to the public's health and safety.

(Comment 52) Some comments question FDA's authority to allow exemptions from DSCSA through rulemaking, because the provisions have been established by Congress through statute.

(Response 52) Congress established in DSCSA that exemptions from section 582 of the FD&C Act are permissible; indeed, the Secretary was given explicit authority to identify such exemptions through a process established by the Agency in guidance (see section 582(a)(3)(A)(iii) of the FD&C Act). The exemptions that were proposed in the NPRM, which is being finalized here, are established in accordance with this statutory authority. Although FDA is establishing these exemptions through rulemaking rather than guidance, we believe this is an appropriate exercise of the section 582 authority because the statute does not foreclose FDA from establishing exemptions through notice-and-comment rulemaking. Because the exemptions identified by FDA in the final rule would apply to SIP participants generally, and because we believe that these exemptions are appropriate only in the context of the requirements established by this rule, including safeguards to protect supply chain security, providing these exemptions concurrently with establishing such safeguards is a sensible and appropriate exercise of FDA's statutory authority in this circumstance. FDA intends to continue to consider and, as appropriate, grant other exemptions consistent with the statutory authority provided in section 582 of the FD&C Act.

(Comment 53) Several comments ask about the availability of laboratories that would meet the statutory and regulatory criteria to become approved qualifying laboratories. In particular, some comments express concerns that the requirement that a qualifying laboratory have an FDA inspection history could result in insufficient options for laboratory partners for SIPs.

(Response 53) We believe there is a sufficient number of FDA-inspected laboratories across the United States capable of doing this testing. About 200 domestic, FDA-inspected laboratories offer CGMP-related contract testing services. Independent laboratories that are contracted to act as a CGMP quality control lab (i.e., laboratories that test samples to satisfy the CGMP regulations (including, for example, §§ 211.165, 211.166, and 211.167 regarding batch testing before distribution) are required to register with FDA and are subject to inspection to verify conformance with the CGMP regulations applicable to laboratory testing and quality control (including, for example, §§ 211.160, 211.194, and 211.22). FDA publishes inspection status information on its website where you can search names of contract laboratories to see their inspection history and FDA classification of compliance status (see the Inspection Classification Database at <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-classification-database>. You can also search FDA's website to see if a warning letter has been issued to a firm at <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters>. As we stated in the NPRM, we intend to approve qualifying laboratories for use by a SIP on a case-by-case basis as part of our review and authorization of a SIP Proposal. In addition, we intend to consider publishing a list of approved qualifying laboratories for the benefit of developing a SIP Proposal.

(Comment 54) One comment opposes requiring qualifying laboratories to hold CGMP certification.

(Response 54) The final rule does not require qualifying laboratories to hold CGMP certification. Qualifying laboratories need to comply with the applicable elements of the CGMP

requirements, including provisions regarding laboratory controls in § 211.160 and regarding laboratory records in § 211.194.

(Comment 55) One comment suggests that because the proposed rule allows the potential for multiple SIP Proposals that include a particular eligible prescription drug, it is important to have clear and consistent quality standards to help ensure that medications have the correct identity, strength, and purity when consumed by patients.

(Response 55) Section 804 of the FD&C Act and the final rule contain numerous provisions that work together to help ensure the quality of products imported under this rule. Among other things, the statute and this final rule require that Statutory Testing either be performed by the manufacturer of an eligible prescription drug or, if such testing is performed by the Importer, that the manufacturer supply the information the Importer needs to authenticate the drug. The final rule specifies that this information includes, among other things, any relevant testing protocols that the manufacturer has developed.

(Comment 56) Several comments suggest that, if a manufacturer does not conduct testing itself, Importers should be allowed to conduct Statutory Testing, or sampling for that testing, in Canada before importation.

(Response 56) FDA declines to make the requested change. Section 804 of the FD&C Act provides that Statutory Testing must be conducted by a qualifying laboratory, and a qualifying laboratory must be in the United States and approved by the Secretary. Sampling upon arrival in the United States helps ensure that the sample is selected from the actual shipment of drugs that arrives in the United States.

(Comment 57) One comment urges FDA to clarify that manufacturers cannot satisfy the Statutory Testing requirements through preexisting release or conformance testing. The

comment also recommends that, if drug products have already undergone release or conformance testing at a qualifying laboratory in the United States, Statutory Testing should be conducted at a separate, independent laboratory to ensure thorough analysis before the products enter the U.S. market.

(Response 57) Section 804 of the FD&C Act and the rule provide that the manufacturer or the Importer must arrange for samples from shipments of eligible prescription drugs to be tested by a qualifying laboratory. We believe it is sufficiently clear that the statute and this regulation do not allow manufacturers to provide testing results, such as those from the manufacturer's batch release or conformance testing. If the manufacturer performs the testing required under section 804(e)(1) of the FD&C Act, the following information must be submitted in electronic format directly to FDA via the Electronic Submissions Gateway (ESG) or to an alternative transmission point identified by FDA: (1) the testing results, (2) a complete set of laboratory records, (3) a detailed description of the selection method for the samples, (4) the testing methods used, (5) complete data derived from all tests necessary to ensure that the eligible prescription drug meets the specifications of the FDA-approved drug that are established in the NDA or ANDA, (6) a Certificate of Analysis, and (7) any other documentation demonstrating that the testing meets the requirements under section 804(e)(1) of the FD&C Act. We do not believe that it is necessary to require in the final rule, for drug products that have undergone release or conformance testing at a qualifying laboratory in the United States, that Statutory Testing be conducted at another, independent laboratory, as long as the approved and CGMP-compliant methods are used.

(Comment 58) One comment recommends that FDA require that sampling be done according to standards issued by the American National Standards Institute (ANSI).

(Response 58) The NPRM proposed to require that a statistical sample of a batch or shipment of section 804 drugs be randomly selected from the batch or shipment being tested or, in the alternative, that the sample be representative of the batch or shipment. We sought comment on whether we should specify a sampling method. We also sought comment on whether we should require that sampling be done according to an established standard such as those issued by the ANSI or by ASTM International. We did not conclude that the comments received provided adequate support for specifying a standard. At this time, we are not specifying a standard in the final rule but may consider providing future guidance on this subject.

(Comment 59) One comment recommends that a manufacturer be allowed no more than 10 calendar days to provide required information to an Importer.

(Response 59) We agree with the comment that a set timeframe for providing required information is appropriate but disagree with the proposed 10-day schedule. We have revised the final rule to require a manufacturer to supply to an Importer, within 30 calendar days of receiving a request, the required attestation and information statement, batch records, transaction information, Statutory Testing information, and authorization to use the FDA-approved labeling for the manufacturer's drug. The 30-day deadline aligns with the timeline for the Importer to submit a Pre-Import Request, which must be submitted 30 days prior to the entry or arrival of a shipment of eligible prescription drugs into the United States.

(Comment 60) One comment contends that drugs refused admission to the United States should be destroyed at the foreign trade zone or at the secured warehouse, and Importers should not be permitted to export them.

(Response 60) We decline to make these changes. The NPRM proposed that if FDA refuses admission into the United States the drug must be exported or destroyed by the Importer

within 90 calendar days of the refusal. This is consistent with section 801(a) and (d)(1) of the FD&C Act, neither of which bar exportation.

In response to the suggestion in the comment that FDA prohibit export for all refused drugs offered for import under a SIP, we recognize that there may be some circumstances where export could be appropriate. For example, in the NPRM we stated that FDA would intend to refuse admission if 6 months have passed from the entry date of the shipment. It is possible that these drugs would not have been relabeled for the U.S. market and may be saleable in Canada. Destruction could prevent the SIP from recouping their loss by exporting the drugs back to the Foreign Seller and add additional cost to the SIP.

Finally, if we have concerns regarding drugs offered for import under a SIP that are refused admission being exported back to Canada or another country, FDA and CBP have tools to address this, such as pursuing destruction of the drugs or notifying the country to which the product would be exported.

(Comment 61) Several comments suggest that if a SIP Sponsor determines that a drug, manufacturer, Foreign Seller, Importer, qualifying laboratory, or other participant in or element of the supply chain in the authorized SIP does not meet all applicable requirements of the FD&C Act, FDA regulations, and the authorized SIP, the SIP Sponsor should not need to immediately stop importation of all drugs under the SIP. One comment asserts that identification of an illegitimate product in the SIP should be grounds for automatic, temporary suspension and potential full revocation of the SIP. One comment notes that if identification of illegitimate product introduced by a SIP were to lead to automatic revocation of the SIP's authorization, it could have the counterproductive result of making trading partners less inclined to identify and report the illegitimate product.

(Response 61) As discussed in the NPRM, under certain circumstances set forth in section 804(g) of the FD&C Act, FDA is required to suspend importation. Section 804(g) of the FD&C Act provides that the Secretary must require that importations of a specific prescription drug or importations by a specific Importer under section 804(b) be immediately suspended on discovery of a pattern of importation of that specific prescription drug or by that specific Importer of drugs that are counterfeit or in violation of any requirement under section 804, until an investigation is completed and the Secretary determines that the public is adequately protected from counterfeit and violative prescription drugs being imported under section 804(b). In some circumstances, as described in the NPRM, FDA may suspend a SIP in whole or in part or FDA may revoke authorization of a SIP, in whole or in part. To ensure that FDA has current relevant information about SIP participants, we have revised the rule to require a SIP Sponsor to inform FDA of any new applicable criminal conviction, violation of law, or disciplinary action.

(Comment 62) Several comments ask FDA to limit requirements that they characterize as duplicative or redundant, citing adverse event reports, individual case safety reports (ICSRs), and recall requirements. In addition, one comment suggests that patients might not know whom to contact regarding an adverse event or a question about medication.

(Response 62) FDA declines to make substantive changes in response to these comments. We have made some minor revisions from the provisions in the NPRM for clarity. For example, in one instance we have revised the wording to align with existing comparable requirements in 21 CFR 314.80 (under § 251.18(d)(9), an Importer must “develop” written procedures to meet their obligations under that subpart because this encompasses the requirement to “maintain” and “follow” such written procedures), but such clarifications do not change FDA’s interpretation of

the scope of existing responsibilities under § 314.80 or other existing safety reporting requirements.

We do not believe the reporting requirements in the final rule are duplicative or redundant. The rule requires an Importer to establish and maintain records and submit to FDA and the manufacturer reports of all adverse events associated with the use of the drug products it imports under section 804 of the FD&C Act and this final rule. An ICSR is a description of an adverse event related to an individual patient or subject. The final rule outlines when and how an Importer must submit ICSRs for domestic adverse events, and follow up reports, to FDA and the manufacturer. As described in the NPRM (84 FR 70796 at 70821), these reports will aid the manufacturer in its pharmacovigilance efforts, and it will provide FDA with information that may be relevant to its review of SIP Proposals and Pre-Import Requests as well as to its oversight of drugs imported under section 804 of the FD&C Act and section 804 in general. In the event of a recall, Importers must, upon request by FDA, provide to FDA the transaction history, information, and statement, as those terms are defined in section 581(25), (26), and (27) of the FD&C Act, for the recalled drugs. We have clarified in the final rule that, in the event of a recall, Foreign Sellers must also provide certain transaction information to FDA upon request.

(Comment 63) Several comments assert that it is inappropriate to establish “medication error” reporting requirements only for SIPs.

(Response 63) We have decided not to establish medication error reporting requirements for SIPs at this time, before establishing such requirements for prescription drugs generally, and have revised the final rule to remove requirements related to reporting medication errors. FDA might at a later time consider whether it should establish medication error reporting requirements for SIPs.

(Comment 64) Several comments request clarification regarding recall responsibilities.

One comment says that the timeframe for adverse event reporting could lead to significant delays in recalls.

(Response 64) The rule requires that each SIP proposal include a recall plan that explains how the SIP Sponsor will obtain additional recall or market withdrawal information, such as by obtaining recall information from an Importer, and how the SIP Sponsor will ensure that recall or market withdrawal information is shared among the SIP Sponsor, the Foreign Seller, the Importer, and FDA, and provided to the manufacturer. In addition, the rule requires that each SIP must have a written recall plan that describes the procedures to perform a recall of the product and specifies who will be responsible for performing the procedures. The recall plan must cover recalls mandated or requested by FDA and recalls initiated by the SIP Sponsor, as well as recalls in Canada or the United States initiated by a drug's manufacturer that implicate a drug imported under a SIP, with which the Foreign Seller or Importer must cooperate. If FDA or any participant in a SIP determines that a recall is warranted, the SIP Sponsor must effectuate the recall in accordance with its written recall plan. We have revised the rule to clarify an Importer's and a Foreign Seller's responsibilities in a recall. We do not believe that the timeframes for adverse event reporting, which are consistent with other FDA requirements for adverse event reporting, would lead to significant delays in effectuating a recall.

(Comment 65) One comment suggests that allowing section 804-imported drugs to coexist on the market with manufacturers' drugs would introduce confusion to real-world data (RWD) collection and bias real-world evidence (RWE) analyses.

(Response 65) The comment assumes that an eligible prescription drug will have quality concerns that could not be accounted for in RWD sources and RWE analysis. However, an

eligible prescription drug would need to meet the conditions in an FDA-approved NDA or ANDA, including quality specifications. In addition, there may be ways of distinguishing eligible prescription drugs imported under section 804 of the FD&C Act in RWD sources, for example, by NDC.

F. Certification

(Comment 66) Several comments address the certification that is required under section 804(l) of the FD&C Act. One comment argues that the certification cannot become null and void for any reason once it is made. Instead, the comment argues that the proper way to address problematic importations is to adopt a proposed new codified provision that would give the Secretary the authority to order the cessation of a particular SIP under certain specified circumstances.

(Response 66) As stated in the NPRM (84 FR 70796 at 70803), the Secretary's certification rests on the authorities and requirements outlined in the regulation issued to implement section 804. If any one of those provisions is invalidated, certification would become null and void because it was based on an understanding regarding how section 804 would be implemented that, under this scenario, would be factually incorrect and legally invalid. We decline to add the codified provision proposed in the comment because this final rule includes § 251.7, also included in the proposed rule, which provides FDA the authority to suspend or revoke a SIP under the circumstances set forth in that section or § 251.18.

(Comment 67) Several comments assert that the NPRM contained no assessment of whether importation under section 804 of the FD&C Act would result in a significant reduction in the cost of covered products to the American consumer and that section 804(l) requires factual findings on cost savings before the certification can be made.

(Response 67) We disagree. For section 804 to become effective, subsection (I) requires the Secretary to certify that the implementation of this section 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. Through this final rule, implementation of section 804(b) through (h) will result in a significant reduction in the cost of covered products to the American consumer. In particular, § 251.3(e)(9), as revised, requires the SIP Sponsor's importation plan to explain, in a manner sufficiently detailed to allow for a meaningful evaluation, how the Sponsor will ensure that the SIP will result in a significant reduction in the cost to the American consumer; and § 251.7(c) provides that FDA may revoke the authorization of a SIP if, among other reasons, the Agency determines that continued implementation of the SIP will not result in a significant reduction in the cost of drugs covered by the SIP to the American consumer. Together, these provisions will ensure that there is a meaningful assessment of whether drugs imported under a particular SIP will result, and are resulting, in a significant reduction in the cost of covered products to the American consumer, which, in turn, allows the Secretary to make the cost-related finding for the certification under section 804(I).

(Comment 68) One comment contends that the Secretary is impermissibly relying on States and Indian Tribes to support his certification decision under section 804(I) because such reliance on third parties to make the certification findings is contrary to the plain language of section 804 of the FD&C Act. The comment further contends that this rule would effectively subdelegate HHS's fact-finding role to SIP Sponsors and cites *U.S. Telecom Ass'n v. FCC*, 359 F.3d 554 (D.C. Cir. 2004) for the proposition that delegating fact-finding to the states is unlawful absent congressional authorization.

(Response 68) In conjunction with this final rule, the Secretary is certifying that implementation of section 804(b)-(h) 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. The final rule is designed to ensure that FDA and other components of HHS receive the necessary information to ensure this certification applies to a particular SIP. Ultimately, it will be the Secretary, acting through FDA, who will find that a particular SIP proposal meets the certification requirements based on the information received as part of the proposal. We note that it is a prohibited act under section 301(aa) of the FD&C Act to import a prescription drug in violation of section 804, falsify any record required to be maintained or provided to the Secretary under such section, or violate the regulations issued under such section. Accordingly, unless the Secretary has reason not to do so, he may consider the information he receives pursuant to this final rule and FDA's evaluation of such information to ensure that a SIP 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. The Secretary has not delegated the certification decision or any other finding to the states or any other third party. Consequently, the comment's reference to *U.S. Telecom Ass'n v. FCC* is inapposite because in that case the court considered, in relevant part, whether a federal agency delegated its authority to make certain *determinations* to a state.

(Comment 69) One comment argues that in order to make the certification under section 804(l), the Secretary must find that implementation of all 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. The comment argues that if the Secretary cannot make this finding with regard to section 804(j), then the certification cannot be made solely with regard to

section 804(b)-(h) of the FD&C Act. The comment cites *Vermont v. Leavitt*, 405 F. Supp. 2d 466 (D. Vt. 2006), in which the court stated that interpreting section 804(l)(1) to apply to only section 804(b)-(h) is “a convoluted and implausible interpretation” and “is undermined by the fact that Congress used the term ‘subsection’ in other provisions of section [804].” The comment also cites *Montgomery County. v. Leavitt*, 445 F.Supp.2d 505, 508 (D. Md. 2006) to support the assertion that FDA has concluded that the certification requirement in section 804 applies to the entire section and does not authorize a specific waiver for a discrete state pilot program.

(Response 69) We disagree that a certification under section 804(l) must cover all of section 804 of the FD&C Act. In general, section 804 contains two importation pathways: (1) commercial importation of drugs from Canada under subsections (b)-(h), and (2) personal importation under subsection (j). Each importation pathway must be certified by the Secretary under section 804(l) to be effective. However, section 804 does not explicitly require a certification to cover both pathways. In stating that this section only becomes effective if the implementation of the section meets the certification criteria, section 804(l) accomplishes two objectives: (1) ensuring that any provision in section 804 does not take effect unless the Secretary certifies that implementation of the provision would meet the certification criteria; and (2) providing for the possibility that implementation could take different forms, including implementing section 804 in a way that only pertains to the commercial importation pathway or the personal importation pathway.

The court’s decision in *Vermont v. Leavitt* does not support the comment’s assertion. In that case, the state of Vermont argued that the personal importation provisions in section 804(j) of the FD&C Act could be implemented without a certification because the certification

provision in section 804(l) only applies to the commercial importation pathway outlined in section 804(b)-(h). The court found this interpretation implausible. We agree with the court's decision that for any provision in section 804 to be in effect, it must be covered by a certification from the Secretary in accordance with section 804(l). The court did not also hold that any certification under section 804(l) must cover all of section 804. In fact, the court expressly did not reach this decision. *See Vermont v. Leavitt*, 405 F. Supp. 2d at 479.

Similarly, in *Montgomery County v. Leavitt*, the plaintiff argued that the certification requirement in section 804(l) of the FD&C Act did not apply to all of section 804, and that FDA could authorize a specific waiver for the proposed importation program before any certification is made. The court held that the certification provision applies to all of section 804 and, therefore, FDA's denial of the county's waiver request for its proposed importation program was mandated by Federal law because no certification had yet been made. Again, we agree with the court's decision that the certification provision applies to all of the provisions of section 804; accordingly, there must be a certification in place for the commercial importation pathway, the personal importation pathway, or both pathways, prior to implementation of such pathway(s).

(Comment 70) One comment argues that the certification under section 804(l) of the FD&C Act can only be made broadly and not with regard to only specific approved SIPs because section 804 contemplates a broad certification finding before the section goes into effect. In support of this argument, the comment states that: (1) section 804 does not provide that certification can be based on state-specific plans for only certain state residents, and if that was the Congressional intent, it could have been so limited; (2) the certification provision refers to the American consumer, not specific American consumers under particular plans; and (3) section 804 permits the opening of the closed U.S. drug distribution system that protects patients from

counterfeit and substandard drugs. In addition, the comment cites *Montgomery County v. Leavitt* and a letter from FDA to Montgomery County to support the proposition that the certification provision in section 804 does not authorize a specific waiver for a discrete state pilot program. The comment also cites to a government brief filed in the *Vermont v. Leavitt* litigation that it argues is inconsistent with the Agency's position on this issue in this final rule.

(Response 70) The Secretary's certification is based on the requirements and safeguards in this final rule. Through this implementation, the certification can be made because importation of drugs under section 804(b)-(h) of the FD&C Act will not increase the risk to the public's health and safety, and will lead to a significant reduction in the cost of covered products to the American consumer. Although the certification provision in section 804(I) does not expressly address the review of sponsored plans for importation, there is nothing in the provision that precludes the Secretary from basing the certification on an implementing regulation that ensures any importations made under section 804 meet appropriate standards, including a requirement that importation plans be sponsored by certain entities and reviewed and authorized by the Secretary. In fact, the certification provision contemplates that the Secretary will base his decision on certain requirements or other policies established by him because the provision asks whether *implementation* of section 804 will lead to the findings necessary to make the certification.

With regard to the argument that because the certification provision refers to the American consumer, the certification must be broad, it is not clear what is meant by the term broad. We do not believe that reference to the American consumer means that before a certification can be made, there must be a finding that all American consumers will benefit from a significant reduction in the cost of covered products. In any case, the Secretary's certification

does not limit the number of American consumers who could benefit from importation of drugs under section 804. A SIP or combination of SIPs could be broad in scope and provide significant cost savings to numerous Americans.

It is not clear how the argument that section 804 opens the closed U.S. distribution system supports the assertion that the certification in section 804(l) of the FD&C Act must be broad. In any case, this final rule does not open the closed U.S. distribution system; instead, it expands it. The SIP Sponsor must demonstrate, among other things, how it will ensure that the supply chain in the SIP is secure, as required by § 251.3(e)(11).

The references to *Montgomery County v. Leavitt* and the letter from FDA to Montgomery County mentioned in that decision do not support this comment's arguments. The court's decision and the cited letter from FDA refer to the ability of FDA to authorize a specific waiver for a discrete state pilot program *in the absence of a certification* under section 804(l). This case, along with the decision in *Vermont v. Leavitt*, agreed with FDA's position and found that such a program could not be authorized before the Secretary makes the required certification under section 804(l) of the FD&C Act.

As noted in the comment, the government's brief in the *Vermont v. Leavitt* litigation (Federal Defendants' Motion to Dismiss Plaintiffs' Complaint and Memorandum in Support) stated that section 804(l) asks the Secretary to certify whether the law should be effective for all Americans, not just those in one particular state. Similar statements were made in the government's brief in the *Montgomery County v. Leavitt* litigation. In contrast, as stated above, the Secretary's certification and this final rule do not limit the number of American consumers who could benefit from importation of drugs under section 804 of the FD&C Act. All states can participate under the rule and, as noted elsewhere, pharmacists or wholesalers may, under certain

circumstances, be able to sponsor a SIP without the cosponsorship of a State or Indian Tribe.

The involvement of a sponsor does not limit the scope of imports; instead it is meant to provide additional oversight to ensure that any such imports are safe.

As stated above, although section 804(*I*) does not expressly address importation plans that are submitted to the Secretary for review and overseen by sponsors, it does not preclude them either. Instead, the certification provision asks whether 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. Section 804(*I*), itself, does not impose any requirements on *how* implementation of section 804 of the FD&C Act would be done in order to enable those findings under the certification. This rule is designed to ensure that any authorized SIP poses no additional risk to the public's health and safety and results in a significant reduction in the cost of covered products to the American consumer, in accordance with the Secretary's certification.

(Comment 71) One comment notes that the proposed rule cites section 804 of the FD&C Act as part of the legal authority for the rule, and that section 804 is not in effect until the Secretary makes the certification required under section 804(*I*). The comment argues that the proposed rule must be withdrawn because it was issued without an effective statutory basis.

(Response 71) In accordance with the Administrative Procedure Act (APA) (5 U.S.C. 553(b)), the proposed rule includes reference to the legal authorities under which it was proposed. As noted by the comment, the referenced legal authorities in the proposed rule include section 804 of the FD&C Act. At the proposed rule stage, the rule is proposed to be issued under one or more legal authorities. The proposed rule does not have legal effect at the time it is issued; therefore, the cited legal authorities do not necessarily need to be in effect at that time.

The Secretary is making the required certification under section 804(l) concurrent with this final rule. Therefore, section 804 is in effect as a legal authority for this final rule. Furthermore, the certification requirement was included in section 804 so that the section would not be implemented before a certification is made. We do not believe that Congress intended for the provision to preclude the issuance of a proposed rule proposing how the section could be implemented in a manner that meets the basis for a certification, once that certification is made. Moreover, under the comment's reasoning, section 804(l) effectively repeals by implication the notice and comment provision of the APA. The Court has consistently noted that repeal by implication is disfavored. *See Morton v. Mancari*, 417 U.S. 535, 549-550 (1974).

(Comment 72) One comment contends that the certification required under section 804(l) of the FD&C Act is a rule within the meaning of the APA and is not subject to any exception from notice and comment requirements in that act. The comment argues that the notice and comment requirements were not met because the public did not have access to the information the Secretary relied on to make the certification and, therefore, could not meaningfully comment on it. The comment goes on to state that FDA should withdraw the proposed rule, place in the public record any basis the Secretary has for certification, and allow the public to comment.

(Response 72) A rule, as defined in the APA, 5 U.S.C. 551(4), is the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy or describing the organization, procedure, or practice requirements of an agency and includes the approval or prescription for the future of rates, wages, corporate or financial structures or reorganizations thereof, prices, facilities, appliances, services or allowances therefor or of valuations, costs, or accounting, or practices bearing on any of the foregoing. We do not agree that the certification under section 804(l) of the FD&C Act is

a rule that must undergo notice and comment rulemaking in accordance with the APA. The certification is a finding that functions as a procedural step that does not itself affect the rights or interests of outside parties. *Cf. Batterton v. Marshall*, 648 F.2d 694, 707-08 (D.C. Cir. 1980). In accordance with section 804(l), the certification is made to Congress. While the certification made by the Secretary leads to section 804(b)-(h) becoming effective, the only consequence of making section 804(b)-(h) effective is that, per section 804(b), the Agency can issue a regulation that was subject to the very process requested by the commenter (notice and comment rulemaking). Thus, the certification has no independent effect on outside parties that warrants notice and comment under section 553 of the APA. Moreover, because this rulemaking constitutes the basis for the certification, the certification *is* effectively undergoing notice and comment in the context of the rulemaking, and any additional notice and comment process for the certification would be duplicative. We also note that, even if the certification were an agency action under the APA, it is more in the nature of a declaratory order that clarifies FDA's position on the matters presented in section 804. See 5 U.S.C. 554(e) ("the agency, with like effect as in the case of other orders, and in its sound discretion, may issue a declaratory order to terminate a controversy or remove uncertainty"); *Wilson v. A.H. Belo Corp.*, 87 F.3d 393, 397 (9th Cir. 1996) (upholding a declaratory order that was issued *sua sponte*, in the absence of any parties before the Agency); *Time Warner Entm't Co., L.P. v. FCC*, 240 F.3d 1126, 1141 (2001) (an agency has "very broad discretion whether to proceed by way of adjudication or rulemaking"). Finally, unlike other provisions of section 804, section 804(l) does not direct the Secretary to implement the provision by issuing a regulation. The lack of such direction indicates that Congress did not intend for the notice and comment requirements to apply.

In any case, we do not agree that the public did not have an opportunity to meaningfully comment on the Secretary's certification. As stated above, the public did have an opportunity to comment on the certification in that it had an opportunity to comment on the rule, which constitutes the basis for the certification. Section 804(l) states that section 804 of the FD&C Act will become effective only if the Secretary certifies to Congress that the implementation of this section 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. The Secretary is making this certification on the basis of this final rule, which contains provisions and safeguards to ensure that any SIP that is authorized by FDA will be consistent with the certification. As stated in response to Comment 67, implementation of section 804(b)-(h) through this rule will result in a significant reduction in the cost of covered products to the American consumer because it requires, among other things, that the SIP Sponsor's importation plan explain, in a manner sufficiently detailed to allow for a meaningful evaluation, how the Sponsor will ensure that the SIP will result in a significant reduction in the cost to the American consumer. Other provisions of this rule ensure that a SIP will not pose an additional risk to the public's health and safety. The Agency sought and received comments on the proposed rule and is issuing this final rule after considering these comments. Because the certification relies on this final rule, the public had an opportunity to meaningfully comment on it.

G. FD&C Act Requirements

(Comment 73) One comment says that the proposed rule would not ensure that each prescription drug imported under section 804 complies with sections 501, 502, and 505 of the FD&C Act, as is required by section 804(c)(1) of FD&C Act. The comment says that as a result FDA will be required to refuse admission to section 804 drugs under section 801(a). The

comment says that a drug imported under this rule will be unapproved because it will differ from the drug approved in the NDA and ANDA. Manufacturing information, specifically information about the relabeler and about the relabeling of a section 804 drug, will not be in the NDA or ANDA of its FDA-approved counterpart, and there will be certain differences set forth in the rule between the labeling of a section 804 drug and the labeling in an FDA-approved NDA or ANDA. The comment says that FDA should apply its procedures for drug approval to each drug imported under section 804.

The comment also says that drugs imported under this rule will be misbranded because their labeling will falsely represent that they are FDA-approved and because the labeling could lead a consumer to mistakenly attribute the drug to the drug's manufacturer. Finally, the comment says that the rule will increase the likelihood that adulterated drugs will enter the U.S. market.

(Response 73) We agree with the comment that for drugs imported under section 804 there will not be "an approval of an application" under section 505(a) of the FD&C Act. Section 804 drugs will not themselves be the subject of an approved NDA or ANDA. They will, however, meet the requirement in section 804(c)(1) of the FD&C Act that they "compl[y] with section 505 (including with respect to being safe and effective for the intended use of the prescription drug)." Specifically, FDA interprets compliance with section 505 to mean that the HPFB-approved drug meets the conditions in an FDA-approved NDA or ANDA. Before a section 804 drug is imported pursuant to this rule, FDA must make a determination, on the basis of the Statutory Testing and information provided by the drug's manufacturer, that the drug meets the conditions in an approved NDA or ANDA.

The comment's alternative interpretation, requiring approval of an application under section 505 of the FD&C Act for drugs imported under section 804 of the FD&C Act, would render section 804 superfluous. If an Importer sought and obtained FDA approval of a drug that was previously only approved for sale in Canada, it would not need to import the drug under section 804. Instead, it could simply import the drug under section 801 of the FD&C Act without meeting any of the additional safeguards imposed under section 804. Thus, it is reasonable for FDA to interpret "complies with section 505 (including with respect to being safe and effective for the intended use of the prescription drug)" to mean that the HPFB-approved drug meets the conditions in an FDA-approved NDA or ANDA, without itself having an approved NDA or ANDA.

Section 804 drugs generally will bear the labeling of their FDA-approved counterparts, with certain exceptions set forth in this rule. Specifically, the labeling of a section 804 drug may differ from the approved labeling to the extent that it includes: (1) the section 804 drug's NDC number, , which will help with supply chain management and security, among other things, (2) the name of the Importer, which will ensure that the persons responsible for the product can be identified, (3) the labeling statement required by § 251.13(b)(4)(iv), which will help avoid confusion between products with the same name, help pharmacists distinguish a section 804 product when selecting the product on the pharmacy shelf, and, potentially, help with pharmacovigilance, and (4) the SIP's website address, which will also help avoid confusion by educating pharmacists, healthcare providers, pharmacy benefit managers, health insurance issuers and plans, as appropriate, and patients.

We disagree with the comment's assertion that section 804 drugs will be misbranded under section 502 of the FD&C Act because they are not FDA-approved. Section 804(h) of the

FD&C Act requires that the manufacturer of a section 804 drug authorize the Importer to use the approved labeling for the drug, while section 804(c)(3) provides that the regulations implementing section 804 must require that safeguards be in place to ensure that section 804 drugs comply with section 502, among other provisions. Section 804 would not require that Importers be authorized to use the approved labeling if doing so would make section 804 drugs misbranded and so not comply with section 502. In addition, the labeling will not mislead consumers about the manufacturer's role in the importation of a section 804 drug because of the labeling statement required by § 251.13(b)(4)(iv), which will make clear that the drug was imported under a SIP without the manufacturer's authorization. Likewise, there is not an increased likelihood that section 804 drugs will be adulterated in violation of section 501 of the FD&C Act, because of the supply chain security, Statutory Testing, and other protections in section 804 and this rule. For these reasons, we disagree with the comment that FDA will be required to refuse admission to section 804 drugs under section 801(a)(3) of the FD&C Act, which provides that articles shall be refused admission if, among other things, they are "adulterated, misbranded, or in violation of section 505."

H. First Amendment

(Comment 74) One comment asserted that the proposed rule, if finalized, would violate the First Amendment on two grounds: (1) the manufacturer's attestation and information statement and Statutory Testing requirements amount to compelled speech and a compelled subsidy and (2) compelled authorization to use the labeling amounts to compelled speech and a compelled subsidy. The comment asserts that, because the speech at issue does not propose any commercial transaction, strict scrutiny applies and the rule would fail under that standard. The

comment also asserts that the proposed rule would fail to pass muster under the four-part *Central Hudson* test applied to government regulation of commercial speech.

(Response 74) We disagree with the comment’s premise that these provisions should be understood as speech regulations that implicate the First Amendment. “[I]t has never been deemed an abridgment of freedom of speech...to make a course of conduct illegal merely because the conduct was in part initiated, evidenced, or carried out by means of language, either spoken, written, or printed.” *Rumsfeld v. Forum for Academic and Institutional Rights, Inc.*, 547 U.S. 47, 62 (2006) (citation omitted); see also *Nicopure Labs, LLC v. FDA*, 944 F.3d 267, 291 (D.C. Cir. 2019) (A “kernel of expression...is not sufficient to bring the activity within the protection of the First Amendment.”) (quoting *City of Dallas v. Stanglin*, 490 U.S. 19, 25 (1989)). The final rule requires manufacturers to engage in the authentication and quality assurance process for drugs imported under a SIP. Manufacturers can participate directly, by conducting the Statutory Testing themselves, or they can facilitate the process by providing the necessary testing information to the Importer. Manufacturers must also provide the attestation and information statement and the executed batch records required by § 251.5(c)(4)(xii), to establish that a section 804 drug meets the conditions in the FDA-approved NDA or ANDA, including any process-related or other requirements for which compliance cannot be established through laboratory testing. Participating in and facilitating authentication and quality assurance are not fundamentally expressive activities, even though there is necessarily information exchanged. Similarly, authorizing the use of FDA-approved labeling neither restricts a manufacturer’s speech nor compels it to express ideas with which it disagrees.

A market regulation that “applies to conduct and is imposed ‘for reasons unrelated to the communication of ideas’” does not implicate the First Amendment and is subject to rational-

basis review. *Nicopure Labs*, 944 F.3d 267 at 291-92 (quoting *Lorillard Tobacco Co. v. Reilly*, 533 U.S. 525, 569 (2001)). As described earlier, these provisions easily survive rational-basis review because they are needed to ensure that drugs imported under a SIP comply with sections 501, 502, and 505 of the FD&C Act, as required by section 804, in addition to other provisions, such as section 804(e) of the FD&C Act. The testing results, attestation and information statement, and executed batch records are needed to ensure that the drugs are authentic, not degraded, and are in compliance with established specifications and standards, and to confirm compliance with any process-related or other requirements that cannot be established through laboratory testing (84 FR 70796 at 70817-70818). The FDA-approved labeling is necessary to ensure that prescribers, pharmacists, and patients have the information they need to prescribe, dispense, and use the drugs appropriately. Without these provisions, it would not be possible to ensure that drugs imported under section 804 meet U.S. legal and regulatory requirements and thus pose no additional risk to the public's health and safety.

Moreover, compelled-speech cases that are subject to review under the First Amendment typically involve a requirement that a speaker "must personally speak the government's message" or "host or accommodate another speaker's message." *Rumsfeld*, 547 U.S. at 63. The fundamental First Amendment concern in such cases is that the government will compel the speaker "to voice ideas with which [it] disagree[s]." *Janus v. AFSCME, Council 31*, 138 S. Ct. 2448, 2464 (2018). That is not the case here, where there is *no* message being compelled. Manufacturers are simply being called upon to help with the process of product authentication, quality control, and product identification.

For example, the comment asserts that the regulatory program as set out in the proposed rule--requiring the manufacturer to make available its product labeling, to provide an attestation

and information statement and executed batch records, and to either conduct testing or disclose testing information--would amount to a significant economic subsidy from the manufacturer to the importer. The comment claims, citing *Janus v. AFSCME, Council 31*, that this economic subsidy is impermissible under the First Amendment unless the government can show that the compelled subsidy serves a compelling state interest that cannot be achieved through means significantly less restrictive of associational freedoms. This caselaw, however, is inapposite. First, as the comment admits, under this rule, there is no direct monetary payment from the manufacturer to the importer. Moreover, the Court in *Janus* found that the subsidies at issue meant that individuals were “coerced into betraying their convictions” by “endors[ing] ideas they find objectionable.” 138 S. Ct. at 2464. *See also United States v. United Foods*, 533 U.S. 405, 410-411 (2001) (finding First Amendment implicated where producers were required to “subsidize speech *with which they disagree.*”) (emphasis added). By contrast, here, the manufacturer is not compelled to itself convey any ideas or subsidize the conveyance of ideas by others.

While the requirement that a drug’s manufacturer authorize an Importer to use the drug’s FDA-approved labeling does not equate to a requirement that the manufacturer convey or subsidize the conveyance of an idea, the comment argues that consumers could mistakenly conclude from the inclusion of a manufacturer’s name and trademarks on the labeling that, among other things, the manufacturer vouches for the safety, efficacy, and quality of its drug when imported by a SIP. The comment also argues that consumers could mistakenly assume that a manufacturer authorized the importation of its drug by the SIP. The comment contends that such mistakes could occur despite the labeling statement required by proposed § 251.13(b)(6)(i): “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.” To address the concern that the use of the FDA-approved labeling might create the misleading impression that the manufacturer is conveying or subsidizing the conveyance of ideas through the labeling of a section 804 drug, we have revised § 251.13(b)(4)(iv) to require the following disclosure: “[This drug was/These drugs were] imported from Canada without the authorization of [Name of Applicant] under the [Name of SIP Sponsor] Section 804 Importation Program.” As explained earlier, we have determined that it is not necessary to require the addition of the manufacturer’s name and place of business if they do not already appear on the FDA-approved labeling. We have also determined that it is not necessary to include the phrase “to reduce its costs to the American consumer” in the labeling statement.

Even if the First Amendment were implicated, any minimal burdens on speech are more than adequately justified by the purposes served by this program. The comment appears to suggest that, because this program does not regulate communications in the realm of commercial marketing, neither *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626 (1985) nor *Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm’n*, 447 U.S. 557 (1980) apply, and instead the requirements of this program should be analyzed under strict scrutiny. We disagree. The Supreme Court has applied strict scrutiny in First Amendment cases involving compelled speech on matters of conscience, and it “trivializes the freedom protected” by those cases to assert that incidental burdens on speech are subject to the same protections. *Rumsfeld*, 547 U.S. at 62.

Accordingly, to the extent a court were to analyze this program under the First Amendment, it would likely apply, instead of strict scrutiny, the test for compelled speech established by *Zauderer* or one of the other more relaxed frameworks under which courts

compare the burden on speech to the asserted government interest. See *S.F. Arts & Athletics, Inc. v. USOC*, 483 U.S. 522, 537 n.16 (1987). Under the framework set out in *Zauderer* and its progeny, which describe the test generally applied to required disclosures of factual and uncontroversial information related to commercial marketing, the Government may require disclosures that are justified by a governmental interest and do not unduly burden protected speech. The provisions at issue here--attesting that a product meets the conditions in its approved NDA or ANDA and supplying related information, supplying testing protocols and executed batch records, and authorizing the use of labeling--all relate to the conveyance of factual and uncontroversial information. The government interest is clear. Prescription drug spending in the United States has increased dramatically in recent years and is projected to account for an increasing share of the country's health care spending. This program is designed to address that problem by allowing for the importation of lower cost prescription drugs from Canada into the United States. And there is no burden on protected speech--nothing in any of these provisions limits manufacturers' ability to speak freely about their products.

The comment asserts that the regulations would compel the manufacturer to provide a false or misleading attestation. We disagree. The rule does not require a manufacturer to attest to anything that the manufacturer does not know or cannot attest to truthfully. If, for example, the drug that the manufacturer manufactures for sale in Canada does not meet the conditions in the FDA-approved NDA or ANDA, a manufacturer could not and should not attest that "but for the fact that [a drug] bears the HPFB-labeling," the drug "meets the conditions in the FDA-approved NDA or ANDA." This is clarified in the final rule in § 251.5(d), which states that if the manufacturer cannot provide the attestation and information statement, it must notify FDA and the Importer of its inability and articulate with specificity the reason or reasons for it. In

addition, a manufacturer's attestation and information statement would be as of the date that the drug in question left the manufacturer's control. A manufacturer could not and should not attest, for example, that the Foreign Seller held the manufacturer's drug in compliance with CGMP.

The program also would be constitutional if reviewed under intermediate scrutiny. Under the test for restrictions on commercial speech articulated in *Central Hudson*, agencies can regulate commercial speech where the regulation directly advances a substantial Government interest and is not more extensive than necessary to serve that interest. *Central Hudson* does not require that the means chosen by the Government be the least restrictive means available for addressing an issue, see *Boards of Trustees. v. Fox*, 492 U.S. 469, 480 (1989), but the Supreme Court has in any event observed that required factual disclosures are less intrusive from a First Amendment perspective than are restrictions on speech. *Zauderer*, 471 U.S. at 651. Because the Government's interest in the goals of this program is substantial and the regulation is no more extensive than necessary to directly advance that interest, the rule withstands review under *Central Hudson*. The increasing cost of prescription drugs is causing hardship to American consumers (84 FR 70796 at 70798-70801). The regulation would directly address this by providing for the importation of lower cost prescription drugs from Canada to significantly reduce the cost of covered products to the American consumer, while posing no additional risk to the public's health and safety. The information that the manufacturer is required to supply is no more extensive than necessary to ensure that section 804 drugs are authentic, not degraded, and meet the conditions in an FDA-approved NDA or ANDA, all of which serves to ensure that the drugs are safe and effective. Likewise, the FDA-approved labeling is necessary to ensure that prescribers, pharmacists, and patients have the information they need to prescribe, dispense, and use the drugs appropriately. As noted earlier, the required labeling statement will help avoid

potential confusion between products with the same name and help pharmacists distinguish a section 804 product when selecting the product on the pharmacy shelf (84 FR 70796 at 70819). The labeling statement may also aid in pharmacovigilance (84 FR 70709 at 70820). Finally, the addition of the explanation that the drug was imported from Canada without the manufacturer's authorization will prevent prescribers, pharmacists, or patients from mistakenly concluding that the manufacturer is conveying an idea or subsidizing the conveyance of an idea.

I. Fifth Amendment Takings

(Comment 75) Some comments say that certain provisions in section 804 and this rule would take manufacturers' private property for public use, entitling manufacturers to just compensation under the Fifth Amendment of the U.S. Constitution. The comments contend that the information that manufacturers would be required to disclose to Importers and qualifying laboratories, including information to be used to conduct the Statutory Testing, could include confidential commercial information and trade secrets in which manufacturers have a constitutionally cognizable property interest. Comments also contend that the provisions of section 804 of the FD&C Act and this rule that require manufacturers to authorize Importers to use the FDA-approved labeling for drugs imported under this rule would effect an unconstitutional taking if the labeling included trademarks such as brand names, company names, logos, and the trade dress reflected in the overall packaging design.

One comment says that because the statute explicitly provides in section 804(h) that manufacturers must provide authorization to use the labeling at no cost, but does not include similar language elsewhere, section 804 of the FD&C Act must be interpreted to permit manufacturers to charge Importers for information (such as the attestation and information statement, the executed batch records, and the Statutory Testing information) or services (such as

conducting Statutory Testing) that section 804 and this rule require them to provide. The comment says that this interpretation is necessary to avoid a Fifth Amendment Takings Clause issue.

(Response 75) “The focus of the regulatory takings analysis is on fundamental fairness-- is it fair for the government to impose the cost of a regulation on private parties rather than on the public as a whole through public spending?” (*Cienega Gardens v. United States*, 503 F.3d 1266, 1278 (Fed. Cir. 2007) (citing *Palazzolo v. Rhode Island*, 533 U.S. 606, 618 (2001); *Penn Central Transp. Co. v. New York City*, 438 U.S. 104, 123 (1978))). “[T]he touchstone of the economic impact question is proportionality: the size of a liability only weighs in favor of finding a taking insofar as it is out of proportion to the legitimate obligations society may impose on individual entities.” (*B&G Constr. Co. v. Dir., OWCP*, 662 F.3d 233, 260 (3d Cir. 2011) (citation and internal quotations omitted)). Indeed, courts have rejected regulatory takings claims even where the government’s actions “impose considerable costs on private actors in the regulated industry.” (*Mobile Relay Assocs. v. FCC*, 457 F.3d 1, 12 (D.C. Cir. 2006)). In addition, as a general rule, the government is not required to pay for the incidental effects of its laws and regulations. (See *Penn Central*, 438 U.S. at 124. “Government hardly could go on if to some extent values incident to property could not be diminished without paying for every such change in the general law.” (*Pennsylvania Coal Co. v. Mahon*, 260 U.S. 393, 413 (1922)).

In this case, the pharmaceutical industry operating in the United States has benefitted from Federal laws and regulations that allow manufacturers to recoup the costs of pharmaceutical research and development and to be rewarded for their investments in it. As explained in the preamble to the proposed rule, however, the increasing cost of prescription drugs is placing a heavy burden on American consumers (84 FR 70796 at 70798-70801). That

Congress chose to place an incidental burden on the pharmaceutical industry to reduce the cost of prescription drugs does not offend any principle of fundamental fairness.

The Supreme Court has explained that a takings analysis involves “essentially [an] ad hoc, factual inquir[y].” (See *Penn Central*, 438 U.S. at 124). A threshold step in that analysis is determining whether the claimant possesses a property interest protected by the Taking Clause. (*Ruckelshaus v. Monsanto*, 467 U.S. 986, 1000 (1984)). The comments assert that manufacturers have property interests in trade secrets and trademarks. The Supreme Court found in *Ruckelshaus v. Monsanto* (467 U.S. at 1003-04) that in certain circumstances there can be a property interest in trade secrets for purposes of the Fifth Amendment’s Takings Clause (“the property right [in a trade secret] is defined by the extent to which the owner of the secret protects his interest from disclosure to others”). We will assume for purposes of this discussion that some of the information that manufacturers are required to disclose under section 804 and this rule would meet the relevant state law definition of a trade secret. The comments did not cite, and we have not found, a case in which a court has held that a manufacturer has a cognizable property interest in a trademark for purposes of the Fifth Amendment Takings Clause, and courts have found that other forms of intellectual property, namely copyrights and patents, do not create cognizable property interests for Takings Clause purposes (*Univ. of Hous. Sys. v. Jim Olive Photography*, 580 S.W.3d 360, 377 (Tex. App. 2019); *Christy, Inc. v. U.S.*, 141 Fed. Cl. 641, 660 (2019)). The question arises whether trademarks are more akin to trade secrets or to copyrights and patents for Fifth Amendment Takings Clause purposes. We find it unnecessary to answer this question here because, even if trademarks were private property protected under the Takings Clause, there has been no taking.

The Supreme Court has held that two categories of regulatory action are generally *per se* takings: (1) when the government “requires an owner to suffer a permanent physical invasion of her property;” and (2) when regulations “completely deprive an owner of ‘all economically beneficial us[e]’ of her property” (*Lingle v. Chevron U.S.A. Inc.*, 544 U.S. 528, 538 (2005) (quoting *Lucas v. S.C. Coastal Council*, 505 U.S. 1003, 1019 (1992))). Neither of those circumstances is present here.

In other circumstances, the Supreme Court has held that “when a regulation impedes the use of property without depriving the owner of all economically beneficial use, a taking still may be found based on ‘a complex of factors,’ including: (1) the economic impact of the regulation on the claimant; (2) the extent to which the regulation has interfered with distinct investment-backed expectations; and (3) the character of the governmental action” (*Murr v. Wisconsin*, 137 S. Ct. 1933, 1943 (2017) (citing *Palazzolo v. Rhode Island*, 533 U.S. at 617) (citing *Penn Central*, 438 U.S. at 124)). The force of any one of these three *Penn Central* factors may be “so overwhelming...that it disposes of the taking question” (*Ruckelshaus*, 467 U.S. at 1005).

1. Provision of Trade Secrets and Confidential Commercial Information

With regard to the first *Penn Central* factor, the economic impact of section 804 of the FDC& Act and this regulation on manufacturers, we note that the government action here is limited. The Supreme Court has explained that “where an owner possesses a full ‘bundle’ of property rights, the destruction of one ‘strand’ of the bundle is not a taking because the aggregate must be viewed in its entirety” (*Andrus v. Allard*, 444 U.S. 51, 65-66 (1979)). (See also *Village of Euclid v. Ambler Realty Co.*, 272 U.S. 365, 384 (1926) (75 percent diminution in value insufficient to prove taking); *Hadacheck v. Sebastian*, 239 U.S. 394, 405 (1915) (92.5 percent diminution insufficient to prove taking)). Because manufacturers will retain the right to exclude

everyone except Importers and qualifying laboratories from the use of their trade secrets and commercial or financial information that is privileged or confidential, their trade secrets and commercial or financial information that is privileged or confidential will retain significant value. An Importer or qualifying laboratory's use of a manufacturer's trade secrets or commercial or financial information that is privileged or confidential will be limited to conducting the Statutory Testing and establishing that an eligible prescription drug meets the requirements of the FD&C Act and the rule. Consistent with section 804 of the FD&C Act, the rule mandates that the trade secrets and commercial or financial information that is privileged or confidential that the manufacturer provides be used only for purposes of testing or otherwise complying with the FD&C Act and the rule. Moreover, the government action here may be further constrained by the fact that there will be a limited number of SIPs working with a limited number of Importers and qualifying laboratories, and by the fact that the SIPs will be time-limited.

The economic impact of the rule will also be constrained by the fact that manufacturers will retain their right to protect their trade secrets against disclosure (*Pharm. Care Mgmt. Ass'n v. Rowe*, 307 F. Supp. 2d 164, 179 (D. Me. 2004) (holding that a "statute's protection from further disclosure inoculates it from constitutional infirmity"). As required by section 804(e)(2) of the FD&C Act, the final rule mandates in § 251.16(g) that the Importer keep any information that the manufacturer provides to authenticate a prescription drug being tested and confirm that the labeling of the prescription drug complies with labeling requirements under the FD&C Act in strict confidence. The final rule also requires that any trade secrets or commercial or financial information that is privileged or confidential that the manufacturer supplies for the purposes of testing or otherwise complying with the FD&C Act be kept in strict confidence. Moreover,

manufacturers have the option of conducting the Statutory Testing themselves, which would obviate the need to disclose the Statutory Testing information to the Importer. While the manufacturer would still need to disclose the Statutory Testing information and results to FDA, FDA would ensure that any trade secrets or confidential commercial information remain confidential consistent with the law (*Full Value Advisors, LLC v. Securities & Exchange Comm.*, 633 F.3d 1101, 1110 (D.C. Cir. 2011) (finding that disclosure to the Securities & Exchange Commission produced no economic harm because the Commission ensured that the information remained confidential).

Turning to the second *Penn Central* factor--interference with distinct investment-backed expectations--regulated industry has been on notice since at least October 28, 2000, when the predecessor to the current section 804 of the FD&C Act was signed into law as part of the Medicine Equity and Drug Safety (MEDS) Act of 2000, that they could be required to disclose information needed for safe importation. Thus, sponsors of NDAs or ANDAs submitted after that date could not have a reasonable investment-backed expectation that is inconsistent with section 804. While a comment points to the fact that prior HHS Secretaries did not make the section 804(l) certification to Congress, it would not be reasonable for manufacturers to expect that such a certification could never be made, especially given the widely-known developments described in the preamble to the proposed rule, including the continued rise of prescription drug prices which has raised concerns among policymakers, healthcare professionals, and American consumers (84 FR 70796 at 70798-70801). With regard to drugs the applications for which were submitted before October 28, 2000, it still would not have been reasonable for manufacturers to expect that a provision like section 804 would not be enacted. Courts have held that those who do business in highly regulated fields are on notice that changes are possible (*Maine Educ. Ass'n*

Benefits Trust v. Cioppa, 695 F.3d 145, 154 (1st Cir. 2012) (finding that “[g]iven the historically heavy and continuous regulation of insurance in Maine, the [Plaintiff], in choosing how and where to allocate its resources, ought to at least be aware of the heightened possibility that new insurance regulations might hinder the use or value of its loss information” (internal citations omitted)); *Connolly v. Pension Ben. Guar. Corp.*, 475 U.S. 211, 226-227 (1986)). The prescription drug industry is such a highly regulated field (*New York v. Actavis PLC*, 787 F.3d 638, 643 (2d Cir. 2015) (describing the pharmaceutical industry as “complex and highly-regulated”).

One comment contends that the protections against disclosure of certain information in the Federal Trade Secrets Act at 18 U.S.C. 1905, in sections 301(j) and 505(l) of the FD&C Act, and in FDA’s regulations at 21 CFR 20.61 and 314.430 support manufacturers’ expectation that they would not have to supply the information specified in section 804 and this rule. In *Ruckelshaus v. Monsanto*, the Supreme Court held that an explicit guarantee of exclusive use created a reasonable investment-backed expectation that EPA would not consider the data when evaluating the application of a subsequent applicant (*Ruckelshaus*, 467 U.S. at 1011). None of the provisions that the comment cites creates an explicit or implicit guarantee that section 804 would not be implemented or that regulations would not be issued requiring manufacturers to provide testing and other information to Importers. We note that we have determined that it is not necessary for FDA to provide Statutory Testing information to Importers, and so we are not finalizing proposed § 251.16(i), which would have provided that “FDA may transmit information that the manufacturer is required to provide to an Importer under this section on the manufacturer’s behalf if the manufacturer has not transmitted such information to the Importer in a timely fashion and if such information is available to FDA in the NDA or ANDA.”

Manufacturers that choose not to conduct the Statutory Testing are required to provide the Statutory Testing information covered by § 251.16(i) to Importers themselves.

The Supreme Court has described the final *Penn Central* factor, the “character of the governmental action,” as a way to assess whether the challenged action “amounts to a physical invasion or instead merely affects property interests through ‘some public program adjusting the benefits and burdens of economic life to promote the common good’ ” (*Lingle*, 544 U.S. at 539 (quoting *Penn Central*, 438 U.S. at 124)). Here, section 804 of the FD&C Act and the rule do not amount to a physical invasion and they have a legitimate public purpose, to significantly reduce the cost of covered products to the American consumer without any additional risk to the public’s health and safety. As noted earlier, the increasing cost of prescription drugs is placing a heavy burden on American consumers. To promote the common good, section 804 and the rule would require manufacturers of certain drugs--those imported under SIPs--to provide limited information to Importers or qualified laboratories under limited circumstances. For these reasons, the third factor of the takings analysis, like the first two factors, compels the conclusion that neither section 804 nor this rule amounts to a regulatory taking of manufacturers’ property that requires compensation under the Fifth Amendment.

We do not agree that section 804 of the FD&C Act is best interpreted to permit manufacturers to charge Importers for information (such as the attestation and information statement, the executed batch records, and the Statutory Testing information) or services (such as conducting Statutory Testing) that section 804 and this rule require them to provide. Section 804(h) explicitly requires manufacturers to authorize Importers to use a drug’s approved labeling at no cost. This does not mean that manufacturers can charge for information or services that they are required to provide. If manufacturers were permitted to charge it would directly

undermine section 804's cost-reducing goal. Moreover, interpreting section 804 to permit manufacturers to charge Importers is not necessary to avoid a Fifth Amendment Takings Clause issue because, as explained earlier, neither section 804 nor this rule effects a taking under the Fifth Amendment.

2. Authorization to Use FDA-Approved Labeling

With regard to the first *Penn Central* factor, the requirement in section 804 of the FD&C Act and this regulation that a manufacturer authorize an Importer to use the FDA-approved labeling for an eligible prescription drug is likely to have little to no impact on the value of the manufacturer's trademarks. Trademarks do not have inherent value (*Marshak v. Green*, 746 F.2d 927, 929 (2d Cir. 1984)). Their only value is in the goodwill with which they are associated. Under this rule, there will be little or no diminution in the goodwill associated with manufacturers' trademarks because section 804 drugs will meet the conditions of the relevant FDA-approved NDA or ANDA. In addition, as discussed earlier, the labeling statement will make it clear that the section 804 drug was imported without the manufacturer's authorization. Turning to the second *Penn Central* factor, a manufacturer could not have a reasonable investment-backed expectation that it would not have to authorize an Importer to use its labeling. Such an expectation would be inconsistent with the current version of section 804. With regard to drugs developed before December 8, 2003, it still would not have been reasonable for manufacturers to expect that a provision like section 804(h) requiring that the manufacturer of a section 804 drug authorize the use of the FDA-approved labeling would not be enacted. Finally, as explained earlier, the third *Penn Central* factor also weighs against a finding that section 804 and this rule effect a regulatory taking, because significantly reducing the cost of covered products to the American consumer without any additional risk to the public's health and safety

“promote[s] the common good” (*Lingle*, 544 U.S. at 539 (quoting *Penn Central*, 438 U.S. at 124)).

(Comment 76) One comment says that section 804 of the FD&C Act and this rule violate provisions of the World Trade Organization’s Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). Specifically, the comment says that section 804 and this rule violate Article 39 of the TRIPS Agreement by requiring manufacturers to disclose trade secrets and confidential commercial information and Article 21 of the TRIPS Agreement by requiring manufacturers to authorize the use of labeling that could include trademarks.

(Response 76) We disagree that section 804 of the FD&C Act and this rule violate the TRIPS Agreement. As a general matter, we note that the United States is in full compliance with its international obligations under the TRIPS Agreement. Article 39 of TRIPS provides that member countries “shall protect undisclosed information in accordance with paragraph 2 and data submitted to governments or governmental agencies in accordance with paragraph 3.” Under section 804 and this rule, Importers and qualified laboratories obtain information from manufacturers under the authority of a statute and implementing regulation. The final rule provides in § 251.16(g), that information supplied by the manufacturer to authenticate the prescription drug being tested and confirm that the labeling of the prescription drug complies with labeling requirements under the FD&C Act, and any trade secrets or commercial or financial information that is privileged or confidential that the manufacturer supplies for the purposes of testing or otherwise complying with the FD&C Act and this rule, must be kept in strict confidence and used only for the purposes of testing or otherwise complying with the FD&C Act and this rule.

With regard to data submitted to governments or governmental agencies, as discussed earlier, we have determined that it is not necessary for FDA to provide Statutory Testing information to Importers, and so we are not finalizing § 251.16(i) from the proposed rule, which would have provided that FDA may transmit information that the manufacturer is required to provide to an Importer under this section on the manufacturer's behalf if the manufacturer has not transmitted such information to the Importer in a timely fashion and if such information is available to FDA in the NDA or ANDA.

We also disagree that section 804 of the FD&C Act and this rule violate Article 21 of TRIPS, which states that "compulsory licensing of trademarks shall not be permitted." The requirement that a manufacturer of a prescription drug authorize an Importer to use the drug's FDA-approved labeling does not constitute compulsory licensing of trademarks. This is at least because the labeling is only used referentially and does not associate the trademark with the Importer. As noted above, the United States is in full compliance with its international obligations under the TRIPS Agreement.

J. Disclosure

(Comment 77) A comment says that FDA's determination that a drug is an eligible prescription drug that can be imported by a SIP discloses trade secrets and confidential commercial information about that drug. When FDA determines that a drug can be imported, FDA has determined that, but for the fact that the drug bears the HPFB-approved labeling when marketed in Canada, it meets the conditions in an FDA-approved NDA or ANDA. The comment says that the information upon which FDA's determination is based--whether a drug manufactured for sale in Canada meets the conditions in an FDA-approved NDA or ANDA--is confidential. Another comment says that FDA should specify that when a manufacturer notifies

an Importer that it cannot or will not make the § 251.5(c)(4)(xii) attestation, because its drug does not meet the conditions in an FDA-approved NDA or ANDA or for some other reason, that is confidential information that the Importer should not be able to disseminate or use.

(Response 77) Section 804 of the FD&C Act directs the Secretary to issue regulations permitting pharmacists and wholesalers to import from Canada drugs that, among other requirements, comply with section 505 of the FD&C Act. FDA interprets compliance with section 505 to mean that the HPFB-approved drug meets the conditions in an FDA-approved NDA or ANDA. Through its labeling requirements, the statute also directs that FDA's determination that a Canadian drug complies with section 505 will be publicly available information, as reflected, for example, in product labeling.

The final rule clarifies in § 251.5(d) that if a manufacturer cannot provide the attestation and information statement, the manufacturer must notify FDA and the Importer and articulate with specificity the reason or reasons why it cannot provide the attestation and information statement. The final rule also requires, in § 251.16(g), that importers keep any trade secrets or commercial or financial information that is privileged or confidential, that the manufacturer supplies for the purposes of testing or otherwise complying with the Federal Food, Drug, and Cosmetic Act and this part, in strict confidence. We note that manufacturers can choose to mark any trade secrets or commercial or financial information that is privileged or confidential that is contained in any of the information that they are required to provide.

We do not believe that the fact that the manufacturer cannot or will not provide the attestation and information statement is likely to be a trade secret or commercial or financial information that is privileged or confidential. The reasons that the manufacturer gives for not providing the attestation and information statement, by contrast, may be trade secrets or

commercial or financial information that is privileged or confidential, which would mean that the Importer would be legally obligated to keep them in “strict confidence” under § 251.16(g).

K. FDA Authority

(Comment 78) A comment states that FDA lacks the authority under section 804 to issue certain provisions regarding manufacturers’ information and manufacturers’ participation in the importation of their drugs by SIPs. The comment states that FDA cannot provide the Importer with the information contained in an approved NDA or ANDA as is provided for by proposed § 251.16(i). The comment also states that FDA cannot require the manufacturer to supply “testing methodologies and protocols that the manufacturer has developed” as FDA proposed in § 251.16(b). The comment states that FDA lacks the authority to issue § 251.5(c)(4)(xii), which requires manufacturers to provide an attestation and information statement that establishes that the drug proposed for import, but for the fact that it bears the HPFB-approved labeling, meets the conditions in the FDA-approved NDA or ANDA. The comment also states that, with regard to § 251.13(a), FDA lacks the authority to deem the manufacturer to have provided authorization to use the FDA-approved labeling for the manufacturer’s drug, if the manufacturer does not provide written authorization to the Importer in a timely fashion. Finally, the comment asks FDA to clarify that section 804(e) of the FD&C Act, which, the comment states, relates to testing, not supply chain information, does not give FDA the authority to issue proposed § 251.14, which requires a manufacturer to provide an Importer with transaction information.

(Response 78) We have determined that it is not necessary to include proposed § 251.16(i) in the final rule. That provision stated that FDA may transmit information that the manufacturer is required to provide to an Importer under this section on the manufacturer’s behalf if the manufacturer has not transmitted such information to the Importer in a timely

fashion and if such information is available to FDA in the NDA or ANDA. Manufacturers are required to provide the Statutory Testing information covered by § 251.16(i) themselves. If they fail to do so, they will have committed a prohibited act under section 301(aa) of the FD&C Act. In addition, as discussed earlier, violations of section 804(e) of the FD&C Act are subject to a penalty under section 303(b)(6) of the FD&C Act.

It is necessary, however, and within FDA's authority under section 804 of the FD&C Act, to issue §§ 251.16(b) and (d), which require that the manufacturer provide the Importer with the information that the Importer needs to conduct the Statutory Testing. Section 804(b) requires that the Secretary issue regulations permitting the importation of certain drugs under section 804. Section 804(e) specifies that these regulations shall require the manufacturer to provide the Importer with the "information needed to authenticate the prescription drug being tested." Sections 804(d)(1)(J)(i)(III) and 804(d)(1)(L) specify that the regulations shall require the Importer to submit to FDA documentation demonstrating that section 804 drugs were tested "for authenticity and degradation" and that the Importer submit to FDA laboratory records including complete data derived from all tests necessary to ensure that the prescription drug is in compliance with established specifications and standards. While sections 804(d)(1)(J)(i)(III) and 804(d)(1)(L) do not state that the regulations must require manufacturers to provide the information needed to conduct these tests, FDA has the authority to require this under section 804(c)(1), which directs the Secretary to issue regulations that require that safeguards be in place to ensure that section 804 drugs comply with section 501, 502, and 505 of the FD&C Act, and under section 804(c)(3), which directs the Secretary to issue regulations that contain any additional provisions determined by the Secretary to be a means to facilitate the importation of prescription drugs.

With regard to the manufacturer's attestation and information statement described in § 251.5(c)(4)(xii), section 804(c)(1) of the FD&C Act specifies that the regulations must require that safeguards be in place to ensure that each drug imported under the regulations complies with the FD&C Act, including sections 501, 502 and 505. It would not be possible to ensure that each drug imported under the regulations complies with sections 501, 502, and 505, as required by section 804(c)(1), without the information from the manufacturer that is captured in the attestation and information statement. For example, only the manufacturer knows whether a drug that was originally intended for the Canadian market was manufactured "in conformity with current good manufacturing practice," as required by section 501. The comment notes that another provision, section 804(d)(1)(K), does not state that the regulations must require the manufacturer to provide the Importer with the information captured in the attestation and information statement. Under section 804(d)(1)(K), the regulations under section 804(b) must require the Importer to submit to FDA a certification from the Importer or the manufacturer that the imported drugs are approved for marketing in the United States and are not adulterated or misbranded, and that they meet all the labeling requirements under the FD&C Act. If the Importer provides the section 804(d)(1)(K) certification, the Importer will need information from the manufacturer, including information about how the drug was manufactured. While section 804(d)(1)(K) does not expressly mandate that the Secretary require the manufacturer to provide the Importer with the information it needs for certification, it is implied because the Importer could not make the certification without certain information from the manufacturer. In any case, the Secretary clearly has the authority to do so under section 804(c)(1) and under section 804(c)(3), which authorizes the Secretary to include regulatory provisions that the Secretary

determines to be appropriate as a safeguard to protect the public health or as a means to facilitate importation of prescription drugs.

With regard to § 251.13(a), the comment contends that FDA would need express statutory authority to deem the manufacturer to have provided authorization to use the FDA-approved labeling for the manufacturer's drug, if the manufacturer does not provide such authorization in a timely fashion. We disagree. While section 804(h) of the FD&C Act, which requires manufacturers to authorize Importers to use their drugs' FDA-approved labeling, does not expressly state that FDA can deem manufacturers to have given their authorization if they fail to do so in a timeframe that FDA determines is reasonable under the circumstances, other provisions of section 804 give FDA the necessary authority. Section 804(c)(1) specifies that the regulations that the Secretary issues must require that safeguards be in place to ensure that each drug imported under the regulations complies with the FD&C Act and section 804(c)(3) directs the Secretary to issue regulatory provisions that it determines will facilitate importation. The provision at issue here will help ensure that section 804 drugs comply with the FD&C Act's labeling requirements and are not misbranded, and will facilitate importation because it will prevent manufacturers from causing unwarranted delay by withholding their authorization to use the FDA-approved labeling.

With regard to § 251.14(b), which requires the manufacturer to provide to the Importer a copy of any transaction documents that were provided from the manufacturer to the Foreign Seller, FDA's authority to require this derives from section 804(c)(3) and (e) of the FD&C Act. Under section 804(e)(2)(A)(i), if the Importer does the Statutory Testing, the manufacturer has to provide certain information, including "information needed to...authenticate the prescription drug being tested." The information needed to authenticate a section 804 drug includes the

transaction documents that the manufacturer provides to the Importer under § 251.14(b). These documents enable the Importer and FDA to conduct a cross check of the transaction documents that the Foreign Seller provides to the Importer under § 251.14(c)(6). This cross check is valuable supporting evidence of the authenticity of the drug, helping to ensure that importation under section 804 poses no additional risk to the public's health and safety.

Under § 251.14(b), manufacturers must provide the transaction documents needed for the cross check regardless of whether the Importer or the manufacturer conducts the Statutory Testing. FDA's authority to require this when the manufacturer conducts the testing derives from section 804(c)(3) of the FD&C Act, which provides that the regulations "shall contain any additional provisions determined by the Secretary to be appropriate as a safeguard to protect the public health or as a means to facilitate the importation of prescription drugs." As noted earlier, the cross check of the transaction documents from the sale of the drug by the manufacturer to the Foreign Seller is a valuable safeguard that protects the public health by providing evidence of the drug's authenticity.

L. Procedural Requirements

(Comment 79) One comment states that the proposed rule failed to comply with certain procedural requirements set forth in statute and executive orders, including the Regulatory Flexibility Act, the Unfunded Mandates Reform Act, the E-Government Act of 2002, and Executive Orders 12866, 13175, 12630, and 13045.

(Response 79) FDA disagrees with this comment. This rulemaking adheres to procedural provisions set forth in statutes and executive orders. For example, as noted in the Final Regulatory Impact Analysis, FDA conducted economic analysis under the Unfunded Mandates Reform Act and the Regulatory Flexibility Act. Further, we do not believe the final rule

establishes a new collection of information under the E-Government Act of 2002. In addition, the Final Rule describes FDA's Economic Analysis of Impacts under Executive Order 12866, the solicitation of comment from Indian Tribes in accordance with Executive Order 13175 and from States in accordance with Executive Order 13132, and FDA considered the applicability of other Executive Orders in the development of the rule.

(Comment 80) One comment states that former Acting Commissioner Brett Giroir did not have authority to sign the proposed rule because he was not the Acting Commissioner on December 18, 2019, which is the date on which the comment asserts the rule was filed with the *Federal Register*.

(Response 80) This statement is incorrect. Acting Commissioner Giroir had signing authority for the proposed rule because he served in the role of Acting Commissioner at the time he signed the rule on December 11, 2019. The date of filing with the *Federal Register* is determined by the time the signed, original, clear and legible copies of a document are received (1 CFR 18.3(c)).

(Comment 81) A comment says that under the Administrative Procedure Act and the Due Process Clause of the U.S. Constitution, NDA or ANDA holders listed in a SIP Proposal must have an opportunity to comment on the SIP Proposal before FDA authorizes it. The comment says that a SIP Proposal is either a rule or an informal adjudication and that, as a result, authorization should not proceed before NDA or ANDA holders have the opportunity to seek judicial review. The comment says that allowing NDA or ANDA holders to comment on SIP Proposals would allow FDA to receive input on appropriate drugs and conserve resources that might otherwise be spent on unworkable or dangerous SIP Proposals.

(Response 81) We disagree with the comment that FDA’s authorization of a SIP Proposal is a rule. Such an authorization would be an order. Under the Administrative Procedure Act (5 U.S.C. 551(4)), a rule is defined as “the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy or describing the organization, procedure, or practice requirements of an agency.” An order is the whole or a part of a final disposition, whether affirmative, negative, injunctive, or declaratory in form, of an agency in a matter other than rule making but including licensing. 5 U.S.C 551(6). Thus, “[t]he term ‘order’ is defined to exclude rules.” S. Rep. 79-752 at 11 (November 19, 1945). While this final rule interprets and implements section 804 of the FD&C Act, when FDA authorizes a SIP Proposal, it will be applying this rule.

We also disagree that the manufacturers that hold the NDAs or ANDAs of the FDA-approved counterparts of the eligible prescription drugs that a SIP seeks to import would necessarily be entitled to participate in FDA’s review of the SIP Proposal or to seek judicial review of FDA’s authorization of a SIP Proposal before it proceeds. Under 21 CFR 10.25, “[a]n interested person may petition the Commissioner [of the FDA] to issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action.” Under 21 CFR 10.35, an interested person may also “request the Commissioner to stay the effective date of any administrative action.” FDA’s regulations further provide that a final administrative decision on such a petition or request for a stay is a prerequisite to filing suit in court (21 CFR 10.45). A manufacturer can follow the procedures set forth in these regulations to petition FDA with regard to, or seek a stay of, the authorization of a SIP.

Finally, we do not believe that FDA’s review of a SIP Proposal would necessarily benefit from input from NDA or ANDA holders. The comment says that NDA or ANDA holders could

offer information such as that antimicrobial, antiviral, or oncology drugs could have a high potential for resistance or death if misbranded or adulterated. We do not think that this is necessary because drugs imported under section 804 of the FD&C Act and this rule will not be any more likely to be adulterated or misbranded than drugs imported with their manufacturer's authorization.

M. Technical Amendments

We are revising § 1.74(a)(2) (21 CFR 1.74(a)(2)) to remove the reference to a biological product regulated by FDA's Center for Drug Evaluation and Research (CDER) that is required to have an approved NDA. In the NPRM, we proposed that information filed in ACE must include, for a biological product regulated by FDA's CDER that is required to have an approved new drug application or an approved biologics license application (BLA), the number of the applicable application. As revised, the text refers to a biological product regulated by FDA's CDER that is required to have an approved BLA. This amendment reflects that after March 23, 2020, a marketing application for a biological product (that previously could have been submitted under section 505 of the FD&C Act) must be submitted in a BLA under section 351 of the PHS Act (see section 7002(e) of the Biologics Price Competition and Innovation Act of 2009 (BPCI Act), enacted as part of the Patient Protection and Affordable Care Act (Pub. L. 111-148)). On March 23, 2020, an approved application for a biological product under section 505 of the FD&C Act was deemed to be a license for the biological product (i.e., an approved BLA) under section 351 of the PHS Act (see section 7002(e)(4)(A) of the BPCI Act; see also section 7002(e)(4)(B) of the BPCI Act). As proposed in the NPRM, we are also adding § 1.74(b), which sets forth the information that ACE filers must submit when they file entry in ACE for drugs that are imported or offered for import under section 804. This information will facilitate the

importation of drugs under section 804 and is a safeguard to ensure that FDA's review of such importation is as protective of the public's health and safety as the Agency's review of entries for other drugs. We have revised the authority citation for Part 1 to reflect that fact that we added § 1.74(b) pursuant to our authority in section 804(c)(3).

In § 251.9(b), we are including language to clarify that when Foreign Sellers register with FDA under section 804 of the FD&C Act, they must submit a unique facility identifier in accordance with the system specified under section 510 of the FD&C Act (21 U.S.C. 360). We have made conforming revisions to § 1.74(b)(1) and the definitions in proposed § 251.2. These revisions align the Foreign Seller registration requirements under section 804 of the FD&C Act with drug establishment registration requirements under section 510 of the FD&C Act.

The definition of "eligible prescription drug" in § 251.2 includes revisions from the definition proposed in the NPRM to clarify that the drug is currently commercially marketed in the United States. This revision aligns the definition with the certification requirement in proposed § 251.19(e). We have made a conforming revision to proposed § 251.3(d)(6).

In § 251.14 we clarify, as discussed in the NPRM, that a Foreign Seller, upon receiving a shipment of eligible prescription drugs from the manufacturer, must, among other things, maintain records associating the SSI with the Canadian DIN and all the records it received from the manufacturer upon receipt of the original shipment intended for the Canadian market for not less than 6 years.

We are making a number of changes throughout the rule for clarity and readability.

VI. Effective/Compliance Date(s)

This rule is effective [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

VII. Economic Analysis of Impacts

We have examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, Executive Order 13771, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct us to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Executive Order 13771 requires that the costs associated with significant new regulations “shall, to the extent permitted by law, be offset by the elimination of existing costs associated with at least two prior regulations.” This final rule has been designated as a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. This rule does not impose new regulatory requirements on small entities that do not participate in SIPs, however we cannot anticipate whether sponsors will contract with small entities to implement their authorized SIP Proposals or whether, under certain circumstances, a small pharmacist or wholesaler might become a sponsor. We also lack information to quantify the total impacts of the final rule. Because we do not have enough information about the effect of the final rule on small entities, we are not certifying that the final rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before issuing “any rule that includes any Federal mandate that may result in the expenditure by State, local,

and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year.” The current threshold after adjustment for inflation is \$156 million, using the most current (2019) Implicit Price Deflator for the Gross Domestic Product. This final rule would not result in an expenditure in any year that meets or exceeds this amount. This final rule allows commercial importation of certain prescription drugs from Canada through time-limited SIPs, sponsored by a State or Indian Tribe, or in certain future circumstances by a pharmacist or wholesale distributor, with possible cosponsorship by a State, Indian Tribe, pharmacist, or wholesale distributor. If such programs allow Importers to leverage drug price differences between the United States and Canada, they may result in cost savings for U.S. consumers.

We received a number of comments on the preliminary economic analysis, including general comments on the analysis as well as comments on costs, benefits, distributional effects, international effects, and effects on small entities. We respond to these comments in the final economic analysis.

Costs of the final rule may accrue to the Federal Government, SIP Sponsors, Importers, and manufacturers of imported eligible prescription drugs. The Federal Government will incur costs to implement the final rule and conduct oversight of authorized programs. SIP sponsors will face costs to prepare proposals, implement approved programs, and produce records and program reports. Drug manufacturers will have to provide certain information to Importers if their drugs are imported into the United States from Canada. SIPs may offer cost savings to patients, as well as participating wholesale drug distributors, pharmacies, hospitals, and third-party payers. As drug distributors realize savings in acquiring imported eligible prescription

drugs and pass some of these savings to consumers and other payors, it is possible that U.S.-based drug manufacturers may experience a transfer in U.S. sales revenues to these parties.

We are unable to estimate the cost savings from this final rule, because we lack information about the likely size and scope of SIPs, the specific eligible prescription drugs that may be imported, the degree to which these imported drugs will be less expensive than non-imported drugs available in the United States, and which eligible prescription drugs are produced by U.S.-based drug manufacturers.

Table 1.--Summary of Benefits, Costs, and Distributional Effects of Final Rule

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Benefits	Annualized Monetized \$millions/year					7%		
						3%		
	Annualized Quantified					7%		
						3%		
Qualitative	Potential cost savings to consumers and third-party payers or entities							
Costs	Annualized Monetized \$millions/year					7%		
						3%		
	Annualized Quantified					7%		
						3%		
Qualitative	Potential costs to Federal Government, SIP Sponsors, Importers, and manufacturers of imported eligible prescription drugs. This framework does not consider the potential implications of private and government insurance and reimbursement as well as other purchasers in the supply chain including hospitals and physicians. We cannot predict the types and volumes of eligible prescription drugs that will be imported under the final rule, which will influence these payors. Moreover, the prices paid by multiple payors, including those affected by discounts, may be different, unobservable, or both.							
Transfers					7%			

Category	Primary Estimate	Low Estimate	High Estimate	Units			Notes
				Year Dollars	Discount Rate	Period Covered	
Federal Annualized Monetized \$millions/year					3%		
From/ To	From:			To:			
Other Annualized Monetized \$millions/year					7%		
					3%		
From/To	From: U.S. drug manufacturers			To: Importers and U.S. consumers			Not Quantified
Effects	State, Local or Tribal Government: Potential costs and cost savings to States and Indian Tribes from sponsoring SIPs Small Business: Potential costs to drug manufacturers; potential costs and cost savings to pharmacists and wholesale distributors Wages: Growth:						

We lack information about the likely size and scope of SIPs, the specific prescription drug products that may become eligible for importation, which eligible prescription drugs are produced by U.S.-based drug manufacturers, and the degree to which these imported drugs will be less expensive than non-imported drugs available in the United States, to estimate the present and annualized values of the costs and cost savings of the final rule over an infinite time horizon. Therefore, we exclude the Executive Order 13771 summary table from this analysis. This is a deregulatory action because the rule is opening a pathway for legal importation that is not currently allowed.

We have developed a comprehensive Economic Analysis of Impacts that assesses the impacts of the final rule. The full analysis of economic impacts, including responses to public comments submitted, is available in the docket for this final rule (Ref. 6) and at <https://www.fda.gov/about-fda/reports/economic-impact-analyses-fda-regulations>.

VIII. Analysis of Environmental Impact

We have determined under 21 CFR 25.30(h) and 25.31(a) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment.

Therefore, neither an environmental assessment nor an environmental impact statement is required.

IX. Paperwork Reduction Act of 1995

This final rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521). The title, description, and respondent description of the information collection provisions are shown in the following paragraphs with an estimate of the annual reporting and recordkeeping burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

Title: Section 804 Importation Program Proposals--21 CFR part 251.

Description: The final rule provides that a SIP Sponsor that seeks to implement a SIP to import eligible prescription drugs from Canada must submit a proposal that includes, among other things, information about the SIP Sponsor, cosponsors if any, and the SIP Sponsor's importation plan including the SIP's compliance plan. In addition, SIP Sponsors must provide FDA with data and information on the eligible prescription drugs the SIP imports and on the SIP's cost savings to the American consumer. Importers have a number of responsibilities related to submitting a Pre-Import Request; screening eligible prescription drugs; and arranging for importation, testing, and relabeling. Manufacturers provide an attestation and information statement, batch records, transaction information, and information needed to test eligible prescription drugs for compliance with section 804 of the FD&C Act and the rule.

Description of Respondents: Respondents would include SIP Sponsors (States or Indian Tribes, or in certain future circumstances pharmacists or wholesale distributors, and any

cosponsor(s)); Importers (pharmacists or wholesaler distributors); and manufacturers of eligible prescription drugs.

FDA anticipates submissions will be made in electronic format through the ESG or to an alternative transmission point identified by FDA.

FDA estimates that there will be 10 SIP Sponsors requiring 360 hours each to research, prepare, and administer requirements annually; 10 Pre-Import Requests requiring 24 hours each annually; and 20 manufacturers also requiring 24 hours each annually to participate in the program. In addition, FDA estimates that a recordkeeping burden of 52 hours will be imposed annually on the 10 SIP Sponsors, and a recordkeeping burden of 24 hours will be imposed annually on each of the 10 Importers and the 20 manufacturers. The 20 manufacturers anticipated to participate in the program will also incur an estimated burden of 24 hours each for copying and providing records to SIP Sponsors and Importers of foreign transactions.

FDA estimates the burden of this collection of information as follows:

Table 2.--Estimated Annual Reporting Burden¹

Type of Information Collection Activity/Respondent	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
SIP Sponsor 251.3; 251.8; 251.14--SIP Proposal Submission Requirements; 251.18--Post-Importation Requirements; 251.19--Reports to FDA	10	1	10	392	3,920
Importer 251.5; 251.12; 251.13; 251.17--Pre-Import Request and Importation Requirements	10	1	10	20	200
Manufacturer 251.16 Laboratory Testing Requirements	20	1	20	28	560
Total					4,680

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

Table 3.--Estimated Annual Recordkeeping Burden¹

Type of Information Collection Activity/Respondent	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
SIP Sponsor 251.8--Modification or Extension of Authorized Importation Programs	10	1	10	52	520
Importer 251.14(d)--Supply Chain Security Requirements; 251.17--Importation Requirements; 251.18 Post-Importation Requirements	10	1	10	24	240
Manufacturer 251.14(b)--Supply Chain Security Requirements	20	1	20	24	480
Total					1,240

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

Table 4.--Estimated Annual Third-Party Disclosure Burden¹

Type of Information Collection Activity/Respondent	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Manufacturer 251.5--Pre-Import Request; 251.14(b)--Supply Chain Security Requirements	20	1	20	24	480

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

The information collection provisions in this final rule have been submitted to OMB for review as required by section 3507(d) of the Paperwork Reduction Act of 1995. Before the effective date of this final rule, FDA will publish a notice in the *Federal Register* announcing OMB's decision to approve, modify, or disapprove the information collection provisions in this final rule. An Agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

X. Federalism

We have analyzed this final rule in accordance with the principles set forth in Executive Order 13132. We have determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we conclude that the rule does not contain policies that have federalism

implications as defined in the Executive Order and, consequently, a federalism summary impact statement is not required.

XI. Consultation and Coordination with Indian Tribal Governments

We have analyzed this rule in accordance with the principles set forth in Executive Order 13175. We have determined that the rule does not contain policies that have substantial direct effects on one or more Indian Tribes, on the relationship between the Federal Government and Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes. Accordingly, we conclude that the rule does not contain policies that have tribal implications as defined in the Executive Order and, consequently, a tribal summary impact statement is not required.

XII. References

The following references are on display at the Dockets Management Staff (see ADDRESSES) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at <https://www.regulations.gov/>. FDA has verified the website addresses, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

1. FDA, 2018, “FDA Launches Global Operation to Crack Down on websites Selling Illegal, Potentially Dangerous Drugs; Including Opioids,” accessed September 21, 2020, <https://www.fda.gov/news-events/press-announcements/fda-launches-global-operation-crack-down-websites-selling-illegal-potentially-dangerous-drugs>.

2. FDA, 2020, “Internet Pharmacy Warning Letters,” accessed September 21, 2020, <https://www.fda.gov/drugs/drug-supply-chain-integrity/internet-pharmacy-warning-letters>.

3. HHS Task Force on Drug Importation, 2004, Report on Prescription Drug Importation, accessed September 21, 2020, <http://www.safemedicines.org/wp-content/uploads/2018/03/HHS-Report1220.pdf>.

4. Government of Canada, Archived, “Consultation: Regulations Amending the Food and Drug Regulations 1447-Good Manufacturing Practices,” accessed September 21, 2020, <https://www.canada.ca/en/health-canada/services/drugs-health-products/public-involvement-consultations/compliance-enforcement/regulations-amending-food-drug-regulations-1447.html>.

5. Government of Canada, Health Canada, “GMP Drug Establishment Good Manufacturing Practices Pre-Application Package: Importers, Distributors and Wholesalers,” accessed September 21, 2020, https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-mps/alt_formats/pdf/compli-conform/gmp-bpf/docs/gmp-package-bpf-eng.pdf.

6. FDA, Regulatory Impact Analysis: Importation of Prescription Drugs, <https://www.fda.gov/about-fda/reports/economic-impact-analyses-fda-regulations>.

List of Subjects

21 CFR Part 1

Cosmetics, Drugs, Exports, Food labeling, Imports, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 251

Exports, Labeling, Packaging and containers, Prescription drugs, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 1 and 251 are amended as follows:

PART 1--GENERAL ENFORCEMENT REGULATIONS

1. The authority citation for part 1 continues to read as follows:

Authority: 15 U.S.C. 1333, 1453, 1454, 1455, 4402; 19 U.S.C. 1490, 1491; 21 U.S.C. 321, 331, 332, 333, 334, 335a, 342, 343, 350c, 350d, 350e, 350j, 350k, 352, 355, 360b, 360ccc, 360ccc-1, 360ccc-2, 362, 371, 373, 374, 379j-31, 381, 382, 384, 384a, 384b, 384d, 387, 387a, 387c, 393; 42 U.S.C. 216, 241, 243, 262, 264, 271; Pub. L. 107-188, 116 Stat. 594, 668-69; Pub. L. 111-353, 124 Stat. 3885, 3889.

2. Revise § 1.74 to read as follows:

§ 1.74 *Human drugs.*

In addition to the data required to be submitted in § 1.72, an ACE filer must submit the following information at the time of filing entry in ACE for drugs, including biological products and eligible prescription drugs as defined in § 251.2 of this chapter that are imported or offered for import under section 804 of the Federal Food, Drug, and Cosmetic Act, intended for human use that are regulated by the FDA Center for Drug Evaluation and Research.

(a) For a drug intended for human use that is not an eligible prescription drug covered under paragraph (b) of this section:

(1) *Registration and listing.* The Drug Registration Number and the Drug Listing Number of the foreign establishment where the human drug was manufactured, prepared, propagated, compounded, or processed before being imported or offered for import into the United States is required to register and list the drug under part 207 of this chapter. For the purposes of this section, the Drug Registration Number that must be submitted at the time of entry filing in ACE is the unique facility identifier of the foreign establishment where the human drug was manufactured, prepared, propagated, compounded, or processed before being imported

or offered for import into the United States. The unique facility identifier is the identifier submitted by a registrant in accordance with the system specified under section 510(b) of the Federal Food, Drug, and Cosmetic Act. For the purposes of this section, the Drug Listing Number is the National Drug Code number of the human drug article being imported or offered for import.

(2) *Drug application number.* For a drug intended for human use that is the subject of an approved application under section 505(b) or 505(j) of the Federal Food, Drug, and Cosmetic Act, the number of the new drug application or abbreviated new drug application. For a biological product regulated by the FDA Center for Drug Evaluation and Research that is required to have an approved biologics license application, the number of the applicable application.

(3) *Investigational new drug application number.* For a drug intended for human use that is the subject of an investigational new drug application under section 505(i) of the Federal Food, Drug, and Cosmetic Act, the number of the investigational new drug application.

(b) For an eligible prescription drug as defined in § 251.2 of this chapter that is imported or offered for import under section 804 of the Federal Food, Drug, and Cosmetic Act:

(1) *Registration and listing.* The Drug Registration Number and the Drug Listing Number. For the purposes of this section, the Drug Registration Number that must be submitted in ACE is the unique facility identifier submitted by the Foreign Seller registrant under § 251.9 of this chapter in accordance with the system specified under section 510 of the Federal Food, Drug, and Cosmetic Act. For the purposes of this section, the Drug Listing Number is the National Drug Code number that the Importer will use when relabeling the eligible prescription drug as required in § 251.13 of this chapter.

(2) *Drug application number.* The number of the new drug application or abbreviated new drug application for the counterpart FDA-approved drug.

(3) *Lot or control number.* The lot or control number assigned by the manufacturer of the eligible prescription drug.

(4) *FDA Quantity.* FDA Quantity, which is the quantity of each eligible prescription drug in an import line delineated by packaging level, including the type of package from the largest packaging unit to the smallest packaging unit; the quantity of each packaging unit; and the volume and/or weight of each of the smallest of the packaging units.

(5) *Pre-Import Request number.* The Pre-Import Request number assigned by FDA.

3. Add part 251 to read as follows:

PART 251--SECTION 804 IMPORTATION PROGRAM

Subpart A--GENERAL PROVISIONS

Sec.

251.1 Scope of the part.

251.2 Definitions.

Subpart B--SECTION 804 IMPORTATION PROGRAM PROPOSALS AND PRE-IMPORT REQUESTS

251.3 SIP proposal submission requirements.

251.4 Review and authorization of importation program proposals.

251.5 Pre-Import Request.

251.6 Termination of authorized importation programs.

251.7 Suspension and revocation of authorized importation programs.

251.8 Modification or extension of authorized importation programs.

Subpart C--CERTAIN REQUIREMENTS FOR SECTION 804 IMPORTATION PROGRAMS

251.9 Registration of Foreign Sellers.

251.10 Reviewing and updating registration information for Foreign Sellers.

251.11 Official contact and U.S. agent for Foreign Sellers.

251.12 Importer responsibilities.

251.13 Labeling of eligible prescription drugs.

251.14 Supply chain security requirements for eligible prescription drugs.

251.15 Qualifying laboratory requirements.

251.16 Laboratory testing requirements.

251.17 Importation requirements.

251.18 Post-importation requirements.

251.19 Reports to FDA.

251.20 Severability.

251.21 Consequences for violations.

The authority citation for part 251 reads as follows:

Authority: 21 U.S.C. 351, 352, 353, 355, 360, 360eee-1, 371, 374, 381, 384.

Subpart A--General Provisions**§ 251.1 *Scope of the part.***

(a) This part sets forth the procedures that Section 804 Importation Program sponsors (SIP Sponsors) must follow when submitting plans to implement time-limited programs to begin importation of drugs from Canada under section 804 of the Federal Food, Drug, and Cosmetic Act. This part also sets forth certain requirements that are necessary for such programs to be

authorized by FDA. Additionally, this part sets forth requirements for eligible prescription drugs and requirements for entities that engage in importation of eligible prescription drugs.

(b) This part includes provisions that exempt eligible prescription drugs that meet certain requirements from section 502(f)(1) of the Federal Food, Drug, and Cosmetic Act. It also includes provisions that exempt certain transactions involving eligible prescription drugs from certain requirements in section 582 of the Federal Food, Drug, and Cosmetic Act.

§ 251.2 *Definitions.*

The definitions of terms in section 804 of the Federal Food, Drug, and Cosmetic Act apply to the terms used in this part, if not otherwise defined in this section. The following definitions apply to this part:

Active ingredient has the meaning set forth in § 314.3 of this chapter.

Adverse event means any untoward medical occurrence associated with the use of a drug product in humans, whether or not it is considered related to the drug product. An adverse event can occur in the course of the use of a drug product; from overdose of a drug product, whether accidental or intentional; from abuse of a drug product; from discontinuation of the drug product (e.g., physiological withdrawal); and it includes any failure of expected pharmacological action.

Combination product has the meaning set forth in § 3.2(e) of this chapter.

Constituent part has the meaning set forth in § 4.2 of this chapter.

Disability means a substantial disruption of a person's ability to conduct normal life functions.

Eligible prescription drug means a drug subject to section 503(b) of the Federal Food, Drug, and Cosmetic Act that has been approved and has received a Notice of Compliance and a Drug Identification Number (DIN) from the Health Products and Food Branch of Health Canada

(HPFB) and, but for the fact that it deviates from the required U.S. labeling, also meets the conditions in an FDA-approved new drug application (NDA) or abbreviated new drug application (ANDA) for a drug that is currently commercially marketed in the United States, including those relating to the drug substance, drug product, production process, quality controls, equipment, and facilities.

Exclusion. The term *eligible prescription drug* does not include:

- (1) A controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C. 802));
- (2) A biological product (as defined in section 351(i)(1) of the Public Health Service Act (42 U.S.C. 262(i)(1)));
- (3) An infused drug (including a peritoneal dialysis solution);
- (4) An intravenously injected drug;
- (5) A drug that is inhaled during surgery;
- (6) An intrathecally or intraocularly injected drug;
- (7) A drug that is subject to a risk evaluation and mitigation strategy under section 505-1 of the Federal Food, Drug, and Cosmetic Act; or
- (8) A drug that is not a “product” for purposes of section 582 as defined in section 581(13) of the Federal Food, Drug, and Cosmetic Act.

Entered (or entry) for consumption has the meaning set forth in 19 CFR 141.0a(f).

Entry means the information or data filed electronically in the Automated Commercial Environment (ACE) or any other U.S. Customs and Border Protection (CBP)-authorized electronic data interchange system to secure the release of imported merchandise from CBP, or the act of filing that information or data.

Foreign Seller means an establishment within Canada engaged in the distribution of an eligible prescription drug that is imported or offered for importation into the United States. A Foreign Seller must have an active Drug Establishment License to wholesale drugs by Health Canada. A Foreign Seller must be registered with provincial regulatory authorities to distribute HPFB-approved drugs. A Foreign Seller must not be licensed by a provincial regulatory authority with an international pharmacy license that allows it to distribute drugs that are approved by countries other than Canada and that are not HPFB-approved for distribution in Canada. A Foreign Seller must also be registered with FDA under section 804 of the Federal Food, Drug, and Cosmetic Act in accordance with the requirements described in this part.

Illegitimate foreign product means a drug purchased by a Foreign Seller from a manufacturer, and intended for sale to the Importer in the United States, where the Foreign Seller has credible evidence that shows that the product:

- (1) Is counterfeit, diverted, or stolen;
- (2) Is intentionally adulterated such that the product would result in serious adverse health consequences or death to humans;
- (3) Is the subject of a fraudulent transaction; or
- (4) Appears otherwise unfit for distribution such that the product would be reasonably likely to result in serious adverse health consequences or death to humans.

Importer means a pharmacist or wholesaler. An Importer must be a State-licensed pharmacist, or a State- or FDA-licensed wholesale distributor, who is the U.S. owner of an eligible prescription drug at the time of entry into the United States. The Importer's pharmacist license or wholesale distributor license (if issued by a State and not FDA) must be issued by a State that is a SIP Sponsor or SIP Co-Sponsor. An Importer's pharmacist or wholesale

distributor license must be in effect (i.e., not expired) and the Importer's license must be in good standing with the licensor.

Individual case safety report (ICSR) means a description of an adverse event related to an individual patient or subject.

ICSR attachments means any document related to the adverse event described in an ICSR, such as medical records, hospital discharge summaries, or other documentation.

Life-threatening adverse event means any adverse event that places the patient, in the view of the initial reporter, at *immediate* risk of death from the adverse event as it occurred, i.e., it does not include an adverse event that, had it occurred in a more severe form, might have caused death.

Manufacturer means an applicant, as defined in § 314.3 of this chapter, or a person who owns or operates an establishment that manufactures an eligible prescription drug. Manufacturer also means a holder of a drug master file containing information necessary to conduct the Statutory Testing, prepare the manufacturer's attestation and information statement, or otherwise comply with section 804 of the FD&C Act or this part.

Minimum data set for an adverse event means the minimum four elements required for reporting an ICSR of an adverse event: An identifiable patient, an identifiable reporter, a suspect drug product, and an adverse event.

Pharmacist means a person licensed by a State to practice pharmacy, including the dispensing and selling of prescription drugs.

Pre-Import Request means a request made to FDA by an Importer that must be granted by FDA before the Importer can start importation under a Section 804 Importation Program.

Qualifying laboratory means a laboratory in the United States that has been approved by FDA for the purposes of section 804 of the Federal Food, Drug, and Cosmetic Act.

Relabel has the meaning set forth in § 207.1 of this chapter.

Relabeler has the meaning set forth in § 207.1 of this chapter.

Repack or repackage has the meaning set forth in § 207.1 of this chapter.

Responsible individual(s) means an individual or individuals who are designated in the Section 804 Importation Program compliance plan. Such individuals are responsible for ensuring compliance with the requirements of the Section 804 Importation Program under their oversight and with the applicable provisions of the Federal Food, Drug, and Cosmetic Act and this part.

Section 804 Importation Program (“SIP”) means a program under section 804 of the Federal Food, Drug, and Cosmetic Act, and this part, that has been authorized by FDA for the importation of eligible prescription drugs from Canada.

Section 804 Importation Program Sponsor (“SIP Sponsor”) means a State or Indian Tribe that regulates wholesale drug distribution and the practice of pharmacy that submits a proposal to FDA that describes a program to facilitate the importation of prescription drugs from Canada under section 804 of the Federal Food, Drug, and Cosmetic Act and is responsible for oversight of the implementation of the program. After an initial 2-year period beginning on the date of the first import entry under any SIP authorized under this rule, the Secretary may determine, based on experience under the program, that there is a sufficient likelihood that a proposal that does not include a State or Indian Tribe as the SIP sponsor could provide the same level of assurance of safety as a proposal that does include such a sponsor, such that FDA may begin receiving, reviewing, and potentially authorizing applications for SIPs without such a

sponsor. After the Secretary makes such a determination, a pharmacist or wholesaler may propose a SIP that does not include a State or Indian Tribe as a sponsor, and FDA may authorize such a SIP if the sponsor demonstrates that the SIP meets the criteria for authorization with the same level of assurance of safety as a proposal that includes a State or Indian Tribe as the SIP sponsor, which FDA shall evaluate consistent with any considerations described in the Secretary's determination, including by evaluating whether the application demonstrates that the proposed sponsor has sufficient relevant experience, such as participating in a SIP and demonstrating compliance with the requirements of the Federal Food, Drug, and Cosmetic Act and this part.

Section 804 Importation Program Co-Sponsor ("SIP Co-Sponsor") means any other State or Indian Tribe, or a pharmacist or a wholesale distributor that, with the SIP Sponsor, signs a proposal to FDA that describes a program to facilitate the importation of prescription drugs from Canada under section 804 of the Federal Food, Drug, and Cosmetic Act.

Section 804 Serial Identifier ("SSI") means a unique alphanumeric serial number of up to 20 characters that is assigned and placed on or affixed by the Foreign Seller to each package and homogenous case of the product that the Foreign Seller intends to sell to an Importer. For purposes of the SSI, "package" means the smallest individual saleable unit of product for distribution that is intended by the Foreign Seller for sale to an Importer located in the United States, and "individual saleable unit" means the smallest container of product sold by the Foreign Seller to the Importer.

Serious adverse event. (1) An adverse event is considered "serious" if it results in any of the following outcomes:

- (i) Death;

- (ii) A life-threatening adverse event;
- (iii) Inpatient hospitalization or prolongation of existing hospitalization;
- (iv) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; and/or
- (v) A congenital anomaly/birth defect.

(2) Other events that may be considered serious adverse events: Important medical events that may not result in one of the listed outcomes in this definition may be considered serious adverse events when, based upon appropriate medical judgment, they may jeopardize the patient or study subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples include: Allergic bronchospasm requiring intensive treatment in an emergency department or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of product dependency or product abuse.

Statutory Testing means the testing of an eligible prescription drug as required by section 804(d)(1)(J) and (L) and section 804(e) of the Federal Food, Drug, and Cosmetic Act, including for authenticity, for degradation, and to ensure that the prescription drug is in compliance with established specifications and standards.

Suspect foreign product means a drug purchased by a Foreign Seller from a manufacturer, and intended for sale to an Importer in the United States, for which the Foreign Seller has reason to believe that such product:

- (1) Is potentially counterfeit, diverted, or stolen;
- (2) Is potentially intentionally adulterated such that the product would result in serious adverse health consequences or death to humans;
- (3) Is potentially the subject of a fraudulent transaction; or

(4) Appears otherwise unfit for distribution such that the product would result in serious adverse health consequences or death to humans.

Transaction means the transfer of product between persons in which a change of ownership occurs, in accordance with section 581(24) of the Federal Food, Drug, and Cosmetic Act. For the purposes of this part, “transaction” includes the sale and transfer of product between the manufacturer and Foreign Seller. The sale and transfer of product between Foreign Seller and Importer also constitutes a “transaction.”

Unexpected adverse event means an adverse event that is not included in the current U.S. labeling for the drug product. Events that may be symptomatically or pathophysiologically related to an adverse event included in the labeling but differ from the labeled event because of greater severity or specificity would be considered unexpected. “Unexpected,” as used in this definition, also refers to adverse events that are mentioned in the product labeling as occurring with a class of products or anticipated from the pharmacological properties of the product but are not specifically mentioned as occurring with the particular product.

(1) *Example of greater severity.* Under this definition, hepatic necrosis would be unexpected if the labeling referred only to elevated hepatic enzymes or hepatitis.

(2) *Example of greater specificity.* Cerebral thromboembolism and cerebral hemorrhage would be unexpected if the labeling included only cerebrovascular accidents.

Unique facility identifier means the identifier required to be submitted by the registrant for drug establishment registration under section 510 of the Federal Food, Drug, and Cosmetic Act in accordance with § 207.25 of this chapter. For Foreign Sellers registering under section 804 of the Federal Food, Drug, and Cosmetic Act, the term “unique facility identifier” means the

identifier required to be submitted under § 251.9 in accordance with the system specified under section 510 of the Federal Food, Drug, and Cosmetic Act.

Wholesaler means a person licensed as a wholesale distributor, as the terms “licensed” and “wholesale distributor” are defined in section 581(9)(A) and 581(29), respectively. The term “wholesaler” does not include a person authorized to import drugs under section 801(d)(1).

Subpart B--Section 804 Importation Program Proposals and Pre-Import Requests

§ 251.3 *SIP proposal submission requirements.*

(a) A SIP Sponsor may delegate implementation activities to a SIP co-sponsor but the SIP Sponsor remains responsible for oversight of the implementation of the program.

(b) A SIP Sponsor must only designate one Foreign Seller and one Importer per initial proposal. Additional Foreign Sellers and Importers may be added to an authorized SIP through a supplemental proposal under § 251.8.

(c) A SIP Sponsor that intends to implement a SIP under this part must submit a proposal to FDA in electronic format via FDA’s Electronic Submissions Gateway (ESG) or to an alternative transmission point identified by FDA. The proposal must include:

(1) A cover sheet containing the following:

(i) Name or names of SIP Sponsor and co-sponsors, if any;

(ii) Name and contact information for a person authorized to serve as the point of contact with FDA during its review of the proposal; and

(iii) The signature of the SIP Sponsor and co-sponsors, if any, or authorized representative who is an employee or agent of the Sponsor or co-sponsor and has been authorized to sign the proposal for the Sponsor or co-sponsor. The signatory must reside or have

a place of business within the United States, and the proposal cover sheet must contain the name, title, and business address of the signatory.

(2) A table of contents;

(3) An introductory statement that includes an overview of the SIP Sponsor's SIP

Proposal; and

(4) The SIP Sponsor's importation plan.

(d) The overview of the SIP Proposal must include:

(1) The name of the SIP, if any, and the name or names and address or addresses of the SIP Sponsor and co-sponsors, if any;

(2) The name, email address, and telephone number of the responsible individual(s);

(3) The name and DIN of each eligible prescription drug that the SIP Sponsor seeks to include in the SIP;

(4) The name and address of the applicant that holds the approved NDA or ANDA for each eligible prescription drug's FDA-approved counterpart, and the approved NDA or ANDA number;

(5) The name and address of the manufacturer of the finished dosage form of the eligible prescription drug, if known or reasonably known;

(6) The name and address of the manufacturer of the active ingredient or ingredients of the eligible prescription drugs, if known or reasonably known;

(7) The name and address of the Foreign Seller;

(8) A copy of the Foreign Seller's Health Canada Drug Establishment License;

(9) The name and address of the Importer;

(10) The name and address of the FDA-registered repackager or relabeler, if different from the Importer, that will relabel the eligible prescription drugs (including any limited repackaging in accordance with the requirements in this part), along with adequate evidence of registration and of satisfactory resolution of any objectionable conditions or practices identified during its most recent FDA inspection, if applicable;

(11) A summary of how the SIP Sponsor will ensure that:

(i) The imported eligible prescription drugs meet the Statutory Testing requirements;

(ii) The supply chain is secure;

(iii) The labeling requirements of the Federal Food, Drug, and Cosmetic Act and this part are met;

(iv) The post-importation pharmacovigilance and other requirements of the Federal Food, Drug, and Cosmetic Act and this part are met; and

(v) The SIP will result in a significant reduction in the cost to the American consumer of the eligible prescription drugs that the SIP Sponsor seeks to import.

(e) The SIP Sponsor's importation plan must:

(1) Identify the SIP Sponsor, including any co-sponsors, identify the responsible individual(s), and identify the applicant that holds the approved NDA or ANDA for each eligible prescription drug's FDA-approved counterpart, the manufacturer(s) of the finished dosage form and the active ingredient or ingredients of each eligible prescription drug that the SIP Sponsor seeks to import, if known or reasonably known, the Foreign Seller, if known or reasonably known, and the Importer, and explain the legal relationship, if any, of each of these entities to the SIP Sponsor.

(2) Include an attestation and information statement containing a complete disclosure of any past criminal convictions or violations of State, Federal, or Canadian laws regarding drugs or devices against or by the responsible individual(s), Foreign Seller, or Importer or an attestation that the responsible individual(s), Foreign Seller, or Importer has not been involved in, or convicted of, any such violations. Such attestation and information statement must include principals, any shareholder who owns 10 percent or more of outstanding stock in any non-publicly held corporation, directors, officers, and any facility manager or designated representative of such manager.

(3) Include a list of all disciplinary actions, to include the date of and parties to any action imposed against the responsible individual(s), Foreign Seller, or Importer by State, Federal, or Canadian regulatory bodies, including any such actions against the principals, owners, directors, officers, quality unit, or any facility manager or designated representative of such manager for the previous 7 years prior to submission of the SIP Proposal.

(4) Include:

(i) The Health Canada inspectional history for the Foreign Seller for the previous 5 years or, if the Foreign Seller has been licensed for less than 5 years, for the duration of its period of licensure; and

(ii) The State and Federal inspectional history for the Importer for the previous 5 years or, if the Importer has been licensed for less than 5 years, for the duration of its period of licensure.

(5) Include the proprietary name (if any), the established name, the approved application numbers, and the DIN and National Drug Code (NDC) for each eligible prescription drug that the SIP Sponsor seeks to import from Canada and for its FDA-approved counterpart. The SIP Sponsor's importation plan must also include as much of the information that is required by

§ 251.5 about the HPFB-approved product and its FDA-approved counterpart as is available, including the name and quantity of the active ingredient, the inactive ingredients, and the dosage form.

(6) Provide adequate evidence that each HPFB-approved drug's FDA-approved counterpart drug is currently commercially marketed in the United States.

(7) Describe, to the extent possible, the testing that will be done to establish that the HPFB-approved drug meets the conditions in the NDA or ANDA for the HPFB-approved drug's FDA-approved counterpart. The SIP Sponsor's importation plan must also identify the qualifying laboratory that will conduct the Statutory Testing for the Importer, if the Importer is responsible for conducting the Statutory Testing, and it must establish that the laboratory is qualified in accordance with § 251.15 to conduct the tests.

(8) Include a copy of the FDA-approved drug labeling for the FDA-approved counterpart of the eligible prescription drug, a copy of the proposed labeling that will be used for the eligible prescription drug, and a side-by-side comparison of the FDA-approved labeling and the proposed labeling, including the Prescribing Information, carton and container labeling, and patient labeling (e.g., Medication Guide, Instructions for Use, patient package inserts), with all differences annotated and explained. The SIP Proposal must also include a copy of the HPFB-approved labeling.

(9) Explain how the SIP Sponsor will ensure that the SIP will result in a significant reduction in the cost to the American consumer of the eligible prescription drugs that the SIP Sponsor seeks to import. The explanation must include any assumptions and uncertainty, and it must be sufficiently detailed to allow for a meaningful evaluation.

(10) Explain how the SIP Sponsor will ensure that all the participants in the SIP comply with the requirements of section 804 of the Federal Food, Drug, and Cosmetic Act and this part.

(11) Describe the procedures the SIP Sponsor will use to ensure that the requirements of this part are met, including the steps that will be taken to ensure that the:

(i) Storage, handling, and distribution practices of supply chain participants, including transportation providers, meet the requirements of part 205 of this chapter and do not affect the quality or impinge on the security of the eligible prescription drugs;

(ii) Supply chain is secure;

(iii) Importer screens the eligible prescription drugs it imports for evidence that they are adulterated, counterfeit, damaged, tampered with, expired, suspect foreign product, or illegitimate foreign product; and

(iv) Importer fulfills its responsibilities to submit adverse event, field alert, and other reports required by the SIP, the Federal Food, Drug, and Cosmetic Act, or this part.

(12) Explain how the SIP Sponsor will educate pharmacists, healthcare providers, pharmacy benefit managers, health insurance issuers and plans, as appropriate, and patients about the eligible prescription drugs imported under its SIP.

(13) Include the SIP's recall plan, including an explanation of how the SIP Sponsor will obtain recall or market withdrawal information and how it will ensure that recall or market withdrawal information is shared among the SIP Sponsor, the Foreign Seller, the Importer, and FDA and provided to the manufacturer.

(14) Include the SIP's return plan, including an explanation of how the SIP Sponsor will ensure that product that is returned after distribution in the United States is properly dispositioned in the United States, if it is a non-saleable return, in order to protect patients from

expired or unsafe drugs, and an explanation of how the SIP Sponsor will prevent the non-saleable returned eligible prescription drugs from being exported from the United States. In the event that a returned eligible prescription drug may be considered saleable, include an explanation for how the returned product will be determined to be saleable and under what circumstances such eligible prescription drugs may be re-distributed in the United States.

(15) Include the SIP's compliance plan, which must include:

(i) A description of the division of responsibilities among co-sponsors, if any, which includes a plan for timely communication of any compliance issues to the SIP Sponsor;

(ii) Identification of responsible individual(s) and a description of the respective area(s) of the SIP, the Federal Food, Drug, and Cosmetic Act, or this part that will be under each responsible individual's oversight;

(iii) The creation of written compliance policies, procedures, and protocols;

(iv) The provision of education and training to ensure that Foreign Sellers, Importers, qualifying laboratories, and their employees understand their compliance-related obligations;

(v) The creation and maintenance of effective lines of communication, including a process to protect the anonymity of complainants and to protect whistleblowers; and

(vi) The adoption of processes and procedures for uncovering and addressing noncompliance, misconduct, or conflicts of interest.

(16) Explain how the SIP Sponsor will ensure that any information that the manufacturer supplies to authenticate a prescription drug being tested and confirm that the labeling of the prescription drug complies with labeling requirements under the Federal Food, Drug, and Cosmetic Act, and any trade secrets or commercial or financial information that is privileged or confidential that the manufacturer supplies for the purposes of testing or otherwise complying

with the Federal Food, Drug, and Cosmetic Act and this part, are kept in strict confidence and used only for the purposes of testing or otherwise complying with the Federal Food, Drug, and Cosmetic Act and this part.

§ 251.4 *Review and authorization of importation program proposals.*

Based on a review of a SIP Proposal or supplemental proposal submitted under this part, FDA may authorize a SIP, modify a SIP, or extend the authorization period of a SIP, that meets the requirements of this part. FDA may use a phased review process to review a SIP Proposal that does not identify a Foreign Seller in an initial submission, under which FDA may notify the Sponsor of such a SIP Proposal whether the Sponsor's SIP Proposal otherwise meets the requirements of this part. In such a case, the required information regarding importers, relabelers, and repackagers still must be included in the initial submission of the SIP Proposal, and the SIP Proposal will be denied if a Foreign Seller is not identified within 6 months of the initial submission date of the SIP Proposal.

(a) FDA may deny a request for authorization, modification, or extension of a SIP, including if a SIP Proposal or supplemental proposal does not meet the requirements of this part. When a SIP Proposal or supplemental proposal meets the requirements of this part, FDA may nonetheless decide not to authorize the SIP Proposal or supplemental proposal. For example, FDA may decide not to authorize a SIP Proposal or supplemental proposal because of potential safety concerns with the SIP; because a Foreign Seller is not identified within 6 months of the initial submission of the SIP Proposal; because of the degree of uncertainty that the SIP Proposal or supplemental proposal would adequately ensure the protection of public health; because of, based on the recommendation of another HHS component as directed by the Secretary, the relative likelihood that the SIP Proposal or supplemental proposal would not result in significant

cost savings to the American consumer; because of the potential for conflicts of interest; or in order to limit the number of authorized SIPs so FDA can effectively and efficiently carry out its responsibilities under section 804 of the Federal Food, Drug, and Cosmetic Act in light of the amount of resources allocated to carrying out such responsibilities.

(b) FDA will notify a SIP Sponsor in writing when FDA receives the SIP Sponsor's SIP Proposal or supplemental proposal.

(c) FDA will make a reasonable effort to promptly communicate to a SIP Sponsor about any information required by § 251.3 that was not submitted in a SIP Proposal.

(1) FDA may notify a SIP Sponsor if FDA believes additional information would help FDA's review of a SIP Proposal or supplemental proposal.

(2) FDA will notify a SIP Sponsor in writing whether FDA has decided to authorize or not to authorize the SIP Sponsor's SIP Proposal or supplemental proposal.

§ 251.5 *Pre-Import Request.*

(a) An eligible prescription drug may not be imported or offered for import under this part unless the Importer has filed a Pre-Import Request for that drug in accordance with this section and FDA has granted the Pre-Import Request.

(b) The Importer must submit a complete Pre-Import Request in electronic format via the ESG, or to an alternative transmission point identified by FDA, at least 30 calendar days prior to the scheduled date of arrival or entry for consumption, whichever occurs first, of an eligible prescription drug covered under an authorized SIP.

(c) A complete Pre-Import Request must include, at a minimum:

(1) Identification of the Importer, including Importer name; business type (wholesale distributor or pharmacist); U.S. license number(s) and State(s) of license; business address;

unique facility identifier if required to register with FDA as an establishment under section 510 of the Federal Food, Drug, and Cosmetic Act or FDA establishment identification number if not required to register under section 510 of the Federal Food, Drug, and Cosmetic Act; and the name, email address, and phone number of a contact person.

(2) Identification of the FDA-authorized SIP, including the name of the SIP, if any; the name or names of the SIP Sponsor and co-sponsors, if any; business address; and the name, email address, and phone number of a contact person.

(3) Identification of the Foreign Seller, including the name of the Foreign Seller; business address; unique facility identifier; any license numbers issued by Health Canada or a provincial regulatory body; and the name, email address, and phone number of a contact person.

(4) Identification and description of each drug covered by the Pre-Import Request, including, for each drug, the following information:

(i) Established and proprietary name of the HPFB-approved drug, as applicable; DIN; and complete product description, including strength, description of dosage form, and route(s) of administration.

(ii) Active pharmaceutical ingredient (API) information, including:

(A) Name of API;

(B) Manufacturer of API and its unique facility identifier; and

(C) Amount of API and unit measure in the eligible prescription drug;

(iii) Established name and proprietary name, as applicable, of the FDA-approved counterpart drug and NDA or ANDA number.

(iv) Manufacturer of the eligible prescription drug with the business address and unique facility identifier.

(v) Copies of the invoice and any other documents related to the manufacturer's sale of the drug to the Foreign Seller that was provided by the manufacturer to the Importer, and copies of the same documents provided by the Foreign Seller to the Importer.

(vi) Quantity, listed separately by dosage form, strength, batch and lot or control number assigned by the manufacturer to the eligible prescription drug intended to be imported under this Pre-Import Request, compared to the quantity of each batch and lot or control number originally received by the Foreign Seller from the manufacturer, and the date of such receipt.

(vii) Expiration date of the HFPB-approved drug, listed by lot or control number assigned by the manufacturer.

(viii) Expiration date to be assigned to the eligible prescription drug when relabeled by the Importer with a complete description of how that expiration date was determined using the manufacturer's stability studies in accordance with the FDA-approved NDA or ANDA.

(ix) NDC proposed for assignment by the Importer.

(x) FDA product code for the eligible prescription drug(s) to be imported.

(xi) Unless the manufacturer has notified the Importer that it intends to conduct the required testing as provided in §251.16(e), a Statutory Testing plan that includes:

(A) A description of how the samples will be selected from a shipment for the Statutory Testing;

(B) The name and location of the qualifying laboratory in the United States that will conduct the Statutory Testing; and

(C) A description of the testing method(s) that will be used to conduct the Statutory Testing.

(xii) Attestation and information statement from the manufacturer that establishes that the drug proposed for import, but for the fact that it bears the HPFB-approved labeling, meets the conditions in the FDA-approved NDA or ANDA, including any process-related or other requirements for which compliance cannot be established through laboratory testing.

Accordingly, the attestation and information statement must include, at a minimum:

(A) Confirmation that the HPFB-approved drug has the active ingredient(s), active ingredient source(s) (including manufacturing facility or facilities), inactive ingredient(s), dosage form, strength(s), and route(s) of administration described in the FDA-approved drug's NDA or ANDA.

(B) Confirmation that the HPFB-approved drug conforms to the specifications in the FDA-approved drug's NDA or ANDA regarding the quality of the drug substance(s), drug product, intermediates, raw materials, reagents, components, in-process materials, container closure systems, and other materials used in the production of the drug.

(C) Confirmation that the HPFB-approved drug was manufactured in accordance with the conditions described in the FDA-approved drug's NDA or ANDA, including with regard to the facilities and manufacturing lines that are used, and in compliance with current good manufacturing practice requirements set forth in section 501 of the Federal Food, Drug, and Cosmetic Act and parts 4 (if a combination product), 210, and 211 of this chapter.

(D) Original date of manufacture or the date used to calculate the labeled expiration date based on the HPFB-approved or scientifically validated expiration period, the expiration period set forth in the FDA-approved drug's NDA or ANDA, and any other information needed to label the drug with an expiration date within the expiration dating period determined by stability studies in the FDA-approved NDA or ANDA.

(E) Information needed to confirm that the labeling of the prescription drug complies with labeling requirements under the Federal Food, Drug, and Cosmetic Act.

(xiii) Information related to the importation, including:

(A) Location of the eligible prescription drugs in Canada and anticipated date of shipment (date the eligible prescription drug(s) leave their location in Canada);

(B) Name, address, email address, and telephone number of the Foreign Seller;

(C) Anticipated date of export from Canada and Canadian port of exportation;

(D) Anticipated date and approximate time of arrival at the port authorized by FDA to import eligible prescription drugs under section 804 of the Federal Food, Drug, and Cosmetic Act;

(E) The name, address, unique facility identifier or FDA establishment identification number, and telephone number of the secured warehouse, location within a specific foreign trade zone, or other secure distribution facility controlled by or under contract with the Importer where the eligible prescription drug will be stored pending testing, relabeling, and FDA determination of admissibility;

(F) Information regarding the facility where the relabeling and any repackaging allowed under the authorized SIP will occur for the eligible prescription drug, including:

(1) The facility's unique facility identifier;

(2) The facility's name, address, and FDA establishment identifier number;

(3) The anticipated date the relabeling and any limited repackaging will be completed;

and

(4) Information about where the relabeled drug will be stored pending distribution, including the FDA establishment identification number of the storage facility, if available.

(d) The manufacturer must provide the attestation and information statement described in § 251.5(c)(4)(xii) to the Importer within 30 calendar days of receiving the Importer's request. If the manufacturer cannot provide the attestation and information statement, it must notify FDA and the Importer of its inability to provide the attestation and information statement and articulate with specificity the reason(s) why it cannot provide the attestation and information statement.

(e)(1) The Importer must provide the executed batch record, including the certificate of analysis, for at least one recently manufactured, commercial-scale batch of the HPFB-approved drug, and at least one recently manufactured, commercial-scale batch of the FDA-approved drug that was produced for and released for distribution to the U.S. market under an NDA or ANDA.

(2) The manufacturer must provide these records to the Importer, within 30 calendar days of receiving the Importer's request, for each manufacturing line that the manufacturer used to produce either or both of the drugs.

§ 251.6 *Termination of authorized importation programs.*

(a) Unless an extension is granted under this part, authorization for a SIP automatically terminates after 2 years, or a shorter period of time if a shorter period of time is specified in the authorization for the SIP.

(b) The authorization period for a SIP begins when the Importer, or its authorized customs broker, files an electronic import entry for consumption for its first shipment of drugs under the SIP.

(c) Notwithstanding paragraph (a) of this section, authorization for a SIP terminates if the Importer, or its authorized customs broker, does not file an electronic import entry for

consumption for a shipment of eligible prescription drugs under the SIP within 1 year of the date that the SIP was authorized.

(d) FDA will terminate authorization of a SIP upon request from the SIP Sponsor.

(e) An eligible prescription drug cannot be shipped into the United States under this part, and is subject to refusal of admission into the United States, if the authorization of the SIP has terminated.

§ 251.7 *Suspension and revocation of authorized importation programs.*

(a) FDA may suspend a SIP under any of the circumstances set forth in § 251.18, or under any other circumstances in FDA's discretion. An eligible prescription drug cannot be shipped into the United States under this part, and is subject to refusal of admission into the United States, if FDA has suspended the SIP or revoked its authorization.

(b) SIP Sponsors and other SIP participants must agree to submit to audits of their books and records and inspections of their facilities as a condition of participation in a SIP. If a SIP Sponsor, manufacturer, Foreign Seller, Importer, qualifying laboratory, or other participant in the supply chain delays, denies, or limits an inspection, or refuses to permit entry, inspection, or audit of its facility or its records, FDA may suspend the SIP, in whole or in part, immediately.

(c) FDA may revoke authorization of a SIP, in whole or in part, including with respect to one or more drugs in the SIP, at any time if FDA determines that:

(1) The SIP Proposal contained an untrue statement of material fact;

(2) The SIP Proposal omitted material information;

(3) The SIP no longer meets the requirements of section 804 of the Federal Food, Drug, and Cosmetic Act, this part, or the SIP, including, among other things, if FDA finds that the

manufacturer, the Foreign Seller, the Importer, or any other supply chain participant is found to be not compliant with section 501(a)(2)(A) or (B) of the Federal Food, Drug, and Cosmetic Act;

(4) Continued implementation of the SIP is reasonably likely to pose additional risk to the public's health and safety;

(5) Confidential manufacturer information was disclosed in violation of § 251.16;

(6) Continued implementation of the SIP is not reasonably likely to result in a significant reduction in the cost of the drugs covered by the SIP to the American consumer;

(7) Continued monitoring of the SIP imposes too much of a burden on FDA or HHS resources for carrying out this part or is inconsistent with FDA or HHS prioritization of resources;

(8) Continued implementation of the SIP is otherwise inappropriate; or

(9) Grounds exist for suspension under § 251.7(a) or (b) and FDA determines it should revoke, either instead of, or after, suspension.

§ 251.8 *Modification or extension of authorized importation programs.*

(a) A supplemental proposal to modify or extend an authorized SIP must be submitted in electronic format via the ESG, or to an alternative transmission point identified by FDA, for FDA's consideration.

(b) FDA's review and authorization of a supplemental proposal to modify or extend an authorized SIP is governed by this part. In reviewing a supplemental proposal, FDA may take into account information learned subsequent to authorization of the SIP.

(c) FDA may authorize a supplemental proposal from a SIP Sponsor to add additional Foreign Sellers or additional Importers to an authorized SIP if FDA determines the SIP Sponsor has adequately demonstrated that the SIP has consistently imported eligible prescription drugs in

accordance with section 804 of the Federal Food, Drug, and Cosmetic Act and this part. Each supply chain under a SIP must be limited to one manufacturer, one Foreign Seller, and one Importer.

(d) If FDA authorizes changes to a SIP, the Importer must submit a new Pre-Import Request in accordance with § 251.5.

(e) A SIP Sponsor must not make any changes or permit any changes to be made to a SIP without first securing FDA's authorization.

(f) A SIP Sponsor may request that FDA extend the authorization period of an authorized SIP. Such a request must be submitted at least 90 calendar days before the SIP's authorization period will expire. To be eligible for an extension of the authorized SIP, a SIP must be up to date on all of the information and records-related requirements of section 804 of the Federal Food, Drug, and Cosmetic Act and this part. FDA may extend the authorization period for up to 2 years at a time.

Subpart C--Certain Requirements for Section 804 Importation Programs

§ 251.9 *Registration of Foreign Sellers.*

(a) Any Foreign Seller(s) designated in a SIP Proposal must be registered with FDA before FDA will authorize the SIP Proposal.

(b) To register, a Foreign Seller must provide the following information:

(1) Name of the owner or operator; if a partnership, the name of each partner; if a corporation, the name of each corporate officer and director, and the place of incorporation;

(2) All names of the Foreign Seller, including names under which the Foreign Seller conducts business or names by which the Foreign Seller is known;

(3) Physical address and telephone number(s) of the Foreign Seller;

(4) Registration number, if previously assigned by FDA;

(5) A unique facility identifier in accordance with the system specified under section 510 of the Federal Food, Drug, and Cosmetic Act;

(6) All types of operations performed by the Foreign Seller;

(7) Name, mailing address, telephone number, and email address of the official contact for the establishment; and

(8) Name, mailing address, telephone number, and email address of:

(i) The U.S. agent;

(ii) The Importer to which the Foreign Seller plans to sell eligible prescription drugs; and

(iii) Each SIP Sponsor with which the Foreign Seller works.

§ 251.10 *Reviewing and updating registration information for Foreign Sellers.*

(a) *Expedited updates.* A Foreign Seller must update its registration information no later than 30 calendar days after:

(1) Closing or being sold;

(2) Changing its name or physical address; or

(3) Changing the name, mailing address, telephone number, or email address of the official contact or the U.S. agent. A Foreign Seller, official contact, or U.S. agent may notify FDA about a change of information for the designated official contact or U.S. agent, but only a Foreign Seller is permitted to designate a new official contact or U.S. agent.

(b) *Annual review and update of registration information.* A Foreign Seller must review and update all registration information required under § 251.9.

(1) The first review and update must occur during the period beginning on October 1 and ending December 31 of the year of initial registration, if the initial registration occurs prior to

October 1. Subsequent reviews and updates must occur annually, during the period beginning on October 1 and ending December 31 of each calendar year.

(2) The updates must reflect new changes not previously required to be reported, along with a summary of the registration updates that were provided to FDA as required during the calendar year.

(3) If no changes have occurred since the last registration, a Foreign Seller must certify that no changes have occurred.

§ 251.11 *Official contact and U.S. agent for Foreign Sellers.*

(a) *Official contact.* A Foreign Seller subject to the registration requirements of this part must designate an official contact. The official contact is responsible for:

(1) Ensuring the accuracy of registration information as required by § 251.9; and

(2) Reviewing, disseminating, routing, and responding to all communications from FDA, including emergency communications.

(b) *U.S. agent.* (1) A Foreign Seller must designate a single U.S. agent. The U.S. agent must reside or maintain a place of business in the United States and may not be a mailbox, answering machine or service, or other place where a person acting as the U.S. agent is not physically present. The U.S. agent is responsible for:

(i) Reviewing, disseminating, routing, and responding to all communications from FDA, including emergency communications;

(ii) Responding to questions concerning those drugs that are imported or offered for import to the United States; and

(iii) Assisting FDA in scheduling inspections.

(2) FDA may provide certain information and/or documents to the U.S. agent. The provision of information and/or documents by FDA to the U.S. agent is equivalent to providing the same information and/or documents to the Foreign Seller.

§ 251.12 *Importer responsibilities.*

(a) The Importer is responsible for:

(1) In accordance with the procedures set forth in § 207.33 of this chapter, proposing an NDC for assignment for each eligible prescription drug imported pursuant to this part;

(2) Examining the Canadian labeling of a sample of each shipment of eligible prescription drugs to verify that the labeling is that of the HPFB-approved drug, and attesting that such examination has been conducted through reports to FDA required under this part;

(3) Screening eligible prescription drugs for evidence that they are adulterated, counterfeit, damaged, tampered with, expired, suspect foreign product, or illegitimate foreign product;

(4) Ensuring the eligible prescription drug is relabeled with the required U.S. labeling, including the container and carton labeling; Prescribing Information; and patient labeling, such as Medication Guides, Instruction for Use documents, and patient package inserts, in accordance with §§ 251.13 and 251.14(d);

(5) Arranging for an entry to be submitted in accordance with § 251.17;

(6) Collecting and submitting the information and documentation to FDA about the imported drug(s) pursuant to section 804(d) of the Federal Food, Drug, and Cosmetic Act, in addition to information about the Foreign Seller, as set forth in § 251.19; and

(7) Submitting the adverse event, field alert, and other reports, and complying with drug recalls, in accordance with § 251.18.

(b) If the Importer is also relabeling the eligible prescription drug, the Importer must also:

(1) Register with FDA as a repackager or relabeler under section 510(b) of the Federal Food, Drug, and Cosmetic Act, in accordance with § 207.25 of this chapter;

(2) Obtain a labeler code from FDA and propose an NDC for each eligible prescription drug pursuant to § 207.33 of this chapter; and

(3) List each eligible prescription drug pursuant to § 207.53 of this chapter.

(c) If the Importer is not itself relabeling the eligible prescription drug, the Importer must:

(1) Obtain its own labeler code from FDA under § 207.33(c) of this chapter;

(2) Ensure that the eligible prescription drug incorporates the NDC the Importer proposed for assignment, which must include the Importer's labeler code; and

(3) Ensure that the entity relabeling an eligible prescription drug on its behalf proposes an NDC pursuant to § 207.33 of this chapter and lists each eligible prescription drug pursuant to § 207.53 of this chapter.

§ 251.13 *Labeling of eligible prescription drugs.*

(a) Upon the request of a SIP Sponsor or Importer, the manufacturer of an eligible prescription drug must provide an Importer written authorization for the Importer to use, at no cost, the FDA-approved labeling for the drug. If the manufacturer fails to do so within 30 calendar days of receiving the Importer's request, FDA may deem this authorization to have been given.

(b) In addition to the exemption provided in subpart D of part 201 of this chapter, an eligible prescription drug imported for purposes of this part is exempt from section 502(f)(1) of the Federal Food, Drug, and Cosmetic Act if all the following conditions are met:

(1) The Importer or the manufacturer certifies that the drug meets all labeling requirements under the Federal Food, Drug, and Cosmetic Act, including the requirements of this part. The Importer of an eligible prescription drug must either:

(i) Propose an NDC for the drug following the procedures in § 207.33 of this chapter and list the drug following the procedures in § 207.53 of this chapter, or

(ii) Take responsibility to ensure that the entity performing relabeling on its behalf lists each eligible prescription drug and incorporates the NDC the Importer proposed for assignment in accordance with the applicable requirements of part 207 of this chapter.

(2) The drug must be:

(i) In the possession of a person (or his or her agents or employees), including Foreign Sellers and Importers, regularly and lawfully engaged in the manufacture, transportation, storage, or wholesale distribution of prescription drugs;

(ii) In the possession of a retail, hospital, or clinic pharmacy, or a public health agency, regularly and lawfully engaged in dispensing prescription drugs; or

(iii) In the possession of a practitioner licensed by law to administer or prescribe such drugs.

(3) The drug is to be dispensed in accordance with section 503(b) of the Federal Food, Drug, and Cosmetic Act.

(4) At the time the drug is sold or dispensed, the labeling of the drug must be the same as the FDA-approved labeling under the applicable NDA or ANDA, except that the labeling must bear conspicuously:

(i) The Importer's NDC for the eligible prescription drug, and such NDC must replace any other NDC otherwise appearing on the label of the FDA-approved drug;

(ii) The lot number assigned by the manufacturer of the eligible prescription drug, on the carton labeling and on the container label;

(iii) The name and place of business of the Importer;

(iv) The statement: “[This drug was/These drugs were] imported from Canada without the authorization of [Name of Applicant] under the [Name of SIP Sponsor] Section 804 Importation Program.” If the SIP maintains a website, the statement could also include the website address. This statement must appear in the HOW SUPPLIED/STORAGE AND HANDLING section for products subject to §§ 201.56(d) and 201.57 of this chapter, or in the HOW SUPPLIED section for products subject to §§ 201.56(e) and 201.80 of this chapter. The statement also must be included on the immediate container label and outside package;

(v) For products subject to §§ 201.56(d) and 201.57(c)(17)(iii) of this chapter, the NDC(s) assigned to the eligible prescription drug in accordance with the procedures in § 207.33 of this chapter must be included in the HOW SUPPLIED/STORAGE AND HANDLING section in place of the NDC(s) assigned to the FDA-approved versions of the drug. The NDC(s) also must be included on the immediate container label and outside package;

(vi) For products subject to §§ 201.56(d) and 201.57(a)(11)(ii) of this chapter, the Adverse Reaction Contact Reporting Statement under the Adverse Reactions heading in the Highlights of Prescribing Information. This statement must include the Importer’s name and the telephone number of the firm to provide a structured process for reporting suspected adverse events; and

(vii) For products subject to §§ 201.56(e) and 201.80(k)(3) of this chapter, the NDC(s) assigned to the eligible prescription drug in accordance with the procedures in § 207.33 of this chapter. The NDC(s) must be included in the HOW SUPPLIED section in place of the NDC(s)

assigned to the FDA-approved versions of the drug. The NDC(s) also must be included on the immediate container label and outside package.

(c) The Importer is responsible for relabeling the drug, or arranging for it to be relabeled, to meet the requirements of this part. The relabeling and associated limited repackaging activities must meet applicable requirements, including applicable current good manufacturing practice requirements under parts 210 and 211 of this chapter. Except for repackaging that is necessary to perform the relabeling described in this part, further repackaging of drugs imported pursuant to a SIP is prohibited. Repackaging the container closure of a drug is not permitted under this part.

(d) The Importer may submit to FDA, in electronic format via the ESG or to an alternative transmission point identified by FDA, under § 251.8, a supplemental proposal to modify the labeling of an eligible prescription drug, for example if the eligible prescription drug's container is too small to fit the additional information required by this section.

§ 251.14 *Supply chain security requirements for eligible prescription drugs.*

(a) *SIP Sponsor.* A sponsor of an authorized SIP must ensure that:

(1) Each drug imported under the SIP is HPFB-approved and labeled for sale in Canada by the manufacturer before it reaches the Foreign Seller;

(2) For each drug that is imported under the SIP and that is manufactured outside Canada, the drug was authorized for import into Canada by the manufacturer and was not transshipped through Canada for sale in another country;

(3) For each drug imported under the SIP, the drug was sold by the manufacturer directly to a Foreign Seller;

(4) For each drug imported under the SIP, the Foreign Seller ships the drug directly to the Importer in the United States;

(5) For each drug imported under the SIP, the Foreign Seller identified in the SIP meets applicable supply chain security requirements of this part;

(6) The Importer identified in the SIP meets the applicable requirements of this part and in sections 582(c) and (d) of the Federal Food, Drug, and Cosmetic Act; and

(7) Returned eligible prescription drugs are properly dispositioned in, and not exported from, the United States.

(b) *Manufacturer.* For each transaction of the eligible prescription drug, the manufacturer must provide to the Importer, within 30 calendar days of receiving the Importer's request, a copy of all transaction documents that were provided from the manufacturer to the Foreign Seller.

(c) *Foreign Seller.*

(1) A Foreign Seller must have systems in place to:

(i) Determine whether a drug in its possession or control that it intends to sell to the Importer under a SIP is a suspect foreign product. Upon making a determination that a drug in its possession or control is a suspect foreign product, or upon receiving a request for verification from FDA that the Foreign Seller has determined that a product within its possession or control is a suspect foreign product, a Foreign Seller must:

(A) Quarantine such product within its possession or control until such product is cleared or dispositioned;

(B) Promptly conduct an investigation, in coordination with the Importer and the manufacturer, as applicable, to determine whether the product is an illegitimate foreign product, and verify the product at the package level, including the SSI; and

(C) If the Foreign Seller makes the determination that a suspect foreign product is not an illegitimate foreign product, promptly notify FDA of such determination for those products that FDA has requested verification.

(ii) Determine whether a drug in its possession or control that it intends to sell to the Importer under a SIP is an illegitimate foreign product. Upon making a determination that a drug in its possession or control is an illegitimate foreign product, the Foreign Seller must:

(A) Quarantine such product within the possession or control of the Foreign Seller from product intended for distribution until such product is dispositioned;

(B) Disposition the illegitimate foreign product within the possession or control of the Foreign Seller;

(C) Take reasonable and appropriate steps to assist a manufacturer or Importer to disposition an illegitimate product not in the possession or control of the Foreign Seller; and

(D) Retain a sample of the product for further physical examination or laboratory analysis of the product by the manufacturer or FDA (or other appropriate Federal or State official) upon request by FDA (or other appropriate Federal or State official), as necessary and appropriate.

(2)(i) Upon determining that a product in the possession or control of the Foreign Seller is an illegitimate foreign product, the Foreign Seller must notify FDA and the Importer that the Foreign Seller received such illegitimate product not later than 24 hours after making such determination.

(ii) Upon the receipt of a notification from the manufacturer, FDA, the Importer or other wholesale distributor, or dispenser that a determination has been made that a product that had been sold by the Foreign Seller is an illegitimate foreign product, a Foreign Seller must identify all illegitimate foreign product subject to such notification that is in the possession or control of the Foreign Seller, including any product that is subsequently received, and perform the activities to investigate the product described in paragraph (c)(1) of this section.

(iii) Upon making a determination, in consultation with FDA, that a notification is no longer necessary, a Foreign Seller must promptly notify the Importer and person who sent the notification that the notification is terminated.

(iv) A Foreign Seller must keep records of the disposition of an illegitimate foreign product for not less than 6 years after the conclusion of the disposition.

(3) Upon request by FDA, or other appropriate Federal or State official, in the event of a recall or for purposes of investigating a suspect foreign product or an illegitimate foreign product, a Foreign Seller must promptly provide the official with information about its transactions with the manufacturer and the Importer.

(4) A Foreign Seller, upon receiving a shipment of eligible prescription drugs from the manufacturer, must:

(i) Separate the portion of drugs intended for sale to the Importer located in the United States, and store such portion separately from that portion of product intended for sale in the Canadian market;

(ii) Assign an SSI to each package and homogenous case intended for sale to the Importer in the United States, unless each such package and homogenous case displayed a manufacturer-

affixed or imprinted product identifier, as such term is defined in section 581(14) of the Federal Food, Drug, and Cosmetic Act, at the time of receipt by the Foreign Seller;

(iii) Affix or imprint the SSI on each package and homogenous case intended for sale to the Importer in the United States. Such SSI must be located on blank space on the package or homogenous case and must not obscure any labeling for the Canadian market, including the DIN; and

(iv) Keep records associating the SSI with the DIN and all the records the Foreign Seller received from the manufacturer upon receipt of the original shipment intended for the Canadian market for not less than 6 years.

(5) Upon receiving a request for verification from the Importer or other authorized repackager, wholesale distributor, or dispenser that is in possession or control of a product such person believes to be distributed by such Foreign Seller, a Foreign Seller must, not later than 24 hours after receiving the request for verification, or in such other reasonable time as determined by the FDA based on the circumstances of the request, notify the person making the request whether the SSI that is the subject of the request corresponds to the SSI affixed or imprinted by the Foreign Seller. If a Foreign Seller responding to a request for verification identifies an SSI that does not correspond to that SSI affixed or imprinted by the Foreign Seller, the Foreign Seller must treat such product as suspect foreign product and conduct an investigation as described in paragraph (c)(1) of this section. If the Foreign Seller determines the product is an illegitimate foreign product, the Foreign Seller must advise the person making the request of such determination at the time such Foreign Seller responds to the request for verification.

(6) For each transaction between the Foreign Seller and the Importer for an eligible prescription drug, the Foreign Seller must provide:

- (i) A statement that the Foreign Seller purchased the product directly from the manufacturer;
- (ii) The proprietary name (if any) and the 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 assigned by the manufacturer;
- (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.
- (7) Upon a request by FDA, or other appropriate Federal or State official, in the event of a recall or for purposes of investigating a suspect foreign product or an illegitimate foreign product, the Foreign Seller must promptly provide the official with information about its transactions with the manufacturer and the Importer.
- (d) Importers.*
- (1) An Importer of an eligible prescription drug must purchase the drug directly from a Foreign Seller in Canada.

(2) Upon receipt of an eligible prescription drug in a transaction from the Foreign Seller, an Importer must facilitate the affixation or imprinting of a product identifier, as defined in section 581(14) of the Federal Food, Drug, and Cosmetic Act, for all eligible prescription drugs. The Importer must ensure that such affixation or imprinting occurs at the same time the product is relabeled with the required U.S.-approved labeling for the drug product and, except for repackaging necessary to perform the relabeling described in this part, cannot otherwise relabel or repackage the product. The Importer may affix or imprint the product identifier, or the Importer may contract with an entity registered with FDA under part 207 of this chapter to accomplish such relabeling, provided that the entity does not otherwise relabel or repackage the product, except for repackaging that is necessary to perform the relabeling described in this part. Any entity with which the Importer contracts to accomplish such labeling must, even if not engaged in a repackaging operation with respect to the eligible prescription drug, have systems and processes in place to meet applicable requirements of a “repackager” under section 582(e) of the Federal Food, Drug, and Cosmetic Act for any transaction involving the eligible prescription drug.

(3) The repackager that affixes or imprints the product identifier on each package and homogenous case of an eligible prescription drug in accordance with section 582 of the Federal Food, Drug, and Cosmetic Act, which may be the Importer or the Importer’s authorized repackager--

(i) May affix or imprint a product identifier only on a package of an eligible prescription drug that has a serial number that was assigned and affixed by the Foreign Seller;

(ii) Must maintain the product identifier information for such drug for not less than 6 years; and

(iii) Must maintain records for not less than 6 years that associate the product identifier the repackager affixes or imprints with the serial number assigned by the Foreign Seller and the Canadian DIN.

(4) An Importer must retain records, for not less than 6 years, that allow the Importer to associate the product identifier affixed or imprinted on each package or homogenous case of product it received from the Foreign Seller, with the SSI that had been assigned by the Foreign Seller, and the Canadian DIN that was on the package when the Foreign Seller received the product from the manufacturer.

(5) An Importer must, upon receipt of an eligible prescription drug and records from a Foreign Seller, compare such information with information the Importer received from the manufacturer, including relevant documentation about the transaction that the manufacturer provided to the Foreign Seller upon its transfer of ownership of the product for the Canadian market.

(6) An Importer must comply with all applicable requirements of section 582 of the Federal Food, Drug, and Cosmetic Act, including requirements that apply to subsequent transactions with trading partners, unless a waiver, exception, or exemption applies.

(7) For transactions of eligible prescription drugs between Importers and Foreign Sellers under a SIP, an Importer is exempt from the following specific supply chain security requirements that are otherwise applicable:

(i) An Importer is exempt from the prohibition on receiving a product for which the previous owner did not provide the transaction history, transaction information, and transaction statement, under sections 582(c)(1)(A) or (d)(1)(A) of the Federal Food, Drug, and Cosmetic

Act, as applicable, provided that the Importer receives from the Foreign Seller the information required under paragraph (c) of this section.

(ii) An Importer is exempt from the prohibition on receiving a product that is not encoded with a product identifier, under sections 582(c)(2) or (d)(2) of the Federal Food, Drug, and Cosmetic Act, as applicable, provided that the product the Importer received from the Foreign Seller has an SSI.

(iii) An Importer is exempt from the prohibition on conducting a transaction with an entity that is not an “authorized trading partner,” under sections 582(c)(3) or (d)(3) of the Federal Food, Drug, and Cosmetic Act, as applicable.

(iv) An Importer is exempt from the requirement to verify that a product in the Importer’s possession or control contains a “standardized numerical identifier” at the package level, under sections 582(c)(4)(A)(i)(II) or (d)(4)(A)(ii)(II) of the Federal Food, Drug, and Cosmetic Act as applicable, provided that the Importer verifies that each package and homogenous case of the product includes the SSI affixed or imprinted by the Foreign Seller.

§ 251.15 *Qualifying laboratory requirements.*

(a) To be considered a qualifying laboratory for purposes of section 804 of the Federal Food, Drug, and Cosmetic Act and this part, a laboratory must have ISO 17025 accreditation.

(b) To be considered a qualifying laboratory for purposes of section 804 of the Federal Food, Drug, and Cosmetic Act and this part, a laboratory must have an FDA inspection history and it must have satisfactorily addressed any objectionable conditions or practices identified during its most recent FDA inspection, if applicable.

(c) To be considered a qualifying laboratory for purposes of section 804 of the Federal Food, Drug, and Cosmetic Act and this part, a laboratory must comply with the applicable

current good manufacturing practice requirements, including provisions regarding laboratory controls in § 211.160 of this chapter and laboratory records in § 211.194 of this chapter.

§ 251.16 *Laboratory testing requirements.*

(a) The manufacturer or the Importer must arrange for drugs imported under an authorized SIP to be tested by a qualifying laboratory.

(b) Unless the manufacturer conducts the Statutory Testing, in accordance with this part, the manufacturer of the drugs imported under an authorized SIP must supply to the Importer, within 30 calendar days of receiving the Importer's request, all information needed to conduct the Statutory Testing, including any testing protocols, Certificate of Analysis, and samples of analytical reference standards that the manufacturer has developed. The manufacturer must also provide the Importer, within 30 calendar days of receiving the Importer's request, with formulation information about the HPFB-approved drug, a stability-indicating assay, and the FDA-approved drug to facilitate authentication.

(c) Testing done on a statistically valid sample of the batch or shipment, as applicable, must be sufficiently thorough to establish, in conjunction with data and information from the manufacturer, that the batch or shipment is eligible for importation under a SIP. The size of the sample must be large enough to enable a statistically valid statement to be made regarding the authenticity and stability of the quantity of the batch in the shipment or the entire shipment, as applicable.

(d) The statistically valid sample of the HPFB-approved drug must be subjected to testing to confirm that the HPFB-approved drug meets the FDA-approved drug's specifications and standards, which include the analytical procedures and methods and the acceptance criteria. In

addition, to test for degradation, a stability-indicating assay provided by the manufacturer must be conducted on the sample of the drug that is proposed for import.

(e) If the manufacturer performs the Statutory Testing at a qualifying laboratory, the testing results, a complete set of laboratory records, a detailed description of the selection method for the samples, the testing methods used, complete data derived from all tests necessary to ensure that the eligible prescription drug meets the specifications and standards of the FDA-approved drug that are established in the NDA or ANDA, a Certificate of Analysis, and any other documentation demonstrating that the testing meets the requirements under section 804 must be submitted in electronic format directly to FDA via the ESG or to an alternative transmission point identified by FDA. The manufacturer must notify the Importer and FDA of the manufacturer's intent to perform the Statutory Testing, and identify the qualifying laboratory for FDA review and approval pursuant to section 804 of the Federal Food, Drug, and Cosmetic Act, within 30 calendar days of receipt of the request from the Importer described in paragraph (b).

(f) Regardless of whether testing under this section is performed by the manufacturer or Importer, the sample of a batch or shipment of drugs must be randomly selected for testing or, in the alternative, the sample must be selected to be representative of the quantity of the batch in a shipment or of a shipment, as applicable.

(g) Information supplied by the manufacturer to authenticate the prescription drug being tested and confirm that the labeling of the prescription drug complies with labeling requirements under the Federal Food, Drug, and Cosmetic Act, and any trade secrets or commercial or financial information that is privileged or confidential that the manufacturer supplies for the purposes of testing or otherwise complying with the Federal Food, Drug, and Cosmetic Act and

this part, must be kept in strict confidence and used only for the purposes of testing or otherwise complying with the Federal Food, Drug, and Cosmetic Act and this part.

(h) To ensure that the information described in paragraph (g) is protected:

(1) The information that the manufacturer supplies about a prescription drug must not be disseminated except for the purpose of testing or otherwise complying with the Federal Food, Drug, and Cosmetic Act and this part; and

(2) The SIP Sponsor must take all of the steps set out in the authorized SIP Proposal to ensure that the information is kept in strict confidence and used only for the purpose of testing or otherwise complying with the Federal Food, Drug, and Cosmetic Act and this part.

§ 251.17 *Importation requirements.*

(a) Importers must ensure that each shipment of eligible prescription drugs imported or offered for import pursuant to this part is accompanied by an import entry for consumption filed electronically as a formal entry in ACE, or another CBP-authorized electronic data interchange system, and designated in such a system as a drug imported pursuant to this part.

(b) The Importer may make entry for consumption and arrival of shipments containing eligible prescription drugs only at the CBP port of entry authorized by FDA to import eligible prescription drugs under section 804 of the Federal Food, Drug, and Cosmetic Act. The Importer must keep the product at a secured warehouse, location within a specific foreign trade zone, or other secure distribution facility controlled by or under contract with the Importer, and under appropriate environmental conditions to maintain the integrity of the products, until FDA issues an admissibility decision. The secured warehouse or other secure distribution facility must be within 30 miles of the authorized Port of Entry for examination.

(c) If the entry for consumption is filed in ACE before the testing and relabeling of the eligible prescription drug, the Importer must submit an application to bring the drug into compliance and must relabel and test the drug in accordance with the plan approved by FDA pursuant to §§ 1.95 and 1.96 of this chapter.

(d) Upon arrival in the United States of an initial shipment that contains a batch of an eligible prescription drug identified in a Pre-Import Request that has been granted by FDA, the Importer must select a statistically valid sample of that batch to send to a qualifying laboratory for Statutory Testing, unless the manufacturer conducts the Statutory Testing at a qualifying laboratory.

(1) In the case of any subsequent shipment composed entirely of a batch of an eligible prescription drug that has already been tested in accordance with this part, the Importer must select a statistically valid sample of the shipment to send to a qualifying laboratory for Statutory Testing.

(2) The Importer must send three sets of the samples sent to the qualifying laboratory in accordance with § 251.16 to the FDA field lab identified by FDA when the Agency granted the Pre-Import Request.

(3) The Importer must submit to FDA a complete set of laboratory records, a detailed description of the sampling method used to select the sample of the eligible prescription drug sent to the qualifying laboratory, the testing protocols used, complete data derived from all tests necessary to ensure that the eligible prescription drug meets the specifications of the FDA-approved drug that are established in the NDA or ANDA, a Certificate of Analysis, and all relevant documentation demonstrating that the testing meets the requirements under section 804(e)(1) of the Federal Food, Drug, and Cosmetic Act, as well as any additional information

FDA deems necessary to evaluate whether the drug meets manufacturing, quality, and safety standards.

(e) If the manufacturer conducts the Statutory Testing, upon arrival in the United States of an initial shipment that contains a batch of an eligible prescription drug identified in a Pre-Import Request that has been granted by FDA, a statistically valid sample of that batch **must be selected** to send to a qualifying laboratory for the Statutory Testing.

(1) In the case of any subsequent shipment composed entirely of a batch or batches of an eligible prescription drug that has already been tested in accordance with this part, the manufacturer must select a statistically valid sample of that shipment to send to a qualifying laboratory for that Statutory Testing.

(2) The manufacturer must send three sets of the samples the manufacturer sent to the qualifying laboratory in accordance with § 251.16 to the FDA field lab identified by FDA when the Agency granted the Pre-Import Request.

(3) The manufacturer must submit to FDA, directly in electronic form to the ESG or to an alternative transmission point identified by FDA, a complete set of laboratory records, a detailed description of the selection method for the sample of the eligible prescription drug sent to the qualifying laboratory, the testing methods used, complete data derived from all tests necessary to ensure that the eligible prescription drug meets the conditions in the FDA-approved drug's NDA or ANDA, a Certificate of Analysis, and all relevant documentation demonstrating that the testing meets the requirements under section 804(e)(1) of the Federal Food, Drug, and Cosmetic Act, as well as any additional information FDA deems necessary to evaluate whether the drug meets manufacturing, quality, and safety standards.

(f) After FDA has reviewed the testing results provided by the Importer or manufacturer and determined that they are acceptable, FDA will notify the Importer and then the Importer must cause the eligible prescription drug to be relabeled with the required U.S. labeling.

(g) After the eligible prescription drug has been shown by testing and relabeling to meet the requirements of section 804 of the Federal Food, Drug, and Cosmetic Act and this part, the Importer or the manufacturer must provide to FDA the written certification described in section 804(d)(1)(K) of the Federal Food, Drug, and Cosmetic Act in electronic format via the ESG or to an alternative transmission point identified by FDA.

§ 251.18 *Post-importation requirements.*

(a) *Stopping importation.* If at any point a SIP Sponsor determines that a drug, manufacturer, Foreign Seller, Importer, qualifying laboratory, or other participant in or element of the supply chain in the authorized SIP does not meet all applicable requirements of the Federal Food, Drug, and Cosmetic Act, FDA regulations, and the authorized SIP, the SIP Sponsor must immediately stop importation of all drugs under the SIP, notify FDA, and demonstrate to FDA that importation has in fact been stopped.

(b) *Field alert reports.* Importers must submit NDA and ANDA field alert reports, as described in §§ 314.81(b)(1) and 314.98 of this chapter, to the manufacturer and to FDA.

(c) *Additional reporting requirements for combination products.* For combination products containing a device constituent part, Importers must submit the reports to the manufacturer and to FDA described in § 4.102(c)(1) of this chapter and maintain the records described in §§ 4.102(c)(1) and 4.105(b) of this chapter.

(d) *Adverse event reports.* (1) *Scope.* An Importer must establish and maintain records and submit to FDA and the manufacturer reports of all adverse events associated with the use of its drug products imported under this part.

(2) *Review of safety information.* The Importer must promptly review all domestic safety information for the eligible prescription drugs obtained or otherwise received by the Importer.

(3) *Expedited ICSRs.* The Importer must submit expedited ICSRs for each domestic adverse event to FDA and the manufacturer as soon as possible but no later than 15 calendar days from the date when the Importer has both met the reporting criteria described in this paragraph (d) and acquired a minimum data set for that adverse event.

(i) *Serious, unexpected adverse events.* The Importer must submit expedited ICSRs for domestic adverse events reported to the Importer spontaneously (such as reports initiated by a patient, consumer, or healthcare professional) that are both serious and unexpected, whether or not the Importer believes the events are related to the product.

(ii) *Other adverse event reports to be expedited upon notification by FDA.* Upon notification by FDA, the Importer must submit as expedited ICSRs any adverse event reports that do not qualify for expedited reporting under paragraph (d)(3)(i) of this section. The notice will specify the adverse events to be reported and the reason for requiring the expedited reports.

(4) *Followup reports for expedited ICSRs.* The Importer must actively seek any missing data elements under paragraph (d)(7) of this section or updated information for any previously submitted expedited ICSR under paragraph (d)(3) of this section. The Importer must also investigate any new information it obtains or otherwise receives about previously submitted expedited ICSRs. The Importer must submit followup reports for expedited ICSRs to FDA and the manufacturer as soon as possible but no later than 15 calendar days after obtaining the new

information. The Importer must document and maintain records of its efforts to obtain missing or incomplete information.

(5) *Nonexpedited ICSRs.* The Importer must submit to FDA and the manufacturer an ICSR for each domestic adverse event not reported under paragraph (d)(3)(i) of this section (all serious, expected adverse events and nonserious adverse events) within 90 calendar days from the date when the Importer has both met the reporting criteria described in this paragraph (d) and acquired a minimum data set for that adverse event.

(6) *Completing and submitting safety reports.* This paragraph (d)(6) describes how to complete and submit ICSRs required under this section. Additionally, upon written notice, FDA may require the Importer to submit any of this section's adverse event reports at a different time period than identified in other paragraphs.

(i) *Electronic format for submissions.* (A) ICSR and ICSR attachments must be submitted in an electronic format that FDA can process, review, and archive, as described in § 314.80(g)(1) of this chapter.

(B) The Importer may request, in writing, a temporary waiver of the requirements in paragraph (d)(6)(i)(A) of this section, as described in § 314.80(g)(2) of this chapter. These waivers will be granted on a limited basis for good cause shown.

(ii) *Completing and submitting ICSRs.*

(A) *Single submission.* Submit each ICSR only once.

(B) *Separate ICSR.* The Importer must submit a separate ICSR for each patient who experiences an adverse event reportable under paragraphs (d)(3)(i) or (ii), (d)(4), or (d)(5) of this section.

(C) *Coding terms.* The adverse event terms described in the ICSR must be coded using standardized medical terminology.

(D) *Minimum data set.* All ICSRs submitted under this section must contain at least the minimum data set for an adverse event. The Importer must actively seek the minimum data set in a manner consistent with its written procedures under paragraph (d)(9) of this section. The Importer must document and maintain records of its efforts to obtain the minimum data set.

(E) *ICSR elements.* The Importer must complete all available elements of an ICSR as specified in paragraph (d)(7) of this section.

(1) The Importer must actively seek any information needed to complete all applicable elements, consistent with its written procedures under paragraph (d)(9) of this section.

(2) The Importer must document and maintain records of its efforts to obtain the missing information.

(F) *Supporting documentation.* When submitting supporting documentation for expedited ICSRs of adverse events, the Importer must:

(1) Submit for each ICSR for a domestic adverse event, if available, a copy of the autopsy report if the patient died, or a copy of the hospital discharge summary if the patient was hospitalized. The Importer must submit each document as an ICSR attachment. The ICSR attachment must be submitted either with the initial ICSR or no later than 15 calendar days after obtaining the document.

(2) Include in the ICSR a list of available, relevant documents (such as medical records, laboratory results, death certificates) that are held in its drug product safety files. Upon written notice from FDA, the Importer must submit a copy of these documents within 5 calendar days of the FDA notice.

(7) *Information reported on ICSRs.* ICSRs must include the following information:

(i) Patient information, which includes:

- (A) Patient identification code;
- (B) Patient age at the time of adverse event, or date of birth;
- (C) Patient gender; and
- (D) Patient weight.

(ii) Adverse event, which includes:

- (A) Outcome attributed to adverse event;
- (B) Date of adverse event;
- (C) Date of ICSR submission;
- (D) Description of adverse event (including a concise medical narrative);
- (E) Adverse drug event term(s);
- (F) Description of relevant tests, including dates and laboratory data; and
- (G) Other relevant patient history, including preexisting medical conditions.

(iii) Suspect medical product(s), which includes:

- (A) Name;
- (B) Dose, frequency, and route of administration used;
- (C) Therapy dates;
- (D) Diagnosis for use (indication);
- (E) Whether the product is a combination product;
- (F) Whether adverse event abated after drug use stopped or dose reduced;
- (G) Whether adverse event reappeared after reintroduction of drug;
- (H) Lot number;

- (I) Expiration date;
- (J) NDC; and
- (K) Concomitant medical products and therapy dates.
- (iv) Initial reporter information, which includes:
 - (A) Name, address, and telephone number;
 - (B) Whether the initial reporter is a healthcare professional; and
 - (C) Occupation, if a healthcare professional.
- (v) Importer information, which includes:
 - (A) Importer name and contact office address;
 - (B) Importer telephone number;
 - (C) Date the report was received by the Importer;
 - (D) Whether the ICSR is an expedited report;
 - (E) Whether the ICSR is an initial report or followup report; and
 - (F) Unique case identification number, which must be the same in the initial report and any subsequent followup report(s).

(8) *Recordkeeping.*

(i) For a period of 10 years from the initial receipt of information, the Importer must maintain records of information relating to adverse event reports under this section, whether or not submitted to FDA.

(ii) These records must include raw data, correspondence, and any other information relating to the evaluation and reporting of adverse event information that is obtained by the Importer.

(iii) Upon written notice by FDA, the Importer must submit any or all of these records to FDA within 5 calendar days after receipt of the notice. The Importer must permit any authorized FDA employee, at reasonable times, to access, copy, and verify its established and maintained records described in this section.

(9) *Written procedures.* The Importer must develop written procedures needed to fulfill the requirements in this section for the surveillance, receipt, evaluation, and reporting to FDA and the manufacturer of adverse event information, including procedures for employee training, and for obtaining and processing safety information from the Foreign Seller.

(10) *Patient privacy.* The Importer must not include in reports under this section the names and addresses of individual patients; instead, the Importer must assign a unique code for identification of the patient. The Importer must include the name of the reporter from whom the information was received as part of the initial reporter information, even when the reporter is the patient. As set forth in FDA's public information regulations in part 20 of this chapter, FDA generally may not disclose the names of patients, individual reporters, healthcare professionals, hospitals, and geographical identifiers submitted to FDA in adverse event reports.

(11) *Safety reporting disclaimer.* (i) A report or information submitted by the Importer under this section (and any release by FDA of that report or information) does not necessarily reflect a conclusion by the Importer or by FDA that the report or information constitutes an admission that the eligible prescription drug imported under section 804 of the Federal Food, Drug, and Cosmetic Act caused or contributed to an adverse event.

(ii) The Importer need not admit, and may deny, that the report or information submitted as described in this section constitutes an admission that the drug product caused or contributed to an adverse event.

(e) *Drug recalls.* (1) The SIP Sponsor must establish a procedure to track the public announcements of the manufacturer of each drug it imports under section 804 of the Federal Food, Drug, and Cosmetic Act, and the SIP Sponsor must also monitor FDA's recall website for recall or market withdrawal information relevant to the drugs that it imports under section 804.

(2) If FDA, the SIP Sponsor, the Foreign Seller, the Importer, or the manufacturer determines that a recall is warranted, the SIP Sponsor must effectuate the recall in accordance with its written recall plan under paragraph (e)(3) of this section.

(3) A SIP must have a written recall plan that describes the procedures to perform a recall of the product and specifies who will be responsible for performing the procedures. The recall plan must cover recalls mandated or requested by FDA and recalls initiated by the SIP Sponsor, the Foreign Seller, the Importer, or the manufacturer. The recall plan must include sufficient procedures for the SIP Sponsor to:

- (i) Immediately cease distribution of the drugs affected by the recall;
- (ii) Directly notify consignees of the drug(s) included in the recall, including how to return or dispose of the recalled drugs;
- (iii) Specify the depth to which the recall will extend (e.g., wholesale, intermediate wholesale, retail or consumer level) if not specified by FDA;
- (iv) Notify the public about any hazard(s) presented by the recalled drug when appropriate to protect the public health;
- (v) Conduct effectiveness checks to verify that all consignees at the specified recall depth have received notification about the recall and have taken appropriate action;
- (vi) Appropriately dispose of recalled product; and
- (vii) Notify FDA of the recall.

(4) In the event of a recall, the Importer must, upon request by FDA, provide transaction history, information, and statement (as these terms are defined in sections 581(25), 581(26), and 581(27) of the Federal Food, Drug, and Cosmetic Act), in accordance with applicable requirements under sections 582(c)(1)(C) and 582(d)(1)(D).

(i) The Importer must also provide to FDA, upon request, information given by the manufacturer under § 251.14(a)(6), including transaction documents that were provided from the manufacturer to the Foreign Seller.

(ii) The Foreign Seller must provide to FDA, upon request, information about its transactions of the recalled drug with the manufacturer and the Importer.

(5) The Foreign Seller and Importer must cooperate with any recalls, including recalls initiated by the SIP Sponsor, FDA, the Foreign Seller, the Importer, or the drug's manufacturer.

§ 251.19 *Reports to FDA.*

(a) A SIP Sponsor must submit a report to FDA each quarter in electronic format via the ESG or to an alternative transmission point identified by FDA containing the information set forth in this section, beginning after the SIP Sponsor files an electronic import entry for consumption for its first shipment of drugs under the SIP. If the SIP Sponsor specifies in such report that the information contained in the report is being transmitted on behalf of the Importer and in order to fulfill the Importer's obligation under § 251.12, the Importer need not separately submit such information to FDA.

(b) The report in paragraph (a) must contain the following information:

(1) The name, address, telephone number, and professional license number (if any) of the Importer;

(2) The name and quantity of the active ingredient of the imported eligible prescription drug(s);

(3) A description of the dosage form of the eligible prescription drug(s);

(4) The date(s) on which the eligible prescription drug(s) were shipped;

(5) The quantity of the eligible prescription drug(s) that was shipped;

(6) The lot or control number assigned to the eligible prescription drug(s) by the manufacturer of the eligible prescription drug(s);

(7) The point of origin (i.e., the manufacturer) and the destination (i.e., the wholesaler, pharmacy, or patient to whom the Importer sells the drug) of the eligible prescription drug(s);

(8) The per unit price paid by the Importer for the prescription drug(s) in U.S. dollars;

and

(9) Any other information that FDA determines is necessary for the protection of the public health.

(c) The Importer must also confirm as part of the report in paragraph (a) that the eligible prescription drug(s) were bought directly from the manufacturer by the Foreign Seller and that the Foreign Seller sold the eligible prescription drug(s) directly to the Importer.

(d) The report in paragraph (a) must include the following documentation:

(1) Documentation from the Foreign Seller specifying the manufacturer of each eligible prescription drug and the quantity of each lot of the eligible prescription drug(s) received by the Foreign Seller from that manufacturer;

(2) Documentation demonstrating that the eligible prescription drug was received by the Foreign Seller from the manufacturer and subsequently shipped by the Foreign Seller to the Importer;

(3) Documentation of the quantity of each lot of the eligible prescription drug(s) received by the Foreign Seller, demonstrating that the quantity being imported into the United States is not more than the quantity that was received by the Foreign Seller;

(4) Documentation demonstrating that the sampling and testing requirements described in section 804(d)(1)(J)(i)(III) of the Federal Food, Drug, and Cosmetic Act were met for each shipment of each eligible prescription drug.

(e) The report in paragraph (a) must include certifications from the Importer for each shipment of each eligible prescription drug that the drug is approved for marketing in the United States and is not adulterated or misbranded and meets all labeling requirements under the Federal Food, Drug, and Cosmetic Act. This certification must include:

- (1) That there is an authorized SIP;
- (2) That the imported drug is covered by the authorized SIP;
- (3) That the drug is an eligible prescription drug as defined in this part;
- (4) That the FDA-approved counterpart of the drug is currently commercially marketed in the United States;
- (5) That the drug is approved for marketing in Canada; and
- (6) That the drug is not adulterated or misbranded and meets all labeling requirements under the Federal Food, Drug, and Cosmetic Act.

(f) The report in paragraph (a) must include laboratory records, including complete data derived from all tests necessary to ensure that each eligible prescription drug is in compliance with established specifications and standards, and documentation demonstrating that the Statutory Testing was conducted at a qualifying laboratory, unless the manufacturer conducted the testing and submitted this information directly to FDA.

(g) The report in paragraph (a) must include data, information, and analysis on the SIP's cost savings to the American consumer for the drugs imported under the SIP.

(h) A SIP Sponsor must submit a report to FDA within 10 calendar days, in electronic format via the ESG or to an alternative transmission point identified by FDA, regarding any applicable criminal conviction, violation of law, or disciplinary action as described in § 251.3(e)(2) and (3).

§ 251.20 *Severability.*

The provisions of this part are not separate and are not severable from one another. If any provision is stayed or determined to be invalid or unenforceable, the remaining provisions shall not continue in effect.

§ 251.21 *Consequences for violations.*

(a) An article that is imported or offered for import into the United States in violation of section 804 of the Federal Food, Drug, and Cosmetic Act or this part is subject to refusal under section 801 of the Federal Food, Drug, and Cosmetic Act.

(b) The importation of a prescription drug in violation of section 804 of the Federal Food, Drug, and Cosmetic Act; the falsification of any record required to be maintained or provided to FDA under such section; or any other violation of this part is a prohibited act under section 301(aa) of the Federal Food, Drug, and Cosmetic Act.

Dated: _____.

Alex M. Azar II,

Secretary,

Department of Health and Human Services.