Appendix H FDA Correspondence

COLORADO
Department of Health Care Policy & Financing

NMDOH
NEW MEXICO DEPARTMENT OF HEALTH

VERMONT
AGENCY OF HUMAN SERVICES

STATE OF NEW HAMPSHIRE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

March 29, 2022

S. Leigh Verbois, Director
Office of Drug Security, Integrity & Response
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Dear Ms. Verbois,

As states leading the way in the development of State Importation Programs (SIPs), we thank you and FDA leadership for your efforts to support us in this process, including establishing a team dedicated to the implementation of SIPs. We are looking forward to our upcoming meeting with you to discuss our progress in implementing Section 804 and hope to have a collaborative discussion around opportunities for further FDA guidance to advance state efforts.

As you know, escalating prescription drug costs continue to be a challenge across the country. Our States are dedicated to advancing importation programs to bring needed prescription drug cost relief to residents and we have been collaborating on this topic for several years— analyzing regulation, evaluating program challenges, and sharing best practices. We have been bolstered by recent federal engagement and the creation of a regulatory structure for implementation and see great opportunities to further enhance the state-federal partnership on Section 804.

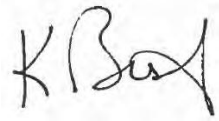
States have identified several areas of regulation in which states would benefit from additional clarity and guidance. These guidance requests focus on two main areas: SIP Application Policy and Operational Policy. Please see the attached guidance requests, including detailed explanations and citations to the specific areas of regulation. We look forward to an opportunity to explore these guidance

recommendations during our upcoming meeting, as well as discuss best practices and other key FDA priorities.

We appreciate your continued partnership.

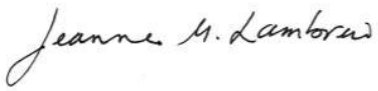
Sincerely,

Kim Bimestefer



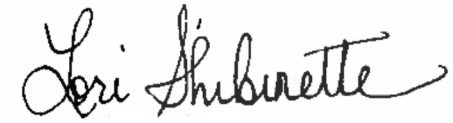
Executive Director
Colorado Department of Health Care Policy & Financing

Jeanne M. Lambrew, PhD



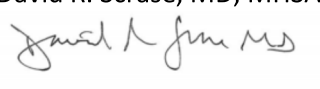
Commissioner
Maine Department of Health and Human Services

Lori A. Shibinette



Commissioner, New Hampshire Department of Health and Human Services

David R. Scrase, MD, MHSA



Acting Cabinet Secretary, New Mexico Department of Health

Ena Backus

Director of Health Care Reform, Vermont Agency of Human Services

FDA Guidance Request
Importation of Prescription Drugs, 21 CFR 1 and 21 CFR 251

SIP Application Policy Issue	Proposed Questions & Answers	Related Final Rule Sections
Demonstrating SIP Cost Savings - As states break new ground establishing new prescription drug marketplaces, it is assumed that initial SIPs will "pilot" Section 804 with narrow drug lists. Early programs will be focused on demonstrating proof of concept. This requires a flexible interpretation of demonstrating cost savings in SIP applications.	Question: The Final Rule provides only a high level explanation of how a SIP Sponsor must justify that their SIP will result in a significant reduction in the cost to the consumer for eligible prescription drugs. Can the FDA clarify that proving cost savings will be assessed with the greatest flexibility given that SIP sponsors are piloting new marketplaces which will take time to establish and yield such savings? Suggested Response: Given state SIP sponsors are establishing new and innovative marketplaces that require time, resources, and a shift in market dynamics to drive cost savings, the FDA will consider demonstration of initial modest savings with the potential for greater savings over time as sufficient in meeting the statutory and regulatory requirements outlined in § 251.3. FDA recognizes that for many states initial SIPs will be piloting the Canadian drug importation program concept and therefore, our assessment of meeting cost savings requirements will take this into account.	§ 251.3 SIP proposal submission requirements.(11) A summary of how the SIP Sponsor will ensure that: (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. § 251.3 SIP proposal submission requirements.(e)The SIP Sponsor's importation plan must: (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.

SIP Review Process and Phased Approval - As states pursue partnerships with manufacturers, insurance carriers and supply chain partners, it is critical that SIP applicants are able to demonstrate progress towards application approval to support the development of such partnerships. FDA communication to a SIP applicant demonstrating progress towards a successful outcome would assist states in such efforts.	Question: The Final Rule indicates that the FDA will make reasonable efforts to communicate about information that is lacking in a SIP application. State SIP applicants would benefit from additional communication regarding FDA's review process, including information regarding meeting certain benchmarks towards a final approval. This will support state efforts to secure partners. Can FDA provide guidance that it intends to share such details during its application review process? Suggested Response: In addition to communications regarding application details that are lacking, FDA will also provide SIP Sponsors with a letter of completeness once all required elements of an application have been received. FDA will also provide applicants with a letter stating that the application review process has been completed and that a final determination is imminent.	251.4 (c) Review and authorization of importation program proposals. "... 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.…"
Drug List in SIP - The process to confirm access to Canadian drug supply is an ongoing and evolving process. The Drug list included in the SIP should be an aspirational list and may not necessarily represent the universe of drugs a SIP Sponsor may be able to import. Market forces in Canada may present opportunities to acquire drugs outside of the original submitted list. States seek flexibility in what they may ultimately submit for each pre-import request.	Question: While the Final Rule requires submission of a drug list with a SIP application, nowhere in the Rule does it state that this list must represent the universe of drugs that may be submitted in pre-import requests. Can the FDA clarify that pre-import requests may include prescription drugs beyond those included in the original SIP application, as long as all statutory and regulatory requirements are met? Suggested Response: As long as FDA approves drugs included in a pre-import request, the SIP Sponsor and their Importer may import such drugs.	§ 251.3 SIP proposal submission requirements.(e)The SIP Sponsor's importation plan must:(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. § 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. § 251.8 Modification or extension of authorized importation programs.
Clarifying SIP Application Safety Requirements - States share FDA's view that safety must be the first priority in establishing importation programs. The Final Rule provides FDA with broad discretion to not authorize a SIP proposal due to "potential safety concerns" which gives SIP sponsors little guidance regarding how to address such concerns in its application.	Question: The Final Rule does not provide details on what the FDA may consider "potential safety concerns" as outlined in § 251.4 that may compel FDA to reject an application. Can FDA release detailed guidance that outlines any anticipated safety concerns that SIP applicants must consider when applying for an approval? Such guidance will help states clarify specific safety measures that align with FDA safety priorities above and beyond what is outlined in the Final Rule. Suggested Response: The FDA appreciates state interest in additional clarifications regarding safety requirements under the Final Rule and intends to release a detailed FAQ that will provide additional guidance to states regarding this aspect of regulation.	§ 251.4 Review and authorization of importation program proposals. (a)...FDA may decide not to authorize a SIP Proposal or supplemental proposal because of potential safety concerns with the SIP.
Operational Policy Issues	Proposed Questions & Answers	Related Final Rule Sections
Pre-Import Requests, Testing Approval Timelines and Communication Plans - Required approvals for pre-import requests and testing of imported products, add significant time to the distribution timeline for imported products. Such approvals will	Question: The Final Rule does not provide any detail on the timing for FDA's review of pre-import requests and testing results which will have negative downstream impacts on the supply chain and related distribution. As states invest in implementation of SIPs once approved, some assurances are needed regarding review timelines. Can FDA provide written guidance including a formalized timeline that prioritizes the shortest possible approval times and clear	§ 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.

require wholesalers to purchase drugs up to an estimated 6 months in advance of distribution which will present a significant financial burden in the supply chain. Creating efficiencies in the review process will be critical to addressing this.	communication strategies (ie. CMS's process for review and approval of Medicaid State Plan Amendments). Additionally, states request a template for a pre-import request. Suggested Response: The FDA appreciates state interest in additional clarifications regarding timelines for approvals of pre-import requests and testing results under the Final Rule and intends to release a detailed FAQ that will provide additional guidance to states regarding this aspect of regulation.	§ 251.16 Laboratory testing requirements. Note: This section does not include any details regarding FDA's review and approval process for laboratory testing results.
US Agent - It is unclear from the Final Rule whether or not this must be an agent employed by the Foreign Seller. This could be a barrier to partnering with such an entity in Canada and therefore, flexibility is requested.	Question: The Final Rule does not specify whether the Foreign Seller's US Agent must be an employee of the Foreign Seller. State's request flexibility in interpretation of this part to allow for individuals other than an employee of the Foreign Seller to act as their US Agent. Suggested Response: The FDA appreciates this question regarding the Foreign Seller's US Agent. This individual does not need to be an employee of the Foreign Seller, rather a contractual, or otherwise, legal relationship will suffice.	§ 251.11 Official contact and U.S. agent for Foreign Sellers.(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.

March 2, 2023

Kim Bimestefer, Executive Director
Colorado Department of Health Care Policy & Financing
1570 Grant Street
Denver, CO 80203

Re: Colorado's Section 804 Importation Program Proposal

Dear Executive Director Bimestefer,

This letter responds to the Section 804 Importation Program (SIP) Proposal that was submitted by the Colorado Department of Health Care Policy & Financing on December 5, 2022.

FDA welcomes your interest in pursuing a SIP and appreciates the efforts you have made to seek authorization of your proposal. Consistent with the July 2021 Executive Order on Promoting Competition in the American Economy, FDA is committed to working with States such as Colorado and Indian Tribes that propose to develop SIPs under section 804 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and the final rule on Importation of Prescription Drugs (see 85 FR 62094; 21 CFR part 251). To assist you with this process, and pursuant to 21 CFR 251.4(c)(1), FDA has identified information that was not provided in your submission but is required pursuant to the final rule. This information was identified after an evaluation of the completeness of your SIP proposal. Additional information may be identified, for example related to your proposals for demonstrating cost savings, after FDA conducts a full evaluation of your SIP proposal. In particular, your proposal did not include the information noted below. You may add the required information to your current SIP proposal or submit a new SIP proposal. We look forward to continuing to work with you toward our shared goal of achieving a significant reduction in the cost of prescription drugs to the American consumer without posing additional risk to the public's health and safety.

Information Missing from the Overview of the SIP Proposal:

- 251.3(d)(5) Provide the name and address of the manufacturer of the finished dosage form of each eligible prescription drug listed on the Drug List, if known or reasonably known.

- 251.3(d)(6) Provide the name and address of the manufacturer of the active ingredient or ingredients of the eligible prescription drugs, if known or reasonably known.

- 251.3(d)(10) Provide adequate evidence of registration for the relabeler, to include a business operation of 'relabel' as required under 21 CFR 207.25(f).

Information Missing from the Importation Plan:

- 251.3(e)(1) Identify 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.
    - Clarify whether the names and addresses in Appendix D, Drug List with Required Data Elements, are for the manufacturer of the finished dosage form of the eligible prescription drug.

- 251.3(e)(6) Provide adequate evidence that each HPFB-approved drug's FDA-approved counterpart drug is currently commercially marketed in the United States. We recommend, at a minimum, including information showing that each drug product is listed in the Active Section of FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly known as the Orange Book.

- 251.3(e)(14) Include 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. Describe:
    - How the importer or designee will ensure non-saleable returned products are properly dispositioned in the United States.
    - How non-saleable returned products will be removed from the pharmaceutical distribution supply chain.

- 251.3(e)(15)(vi) Include the adoption of processes and procedures for uncovering and addressing conflicts of interest.

- 251.9(a) Any Foreign Seller(s) designated in a SIP Proposal must be registered with FDA before FDA will authorize the SIP Proposal. Ensure that the proposed Foreign Seller is registered with a business operation 'SIP Foreign Seller'. Please contact edrls@fda.hhs.gov for questions and assistance with registration.

Information on the Eligible Prescription Drugs:

- 251.3(e)(11)(i) 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 storage, handling, and distribution practices of supply chain participants, including transportation providers, meet the requirements of 21 CFR part 205 (requirements for state licensing of wholesale prescription drug distributors) and do not affect the quality or impinge on the security of the eligible prescription drugs.
    - For sterile drugs or drugs that require special storage conditions such as temperature control, please explain how the SIP Sponsor 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.

Information on the Proposed Labeling:

- 251.3(e)(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.
    - Ensure that this side-by-side comparison of the FDA-approved labeling and the proposed labeling is provided for each drug identified in the SIP Proposal.
    - Ensure that all approved and proposed labeling is provided in the SIP Proposal including all the carton and container labeling.
    - If your SIP Proposal does not include all the package sizes available for the FDA-approved counterpart, then please revise the HOW SUPPLIED/STORAGE AND HANDLING section of the proposed Prescribing Information (PI) to delete package sizes that are not being proposed for importation.
    - Ensure that your proposed labeling is based on the most recent version of the FDA-approved labeling.
        - The FDA-approved labeling for the NDA drug products can be found on Drugs@FDA. If such labeling is not available on Drugs@FDA, you may be able to obtain the labeling from the manufacturers. You can also obtain it through a Freedom of Information Act (FOIA) request.
        - The FDA-approved labeling for ANDA drug products is typically not posted on Drugs@FDA. The labeling for FDA-approved ANDA drug products can be obtained through a FOIA request. You may also be able to obtain it from the manufacturers.
        - The revision date should match the revision date of the latest FDA-approved labeling.

- 251.13(b)(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, with certain exceptions. An eligible prescription drug's labeling can only deviate from the FDA-approved labeling in the ways listed at 251.13(b)(4)(i)-(vii). Ensure that the content and format of the container and carton labeling of each eligible prescription drug included in the SIP Proposal is the same as the FDA-approved carton and container labeling.

- 251.13(b)(4)(i) The Importer's NDC for the eligible prescription drug must replace any NDC appearing on the label of the FDA-approved drug.

- 251.13(b)(4)(iii) The labeling must bear conspicuously, among other things, the name and place of business of the Importer.
    - We recommend you add the Importer's name and place of business at the end of the PI in addition to the HOW SUPPLIED/STORAGE AND HANDLING section. We also recommend you add the Importer's information at the end of the Medication Guide, Instructions for Use, and/or patient package inserts.
        - The statement of the place of business should include the street address, city, state, and ZIP Code. The street address can be omitted if it is shown in a current city directory or telephone directory. If the importer's street address is not shown in a current city directory or telephone directory, the street address of the importer should be added.
    - The Importer may submit to FDA 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 required information, in accordance with 251.13(d).

- Consistent with 21 CFR 251.13(c), provide the written procedure for the relabeling process of your proposed imported prescription drugs.
    - 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 as per the rule. The final rule does not allow repackaging of drugs that breaches the container closure system, such as a blister pack, which could introduce unnecessary risk of adulteration, degradation, and fraud for drugs imported under a SIP. The final rule also does not permit affixing a conforming label to the outside of the container closure system in lieu of relabeling the immediate container of the product. For example, Farxiga (Forxiga in Canada) tablets listed in the Drug List are packaged in blister packs according to the HPFB-approved labeling. If relabeling the drug product would require breaching the container closure system (e.g., breaking the foil on a blister pack), then the product cannot be imported under a SIP.

Please indicate by April 7, 2023, if you intend to provide the additional required information or if you would like to withdraw the current submission and potentially resubmit it at a later time. If you do not respond by the above date indicating your intention to respond to this request, we will conclude our review of the December 2022 proposal and deny authorization of that submission.

If you submit additional or revised information to the SIP Proposal, please describe the changes that have been made since your previous submission. Please submit any questions, requests to meet, or any revisions to your SIP Proposal for agency review to: SIPDrugImportsandRFP@fda.hhs.gov.

Additional Comments:

In the December 2022 proposal, you requested additional information on (1) FDA's SIP proposal review process; (2) standards on demonstrating cost savings; and (3) flexibility on the list of eligible prescription drugs that may be imported under an approved SIP. In March 2022, FDA held a meeting with representatives from several states, the National Academy for State Health Policy, and the U.S. Department of Health and Human Services to discuss the development of Section 804 Importation Program proposals. FDA's presentation on "Section 804 Importation Program: Overview of Final Rule and Implementation" and HHS's presentation on "Projecting Cost Savings for the American Consumer" are available on FDA's website at https://www.fda.gov/about-fda/reports/importation-drugs-originally-intended-foreign-markets. In May 2022, FDA issued guidance titled *Importation of Prescription Drugs Final Rule Questions and Answers*, which is intended to summarize in plain language the legal requirements in the final rule.

Your SIP Proposal indicates that imported medications will enter through the port of entry located in Buffalo, New York. The final rule specifies that entry and arrival of a shipment containing an eligible prescription drug is limited to the U.S. Customs and Border Protection (CBP) port of entry authorized by FDA; see 21 CFR 251.17(b). At this time, the only port of entry that has been authorized by FDA is located in Detroit, Michigan. *See*, FDA Supplemental Guide for the Automated Commercial Environment/International Trade Data System (ACE/ITDS), at https://www.cbp.gov/document/guidance/fda-supplemental-guide (p. 16).

With regard to the prescription drugs that you may seek to import, we note that some of the drug products in your SIP Proposal may not be "eligible prescription drug[s]" as defined in 21 CFR 251.2. Under 21 CFR 251.2, the Canadian drug product must "meet[] 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." The Canadian varenicline drug product in Appendix G appears to have a different manufacturer, inactive ingredients, tablet characteristics, and storage and handling conditions than the varenicline drug product that is presented as its FDA-approved counterpart. To give another example, the Canadian Pulmicort Turbuhaler products listed in Appendix D appear to have different strengths and different inactive ingredients than the Pulmicort Flexhalers that are presented as their FDA-approved counterparts.

We also note that it may be more efficient to gather information only for the eligible prescription drug product(s) identified in your SIP Proposal that you intend to include in an initial Pre-Import Request. Accordingly, you may choose to submit information for a smaller selection of drug products. FDA can then evaluate the information about this smaller selection of drug products and you may submit a supplemental proposal to add eligible prescription drugs at a later time.

The December 2022 proposal additionally indicates that you intend to work directly with manufacturers and that manufacturers will authorize eligible prescription drugs to be included in your importation program. If a drug that was originally intended to be marketed in a foreign country is authorized by its manufacturer to be marketed in the U.S., and if the manufacturer

"cause[s] the drug to be labeled to be marketed in the [U.S.]," the drug may be imported under section 801 of the FD&C Act, rather than under section 804. There is information on manufacturer-authorized importation of drugs originally intended to be marketed in a foreign country in our guidance *Importation of Certain FDA-Approved Human Prescription Drugs, Including Biological Products, and Combination Products under Section 801(d)(1)(B) of the Federal Food, Drug, and Cosmetic Act*.

We note that the protections that are set forth in section 804 and 21 CFR part 251, including those related to the establishment of a SIP and to foreign sellers, importers, labeling, supply chain security, and laboratory testing, are necessary to ensure that importation of eligible prescription drugs without the manufacturer's authorization poses "no additional risk to the public's health and safety." Likewise, the provisions in the statute and the regulation that place requirements on manufacturers, for example, the requirement in section 804(h) that the manufacturer give the importer "written authorization" for the importer to use a drug's approved labeling, are necessary because the importation is occurring without the manufacturer's authorization. As you point out, 21 CFR 251.13(b)(4)(iv) requires that the labeling of a drug imported by a SIP bear a statement indicating that the product was imported without the manufacturer's authorization. The preamble to the final rule promulgating 21 CFR part 251 explains that this "will help to prevent potential misperceptions regarding whether the manufacturer authorized the product to be imported." (85 Fed. Reg. 62094, 62105 (Oct. 1, 2020)). We would be happy to discuss further with you details about your planned outreach to manufacturers, in order to discern the extent to which the importation would occur with the manufacturer's authorization.

Sincerely,

S. Leigh Verbois, PhD
Director
Office of Drug Security, Integrity & Response
Office of Compliance
Center for Drug Evaluation and Research

COLORADO
Department of Health Care Policy & Financing

1570 Grant Street
Denver, CO 80203

March 23, 2023

Ms. Leigh Verbois
Center for Drug Evaluation and Research
Food and Drug Administration
Department of Health and Human Services
1001 New Hampshire Avenue
Hillandale Building, 4th Floor
Silver Spring, MD 20993

RE: Intent to Respond to FDA's Request for Information

Dear Ms. Verbois:

Please accept this letter as Colorado's formal intent to respond to the FDA's Request for Information (RFI), as shared during our meeting with the FDA on March 2. Our intention is to address the requested information within our Section 804 Importation Program (SIP) submitted on December 5, 2022 and submit a formal response as soon as feasible.

As discussed at our meeting on March 2, we would like to explore creative strategies to address a specific challenge for state-led importation programs. As you know, Colorado must negotiate with drug manufacturers to secure supply for our program. It has been made clear that potential partners will be more interested in committing to participate once our program has been approved by the FDA. While we understand the regulatory framework does not permit for a provisional approval, we know that showing progress towards an approved program will aid in our negotiations with drug manufacturers. We would like to discuss this further with you in an upcoming meeting to be scheduled at your convenience, as well as other process related questions, outlined below.

- Should the State of Colorado expect additional RFIs? If yes, will these build on the content included in the RFI dated March 2nd or should we expect other RFIs covering other aspects of the application outside the scope of that letter?
- Once the responses to all RFI requests have been submitted, what is the timeline for a final review of these outstanding items?

In reviewing the RFI, we identified two different categories of requests. The first, which we refer to as short term, are in process or completed as of submission of this letter. The

detailed changes will be included in our updated SIP application to be submitted at a later date.

Short Term Requests

- 251.3(d)(10): Adequate evidence of registration for the relabeler
- 251.3(e)(14): Disposition of non-saleable products
- 251.9(a): Foreign Seller registration
- 251.3(e)(11)(i): Special storage conditions
- Port Entry changed to Detroit, MI

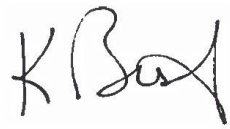
The second category is requests that are longer term, require significantly more time to address, and in most cases are dependent upon the outcome of our negotiations with drug manufacturers. We cannot assess the exact timeframe for responses to these items, but below is a summary of the long term requests.

Long Term Requests

- 251.3(d)(5): Name and address of manufacturer of finished dosage form of each eligible prescription drug on the Drug List.
- 251.3(d)(6): Name and address of the manufacturer of the active ingredient or ingredients of the eligible prescription drugs.
- 251.3(e)(1): Name and address of manufacturer of finished dosage form of each eligible prescription drug on the Drug List.
- 251.3(e)(6): Provide adequate evidence that each HPFB-approved drug's FDA-approved counterpart drug is currently commercially marketed in the United States.
- 251.3(e)(15)(vi): Include the adoption of processes and procedures for uncovering and addressing conflicts of interest.

We look forward to additional engagement on these matters. Should the FDA have any questions during the review process, please contact Lauren Reveley, Colorado Department of Health Care Policy & Financing Drug Importation Program Manager, at Lauren.Reveley@state.co.us.

Sincerely,



Kim Bimestefer
Executive Director
Colorado Department of Health Care Policy & Financing

COLORADO
Department of Health Care Policy & Financing

1570 Grant Street
Denver, CO 80203

May 17th, 2023

Ms. Leigh Verbois
Center for Drug Evaluation and Research
Food and Drug Administration
Department of Health and Human Services
1001 New Hampshire Avenue
Hillandale Building, 4th Floor
Silver Spring, MD 20993

RE: Advance Preparation for May 25 Engagement

Dear Ms. Verbois:

Colorado looks forward to its planned meeting with the FDA on May 25 to further collaborate on the implementation of Colorado's Canadian Drug Importation Program. This letter provides an overview of several key issues we are facing, with a particular focus on sourcing products. We are at a critical juncture in our program's development and collaboration with and guidance from the FDA are essential to our next steps.

In our letter dated Mar. 23, we suggested discussing the following process-related items at an upcoming meeting; however, we would like to use the time in our May 25 meeting to discuss more critical topics, as outlined below. Therefore, we would appreciate written responses to the following questions:

- Should the State of Colorado expect additional RFIs? If yes, will these build on the content included in the RFI dated March 2nd or should we expect additional RFIs covering other aspects of the application outside the scope of that letter?
- Once the responses to all RFI requests have been submitted, what is the timeline for a final review of these outstanding items?

For the purposes of our upcoming meeting agenda, we would like to focus on sourcing challenges and related issues in the Final Rule's framework that will impact our implementation success.

First, we believe there is a foundational disconnect between the rule and what is practically required to secure Canadian drug supply. As we discussed in our March 2

meeting, manufacturer contracts with wholesalers in Canada include clauses that expressly prohibit the exportation of their products to the U.S. Due to standard contract language that we have verified with our Foreign Seller partner, direct negotiation with manufacturers is the only path forward.

This is illustrated, for example, by the rule's inclusion of a requirement that imported drugs include the following label:

- *"[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."*

Drugs imported through our program must have the express permission of the manufacturer, and we do not believe a manufacturer would agree to such a statement appearing on the relabeled eligible prescription drugs.

Further, if it were possible to implement a program without manufacturer negotiations, we have concerns about provisions in the rule that rely wholly on manufacturer participation. There is no reason to believe (especially considering that manufacturers thus far are not readily agreeing to participate via negotiation) that a manufacturer would supply all the necessary information to our Importer for an attestation and Pre-Import Request.

Given these concerns, we hope to discuss during our upcoming meeting the fundamental challenges we are experiencing in sourcing prescription drugs for our program. We wish to hear from FDA how the agency envisions the rule's operational implementation in a scenario where manufacturer negotiations are not required and importantly, how the interpretation of Section 804 and the rule may be flexible given the need for negotiations.

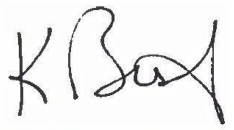
While sourcing is our primary focus for the May 25 meeting, it is also important to note that challenges absent direct manufacturer negotiations do exist. For example,

- Because attestations are required to ensure an imported drug "otherwise meets the conditions" of an FDA-approved drug and the rule appears to allow for some flexibility on who can provide such information (beyond the "applicant"), **we seek clarification regarding what entities FDA would deem "appropriate manufacturers" in providing such information.**
- The labeling requirements outlined in the rule are so extensive and so restrictive that they may disqualify a large percentage of the drugs we included on the aspirational list of 112 drugs included in our Dec. 5th SIP submission. **We would like to understand how the labeling requirements align with what is required in the market more broadly.**
- Given that negotiations are foundational to the implementation of this program, the lack of clarity in the approval process makes potential partners hesitant to commit to

the program. A showing of public support from the FDA that approval of a SIP is likely is paramount to successful negotiations with drug manufacturers, as well as for downstream partners, including health plans, pharmacy benefit managers, and pharmacies. **We would like to work with the FDA to come up with creative solutions to show forward momentum and progress on our program.**

We look forward to hearing the FDA's thoughts on these matters at our May 25 meeting and would like to pursue tangible and collaborative solutions to these critical challenges. Should the FDA have any questions, please contact Lauren Reveley, Colorado Department of Health Care Policy & Financing Drug Importation Program Manager, at Lauren.Reveley@state.co.us.

Sincerely,



Kim Bimestefer
Executive Director
Colorado Department of Health Care Policy & Financing

Meeting Summary Memorandum

MEETING DATE: June 16, 2023
TIME: 11:00 AM - 12:00 PM ET
LOCATION: Teleconference

ORGANIZATION: Colorado Department of Health Care Policy and Financing
TYPE OF MEETING: Stakeholder
MEETING TOPIC: Colorado Section 804 Importation Program (SIP) Proposal
MEETING CHAIR: Leigh Verbois, Director, ODSIR
MEETING RECORDER: Mike Airumian, Health Science Project Manager

ATTENDEES:

Food and Drug Administration (FDA):

Office of Policy, Legislation, and International Affairs (OC/OPLIA), Office of the Commissioner

Nicholas Alexander, Director of Intergovernmental Affairs
Christopher Campbell, Senior Intergovernmental Affairs Specialist

Office of Compliance, Center for Drug Evaluation and Research (CDER)

Leigh Verbois, Director, Office of Drug Security, Integrity, and Response (ODSIR)
Carole Jones, Director, Division of Global Drug Distribution and Policy (DGDDP), ODSIR
Andrei Perlloni, Branch Chief, Imports Compliance Branch (ICB), DGDDP, ODSIR
Paul Gouge, Senior Regulatory Counsel, DGDDP, ODSIR
Olivia Han, Consumer Safety Officer, ICB, DGDDP, ODSIR
Mikhael Airumian, Health Science Project Manager, Program and Regulatory Operations Staff I (PRO-I), Office of Program and Regulatory Operations (OPRO)

Office of Regulatory Policy (ORP), CDER

Aaron Young, Senior Regulatory Counsel, Division of Regulatory Policy II

EXTERNAL ATTENDEES:

Lauren Reveley, Drug Importation Program Manager, Pharmacy Office,
Colorado Department of Health Care Policy & Financing
Kelly Swartzendruber, Drug Importation Pharmacist, Pharmacy Office,
Colorado Department of Health Care Policy & Financing
Mara Baer, Policy Advisor and Consultant

BACKGROUND:

- The Food and Drug Administration (FDA) is working with States and Indian Tribes

that propose to develop section 804 importation program (SIP) proposals in accordance with section 804 of the FD&C Act and FDA's implementing regulations to reduce the cost of covered products to the American consumer without imposing additional risk to public health and safety.

- The Colorado Department of Health Care Policy & Financing (Colorado) submitted a SIP proposal to FDA on December 5, 2022. On February 6, 2023, Colorado requested a meeting with FDA to address issues in the State's SIP proposal so the State could begin taking the necessary steps to resolve those issues. Colorado sent several questions in advance of the meeting about the status of FDA's review, opportunities for collaboration with FDA, the possibility of partial approval of a SIP proposal, and engagement on cost analysis.
- On March 2, 2023, FDA sent Colorado a Request for Information (RFI) letter to request information that was not provided in the State's submission but is required by FDA's regulations. The rigorous review of all aspects of submitted SIP proposals is essential to ensuring that the requirements of section 804 are met, including the requirement that drugs imported under the section must "pose no additional risk to the public's health and safety." FDA is committed to working with States such as Colorado and Indian Tribes on their SIP submissions throughout the process.

MEETING OBJECTIVES:

- This meeting was scheduled at Colorado's request to discuss Colorado's Section 804 Importation Proposal (SIP Proposal) to be an opportunity for Colorado to provide feedback and ask questions. FDA arranged this meeting as soon as possible for the participants.
- As the SIP Proposal is still under review, the information provided was not final or intended to be all-inclusive and may differ from the final evaluation of Colorado's proposal. FDA will evaluate the sufficiency of the SIP proposal to ensure it meets the requirements under the final rule.
- Attendees were reminded that they should not make audio or video recordings of discussions at this meeting. Consistent with 21 CFR 10.65(e), the official record of this meeting will be the FDA-generated minutes.

DISCUSSION POINTS:

FDA considers this meeting important in terms of working to evaluate sufficiency of the proposal. FDA has committed to provide minutes to Colorado after this meeting. FDA emphasized its commitment to working with Colorado.

Colorado was offered an opportunity to ask opening general questions at the beginning of the meeting. Colorado requested a clarification regarding the status of the Section 804 program when FDA stated that Section 804 "was still under review.". FDA indicated that the FDA Section 804 program is operational, and that FDA is currently reviewing Colorado's submission. FDA requested a confirmation that written responses sent via email on June 14 to questions Colorado submitted in advance were received and there were no follow up questions. Colorado confirmed that the answers received via email were very clear and there were no follow up questions at this time.

Colorado indicated that Canadian contracts between manufacturers and wholesalers prohibit wholesalers from distributing products intended for the Canadian market to the United States and said that it appears to be a nationwide issue. Colorado indicated that they have heard that such language also exists in US contracts, thereby prohibiting wholesalers from importing drugs directly from overseas. Per Colorado: manufacturers can cut off supply if they discover export to the United States. These contracts bar exportation and it is understood broadly that wholesalers need to go to manufacturers and ask for permission. Manufacturers have total control over supply chain and distribution. Given that manufacturers track everything electronically, they have visibility into the supply chain and will find out about any wholesale distribution because they can see the path drugs take. This supply chain visibility extends from leaving the manufacturing plant all the way to dispensing at the pharmacy in Canada. Therefore, manufacturers will be informed immediately if a wholesaler sells outside of its contract. Wholesalers in Canada are not willing to put their businesses at risk by selling without the permission of manufacturers. None of the manufacturers have agreed to such proposals from Colorado so far.

- Per Colorado, the foundational issue that poses a risk to the success of an importation program is sourcing. Manufacturers are opposed, and contracts prohibit export to the United States. Wholesalers all say they would have to negotiate with the manufacturers. There appears to be fear on the part of Canadian suppliers that there could be an effort of retaliation from manufacturers.
- Colorado said it does not have a solution to fix this contracting issue in Canada and asked if FDA has a way to penalize foreign entities who refuse to comply. In other words, what enforcement options are at FDA's disposal when manufacturers respond that they are not prepared to cooperate voluntarily, particularly given that said manufacturers are global companies and Colorado would be working with a Canadian arm of that business. Colorado asked what jurisdiction the U.S. government has in enforcing U.S. regulation in Canada. Colorado suggested to conduct a mapping exercise about FDA authority to introduce penalties on US counterparts and how this could affect sourcing without negotiating directly with manufacturers. Currently, everything seems to stop at the manufacturers' level and it is not clear how a Section 804 regulatory structure would exist absent negotiations with them.
- Colorado shared that their supply chain partners have experienced feedback from manufacturers and other stakeholders. FDA suggested that Colorado document processes and organizations that give retaliatory responses. FDA plans to communicate to manufacturers about this program in the future regarding their responsibilities related to statutory testing and recordkeeping requirements.
- Colorado asked if the Agency's suggestion was to start building a case against the manufacturers who refuse to cooperate.
- FDA responded that this would depend on whether non-cooperation is entity-specific or characteristic of the entire industry. FDA pointed out that it is not the only agency that may have regulatory authority in this context.
- Colorado emphasized that this issue is highly sensitive and perhaps a better

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Deleted: forcing wholesalers not to sell to distributors.

Commented [RL1]: Colorado does not recall this being said in the meeting and would be interested in additional detail.

Deleted: Colorado said it did not seem like retaliation because the contracts have been in existence before the final rule.

short-term solution would involve legislation as a pathway to sourcing. Pursuing retaliation by manufacturers is a secondary approach and not a priority to them in a short term or even long term.

FDA asked about Colorado's efforts to identify foreign sellers and if they have approached others.

- Colorado stated it made in person site visits to 3 different smaller Canadian wholesalers who responded during Colorado's procurement process. Prior to releasing the state's Request for Proposal, Colorado made about 40 cold calls and met with 6-7 Canadian wholesalers who agreed to speak. All identified the same issue: wholesalers' contracts with manufacturers prohibit export to the U.S. While contracts between wholesalers and manufacturers bar importation, it is understood that manufacturers can be asked for permission.
- Per Colorado, McKesson a multinational and Canadian wholesaler, has a monopoly controlling 80% of the market. They appear to buy out smaller competitors once they reach a certain level of sales. Colorado was unable to find somebody at McKesson who would talk to them.
- Colorado never anticipated that large wholesalers would participate in this program from the start because they are benefiting from the status quo. Colorado therefore tries to reach out to manufacturers but to no avail. Furthermore, manufacturers and wholesalers have trade associations and they publish their position on their websites.
- FDA stated that it will think about additional channels of communication.

Colorado asked about attestations:

- Because attestations are required to ensure an imported drug "otherwise meets the conditions" of an FDA-approved drug, and the rule appears to allow for some flexibility on who can provide such information, who is a manufacturer under the rule? On page 17 of the rule, FDA uses this language, "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."
- FDA responded that under the final rule, "Manufacturer" means an applicant, 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 Federal Food, Drug, and Cosmetic Act or this part.
- FDA indicated that it has regulatory tools to help ensure that manufacturers provide attestations. Section 303(b)(6) of the FD&C Act (21 U.S.C. 333(b)(6)) provides for penalties for manufacturers or importers that knowingly fail to comply with a requirement of section 804(e).

Colorado said there are a few big issues that affect brand manufacturers, after engaging with several throughout their negotiations thus far:

- First, manufacturers are concerned about the reaction of the Canadian

Commented [RL3]: Colorado does not recall discussing potential legislation as a solution to sourcing issues. We are not sure there is a legislative fix that's reasonably possible.

Commented [RL4]: The potential retaliation Colorado brough to light is unrelated to when the contracts were put into place (likely early 2000s vs. recently).

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government.

- Second, there is concern about supply. The supply chain has not returned to normal from Covid times. Canadian partners don't have much tolerance for any changes in the supply chain and respond with a hard "no" on the calls.
- Third, there is concern about liability, including liability for recalls and returns in case of failed testing. Manufacturers don't like relabeling because of the responsibility generally placed on them. There are problems with relabeling. For example, manufacturers worry that products can be opened and tampered with and it's not clear to manufacturers what their liability is in such cases.

Liability for Relabeling

- Colorado's understanding is that manufacturers cannot control relabeling in an importation program.
- FDA stated that regulatory responsibilities in regard to compliance are covered in the Rule and all requirements are spelled out as to Who, What, When and How. The final rule says that the SIP sponsor has a responsibility for recalls and relabeling. Colorado would need to describe in the proposal how it will do this. Colorado expressed their belief that the burden and responsibility would need to be shared between Colorado and FDA. FDA indicated that there are processes for recalls and importation that could also apply to this program.
- Colorado asked how liability is decided, for example if it needs to open a box to change labeling. FDA stated that the rule excludes certain products from eligibility because of these very concerns.

Colorado said that many products come with package inserts inside of the box and indicated that the rule is frustrating because so many drugs don't qualify just because of this.

FDA concluded the meeting reemphasizing its commitment to work closely with the states and all stakeholders. The Agency recognized that it is important to continue to have conversations and transparency is imperative. All information provided by Colorado has a critical role and FDA confirmed concerns were adequately addressed.

DECISIONS (AGREEMENTS) REACHED:

No decisions

UNRESOLVED ISSUES OR ISSUES THAT MAY REQUIRE FURTHER DISCUSSION:

Relabeling Questions were raised. Per FDA's request, Colorado agreed to send the questions in writing.

ACTION ITEMS:

FDA confirmed that Colorado would receive a copy of the minutes of this call.

The State may, at any time, submit questions, requests to meet, or revisions to the SIP Proposal for Agency review to the Section 804 mailboxat:

Commented [RL5]: Colorado believes this is a mis-characterization. During the meeting Colorado shared our concern that the way the rule is constructed regarding recalls and returns puts our partners at risk of carrying the financial weight of products that cannot be sold but will not be accepted as returns by manufacturers (as the products have crossed the border and have been relabeled by a third party not affiliated with the manufacturer).

Commented [RL6]: Colorado disagrees. While we will continue to refine our SIP and develop a complete response to FDA's RFI from March 2, we do not feel our concerns about sourcing and the rule's lack of contemplation of the realities of the market in the context of importation programs have been adequately addressed.

SIPDrugImportsandRFP@fda.hhs.gov.

ATTACHMENTS/HANDOUTS:

No attachments or handouts.

Date:_____7/20/2023_____ Signature: Carole L. Jones -S Digitally signed by Carole L. Jones -S Date: 2023.07.20 13:38:16 -04'00'

COLORADO
Department of Health Care Policy & Financing

1570 Grant Street
Denver, CO 80203

September 5, 2023

Ms. Leigh Verbois
Center for Drug Evaluation and Research
Food and Drug Administration
Department of Health and Human Services
1001 New Hampshire Avenue
Hillandale Building, 4th Floor
Silver Spring, MD 20993

RE: SIP Implementation Questions

Dear Ms. Verbois:

In follow up to our meeting on June 16, Colorado is reaching out to request further clarification regarding key questions posed in our May 17 letter. We appreciated the opportunity to meet with the FDA and have reviewed the follow up minutes you provided. While we appreciate these minutes, our Executive Director, Kim Bimestefer, has asked that we request that you adopt Colorado's suggested edits and clarifications (attached to this letter) to more appropriately portray and describe the content of the meeting.

We continue to require additional collaboration and information from the FDA that will be critical to realizing success for state-led importation programs. We are particularly interested in continuing to engage on ongoing sourcing concerns, manufacturer requirements, and operational challenges related to relabeling.

We respectfully request responses in writing to the following outstanding questions and concerns:

- **Sourcing absent direct negotiation -** The FDA seemed to indicate that the Foreign Seller should be able to source drugs without direct negotiation/agreement with manufacturers. Please clarify:
    - Section 804 and the Final Rule require programs to purchase eligible drugs directly from manufacturers. How do SIPs source eligible drugs without manufacturer approval or agreement? If a manufacturer will not sell eligible drugs to our Foreign Seller, how is a program to secure supply for a SIP?

        - We briefly discussed the manufacturer feedback we have received regarding Colorado's program to date. We are attaching a summary of our engagement with the pharmaceutical industry thus far to this letter.
    - Because attestations are required to ensure an imported drug "otherwise meets the conditions" of an FDA-approved drug and the rule appears to allow for some flexibility on who can provide such information (beyond the "applicant"), we seek clarification regarding what entities FDA would deem "appropriate manufacturers[1]" in providing such information.
    - You indicated that the FDA has regulatory "teeth" to require manufacturers to provide information to support attestations and Pre-Importation requests.
        - Given the challenges Colorado has faced in working directly with manufacturers, is the FDA able to help us by requiring manufacturers to provide such information through the exercise of its regulatory enforcement powers?

- **Sourcing and direct negotiation -** As discussed during our call, Canadian manufacturers broadly require wholesalers to sign contracts prohibiting exportation to the U.S. This means that direct negotiation with manufacturers is required to source Canadian prescription drugs. The rule is not structured in a way that contemplates this reality. We are still looking for clarification of how the rule can be implemented in this scenario. Please provide specific details regarding how SIP programs can be implemented in this scenario and still remain compliant with federal regulation (i.e., labeling requirements, manufacturer attestations, etc.).

- **Talking points and regulatory citations -** During the June 16 meeting, you delivered talking points that were clearly intended to respond to some of our questions and concerns. These talking points included specific citations of U.S. law and regulations which we requested in writing during the meeting. These do not appear to be fully included in the provided minutes. It would help us to have those citations in writing so that we can better understand your responses to our questions. Are you able to provide those, we note they are not included in the meeting minutes.

- **Relabeling clarification** - At the June 16 meeting, we committed to sharing our outstanding labeling question in writing regarding FDA-approved labeling changes to program approved eligible drugs. We include that question here:
    - Does FDA concur that once an eligible drug has been distributed to participating pharmacies that drug may be dispensed regardless of subsequent changes that are made to FDA-approved labeling? If you do not concur can you please explain why not?

[1] Referenced from page 17 of the Final Rule. https://www.hhs.gov/sites/default/files/importation-final-rule.pdf

We look forward to receiving a written response from the FDA on these matters which are critical to Colorado's progress in successfully implementing its importation program. As we continue to refine our response to FDA's RFI, we are likely to have additional regulatory questions and request to meet with FDA on or around November 15 to address outstanding questions, ahead of our planned resubmission of Colorado's SIP in early 2024.

Lastly, the Department is statutorily required to annually update the Colorado General Assembly on December 1 regarding the status of the importation program. This will include details of our ongoing engagements with manufacturers as well as our correspondence and collaboration and efforts with FDA to address outstanding concerns and challenges with implementation.

Should the FDA have any questions, please contact me via email at Lauren.Reveley@state.co.us.

Sincerely,

Lauren Reveley
Drug Importation Program Manager
Colorado Department of Health Care Policy & Financing

Enclosure(s)

cc: Kim Bimestefer, Executive Director, Colorado Department of Health Care Policy & Financing

COLORADO

Department of Health Care Policy & Financing

	Company Name	Initial Outreach	Response
1	Allergan	April 2023	No response received after 2 outreach emails in April and May 2023
2	Amgen	August 2023	Response received 8/30/23: "... regarding the state of Colorado's proposed Canadian Drug Importation Program, I want to notify you that Amgen will not be participating in the importation program."
3	Apotex	February 2023	Initial response from US representatives: "Not an opportunity we are prepared to pursue for the time being." Follow up meeting with Canadian representatives in June 2023 did not result in further progress.
4	Astellas Pharma US	April 2023	No response received after 2 outreach emails in April and May 2023
5	AstraZeneca	April 2023	Response received 5/2/23: "We appreciate you initiating a dialogue on this subject, but respectfully we are unable to participate in the program at this time."
6	Bayer	May 2023	No response received after an outreach email in May 2023
7	Boehringer Ingelheim	April 2023	Response received 5/2/2023: "Thank you for your outreach regarding the Canadian Drug Importation Program that Colorado is pursuing. We appreciate the acknowledgement of the importance of manufacturers in this process. We are tracking the SIP, and at this time, we are not prepared for a dialogue with the Department. We will be sure to reach out as this process progresses should we have any questions or thoughts."
8	Bristol-Myers Squibb	April 2023	No response received after 2 outreach emails in April and May 2023
9	Eli Lilly	April 2023	No response received after 2 outreach emails in April and May 2023
10	Gilead	April 2023	Response received May 2023: "Gilead is committed to enabling safe access to its medicines and is open to dialogue. While we do not grant permission to import any Gilead (including its affiliates and licensees) drug via Colorado's SIP program, we would appreciate the opportunity to speak with you to discuss your inquiry and explain our rationale in greater detail." A follow up meeting on July 17th did not result in further negotiation.
11	GlaxoSmith Kline	April 2023	No response since an initial reply received June 13
12	Janssen	April 2023	Meeting on 5/12/23 between Janssen & representatives of the State. Janssen indicated they were open to a discussion but that they are not willing to move forward due to supply chain challenges associated with Covid-19, product integrity risks associated with testing and relabeling, and the potential to negatively affect their relationship with Health Canada due to the Interim Order.
13	Merck	April 2023	Response received 5/2/23: "To be clear, Merck does not support the efforts by Colorado or any other state to import Merck products from Canada, nor is Merck prepared to cooperate voluntarily in those efforts."
14	Novartis	April 2023	No response received after 2 outreach emails in April and May 2023.
15	Novo Nordisk	April 2023	An initial response was received after 2 outreach emails in April and May 2023; no response has been received since.

COLORADO
Department of Health Care Policy & Financing

	Company Name	Initial Outreach	Response
16	Pfizer	April 2023	An initial response was received after 2 outreach emails in April and May 2023; no response has been received since.
17	Sandoz	February 2023	Response Received 7/27/23: "We have reviewed your request and have decided to decline this project."
18	Sunovion	April 2023	Response Received 5/2/23: "Thank you for your note and providing us the opportunity to discuss the program. We are declining the invitation, but appreciate you taking the time to reach out."
19	Takeda	August 2022	They did not want to participate in an importation program but offered Colorado an opportunity for Drug Discount Cards.
20	Teva	February 2023	Response received 8/8/23: "We do not believe the approach proposed by the State of Colorado reflects the realities of supply chain safety or affordability for its residents and are therefore unable to assist with your request. "
22	Vertex	August 2023	Pending
23	Viiv Healthcare Company	April 2023	Response received 6/23: "Thank you for this information regarding Colorado's drug importation program. At this time, ViiV Healthcare is not interested in engaging in this program as we maintain a program like this could threaten the integrity of the US supply chain and the safety of US consumers. Thank you."

October 27, 2023

Lauren Reveley, Drug Importation Program Manager
Colorado Department of Health Care Policy & Financing
1570 Grant Street
Denver, CO 80203

Re: Colorado's Letter to FDA in follow up to June 16 Importation Meeting

Dear Lauren Reveley,

This letter responds to Colorado's letter to FDA on September 5, 2023 that presented outstanding questions regarding Section 804 Importation Program (SIP).

1. Colorado's Question: *Sourcing absent direct negotiation - The FDA seemed to indicate that the Foreign Seller should be able to source drugs without direct negotiation/agreement with manufacturers. Please clarify:*

- *Section 804 and the Final Rule require programs to purchase eligible drugs directly from manufacturers. How do SIPs source eligible drugs without manufacturer approval or agreement? If a manufacturer will not sell eligible drugs to our Foreign Seller, how is a program to secure supply for a SIP?*
  - *We briefly discussed the manufacturer feedback we have received regarding Colorado's program to date. We are attaching a summary of our engagement with the pharmaceutical industry thus far to this letter.*

FDA Response:

Section 804 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 384) does not require manufacturers to sell drugs approved for sale in Canada to potential purchasers in the United States. Rather, section 804 gives FDA the authority to authorize the importation of certain prescription drugs from Canada into the US to reduce the cost of these drugs to the American consumer, without imposing additional risk to public health and safety.

- *Because attestations are required to ensure an imported drug "otherwise meets the conditions" of an FDA-approved drug and the rule appears to allow for some flexibility on who can provide such information (beyond the "applicant"), we seek clarification*

regarding what entities FDA would deem "appropriate manufacturers" in providing such information.

FDA Response:

Under 21 CFR 251.2, "manufacturer" is defined as an applicant or a person who owns or operates an establishment that manufactures an eligible prescription drug. Applicant means any person who submits an NDA or ANDA (including a supplement or amendment to an NDA or ANDA) to obtain FDA approval of a new drug. "Manufacturer" also includes 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 FDA's regulations. The appropriate manufacturer to make the required attestation would be the applicant, owner/operator, or holder of a drug master file who had the necessary information.

An Importer will determine which manufacturer, as described above, 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 (which may not be the applicant), and that entity would be required to provide those records if the records are in the facility's possession or control.

- *You indicated that the FDA has regulatory "teeth" to require manufacturers to provide information to support attestations and Pre-Importation requests.*
  - *Given the challenges Colorado has faced in working directly with manufacturers, is the FDA able to help us by requiring manufacturers to provide such information through the exercise of its regulatory enforcement powers?*

FDA's Response:

The obligations on manufacturers under section 804 and the implementing regulation 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. Additionally, 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 could also be fined under 18 U.S.C. 3571. These tools would only apply if a manufacturer did not comply with the requirements of section 804 (e.g., did not provide the required attestation). FDA, working with the U.S. Department of Justice, determines whether to bring a judicial action enforcing these provisions on a case-by-case basis, and generally retains discretion in their enforcement.

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, FDA's regulation 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.

2. Colorado's Question: *Sourcing and direct negotiation - As discussed during our call, Canadian manufacturers broadly require wholesalers to sign contracts prohibiting exportation to the U.S. This means that direct negotiation with manufacturers is required to source Canadian prescription drugs. The rule is not structured in a way that contemplates this reality. We are still looking for clarification of how the rule can be implemented in this scenario. Please provide specific details regarding how SIP programs can be implemented in this scenario and still remain compliant with federal regulation (i.e., labeling requirements, manufacturer attestations, etc.).*

FDA's Response:

FDA's regulations are intended to afford 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.

If a drug that was originally intended to be marketed in a foreign country is authorized by its manufacturer to be marketed in the U.S., and if the manufacturer "cause[s] the drug to be labeled to be marketed in the [U.S.]," the drug may instead be imported under section 801 of the FD&C Act, rather than under section 804. There is information on manufacturer-authorized importation

of drugs originally intended to be marketed in a foreign country in our guidance *Importation of Certain FDA-Approved Human Prescription Drugs, Including Biological Products, and Combination Products under Section 801(d)(1)(B) of the Federal Food, Drug, and Cosmetic Act*.

3. Colorado's Question: *Talking points and regulatory citations - During the June 16 meeting, you delivered talking points that were clearly intended to respond to some of our questions and concerns. These talking points included specific citations of U.S. law and regulations which we requested in writing during the meeting. These do not appear to be fully included in the provided minutes. It would help us to have those citations in writing so that we can better understand your responses to our questions. Are you able to provide those, we note they are not included in the meeting minutes.*

FDA's Response:

We are happy to provide any citations you require. However, we are unaware of which citations you are referencing.

4. Colorado's Question: *Relabeling clarification - At the June 16 meeting, we committed to sharing our outstanding labeling question in writing regarding FDA-approved labeling changes to program approved eligible drugs. We include that question here:*

- *Does FDA concur that once an eligible drug has been distributed to participating pharmacies that drug may be dispensed regardless of subsequent changes that are made to FDA-approved labeling? If you do not concur, can you please explain why not?*

FDA's Response:

At the time an eligible prescription drug is sold or dispensed, it has to have been relabeled to be consistent with the FDA-approved labeling under the applicable NDA or ANDA, except for items described under 21 CFR 251.13(b)(4). FDA's regulations also include post-importation requirements. For example, under 21 CFR 251.18(d)(2), an importer must promptly review all domestic safety information for the eligible prescription drugs obtained or otherwise received by the Importer. As explained in Response 38 of the Final Rule, we interpret the phrase "sold or dispensed" to apply to the Importer. (The Importer is responsible for facilitating re-labelling, and as explained in the rule an Importer can be engaged in either selling/distributing the drug to participating pharmacies (i.e., as a wholesale distributor), or engaged in dispensing the drug to patients (i.e., if the

Importer is a pharmacist)). If an Importer acting as a wholesale distributor distributes eligible drugs that are relabeled to be consistent with the FDA-approved labeling to pharmacies, we think it is generally the case that those drugs may be dispensed by those participating pharmacies. Note that, as described below, the Importer is responsible for monitoring for any FDA-approved drug labeling changes to the applicable NDA or ANDA, and for engaging with FDA regarding required revisions to the labelling. We also note that under certain circumstances, as per 21 CFR 251.18(e)(2), FDA may determine a recall of an eligible drug is warranted.

Prompt revision, submission to the Agency, and implementation of revised labeling are important to ensure that the imported drugs under a SIP continue to be as safe and effective as the corresponding FDA-approved source drugs. Thus, FDA recommends that you promptly submit revised importer labeling after a new version of the source drug labeling is approved by the FDA. It is the importer's responsibility to monitor for FDA-approved drug labeling changes under the applicable NDA or ANDA, (e.g., using Drugs@FDA) and to promptly submit revised proposed importer labeling to FDA.

We look forward to meeting you again in our scheduled meeting in November and continuing our partnership.

Please submit any questions, requests to meet, or revisions to your SIP proposal for agency review to SIPDrugImportsandRFP@fda.hhs.gov.

Sincerely,

Sandi L. Verbois -S

Digitally signed by Sandi L. Verbois -S
Date: 2023.10.27 17:14:23 -04'00'

S. Leigh Verbois, PhD
Director
Office of Drug Security, Integrity & Response
Office of Compliance
Center for Drug Evaluation and Research

STATE OF COLORADO

Swartzendruber - HCPF, Kelly <kelly.swartzendruber@state.co.us>

Re: [EXTERNAL] Follow Up from 6/16 Meeting with Colorado

1 message

Swartzendruber - HCPF, Kelly <kelly.swartzendruber@state.co.us> Mon, Oct 30, 2023 at 4:08 PM
To: SIPDrugImportsandRFP <SIPDrugImportsandRFP@fda.hhs.gov>
Cc: "Reveley - HCPF, Lauren" <lauren.reveley@state.co.us>, "Campbell, Christopher C" <Christopher.Campbell@fda.hhs.gov>, SIPDrugImportsandRFP <SIPDrugImportsandRFP@fda.hhs.gov>, "Verbois, Leigh" <Leigh.Verbois@fda.hhs.gov>, "Alexander, Nicholas" <Nicholas.Alexander@fda.hhs.gov>, Ciara O'Neill - HCPF <ciara.oneill@state.co.us>
Bcc: Mara Baer <mara@agohealth.com>

Good afternoon,

Thank you for your letter received Friday, October 27, in response to our letter sent September 5. We are analyzing your responses and will reach out with follow up questions and will likely be requesting a separate meeting to discuss. For our upcoming meeting on November 29, we would like to focus on the set of attached questions that will inform our updated SIP submission. We would appreciate written responses to these questions in advance of the meeting if possible to inform our discussion.

We appreciate our partnership on Section 804 and look forward to meeting with you soon. Please reach out to me directly if you have any follow up questions.

Thank you,
Kelly

Kelly Swartzendruber, PharmD
Drug Importation Program Manager
Pharmacy Office
COLORADO
Department of Health Care Policy & Financing

P 303.866.3632 | F 303.866.3590 State Relay: 711
303 E. 17th Avenue, Denver, CO 80203
kelly.swartzendruber@state.co.us | colorado.gov/hcpf/drug-importation

On Fri, Oct 27, 2023 at 3:24 PM SIPDrugImportsandRFP <SIPDrugImportsandRFP@fda.hhs.gov> wrote:

> Dear Lauren Reveley,
>
> Attached is our written response to your letter on September 5, 2023.
>
> Regards,
>
> Office of Drug Security, Integrity and Response

Office of Compliance

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

SIPDrugImportsandRFP@fda.hhs.gov

From: Reveley - HCPF, Lauren <lauren.reveley@state.co.us>
Sent: Tuesday, September 5, 2023 2:10 PM
To: SIPDrugImportsandRFP <SIPDrugImportsandRFP@fda.hhs.gov>
Cc: Campbell, Christopher C <Christopher.Campbell@fda.hhs.gov>; Kelly Swartzendruber - HCPF <kelly.swartzendruber@state.co.us>
Subject: [EXTERNAL] Follow Up from 6/16 Meeting with Colorado

Good afternoon,

Hope you all had a nice Labor Day weekend.

Attached you will find a letter from Colorado. There are two attachments: Colorado's edits to the minutes shared by FDA from our June 16 meeting and a table showing the outcome of our initial attempts at negotiating with drug manufacturers to secure supply for our program.

Please let me know if you have any questions.

Thank you,
Lauren

Lauren Reveley
Government Relations Director
Drug Importation Program Manager

Policy, Communications & Administration Office

P 303-866-2718 | F 303-866-4411 | State Relay: 711

1570 Grant Street, Denver, CO 80203

Lauren.Reveley@state.co.us I Colorado.gov/hcpf

HCPF.FDA Questions 11.29.23.pdf
463K

Colorado's Drug Importation Program

November 29, 2023

§ 251.17(c) Application Clarification

Can the Agency clarify what it would like to see for Colorado to comply with §251.17(c)? Is the "**application**" referenced assumed to be the Pre-Import request? The SIP Application itself? If no to both of these, can the Agency define the **application** in context of the rule?

*"...(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…"*

Admissibility Decision Clarifications

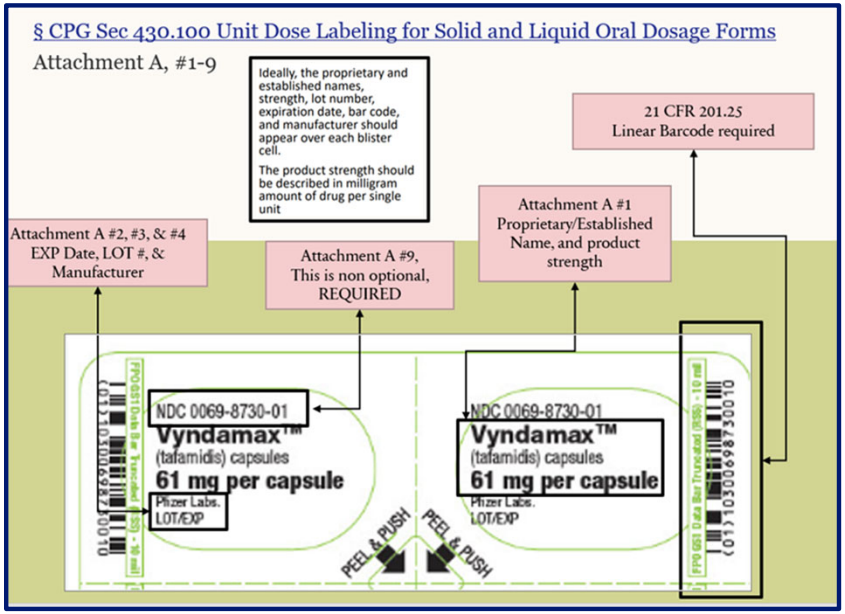
- We now understand that the Agency issues an admissibility decision as listed in §251.17(b) after relabeling occurs, not after testing occurs. We understand this to mean the drugs will leave the Customs and Border Patrol (CBP) secure warehouse under the importer's control, be relabeled, and come back to the CBP warehouse. C**an the Agency confirm this order of events?**

- How do the post-labeling admissibility requirements interact with the 30-mile rule as listed in §251.17(b)? For example, how would Agency requirements address relabeling that occurs more than 30 miles from CBP?

- In addition to the Agency inspecting the relabeled products, what other documents or items will be required for review by the Agency to receive an admissibility decision?

Labeling Question - Blister Pack

Does the Agency agree that when relabeling a non-perforated multi-dose blister package, it is sufficient to list required information per CPG Sec 430.100, “Unit Dose Labeling for Solid and Liquid Oral Dosage Forms,” once on each blister card?



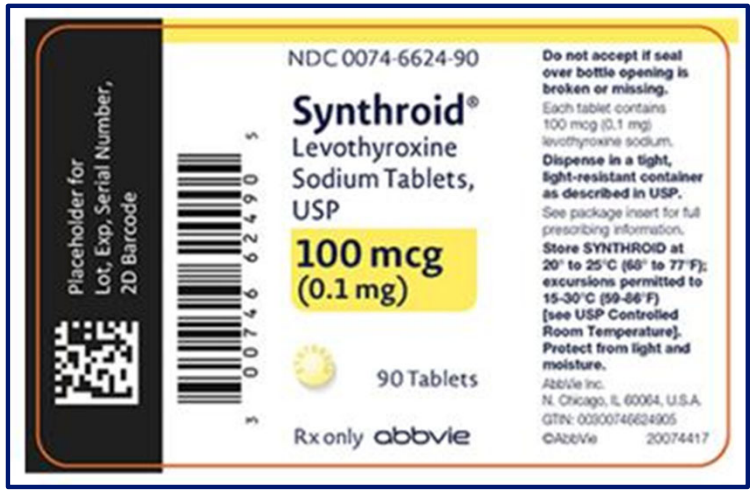
Canadian Ibrance Blister Pack

Labeling Question - Company Branding

Synthroid® US is distributed by Abbvie and Synthroid® CAN is distributed by Mylan. Both products are manufactured by Abbvie. Does the Agency agree that to meet the requirements listed in § 251.14(d)(2), the relabeler should add Abbvie branding and remove Mylan branding to reflect the FDA-approved US label?

US Label

CAN Label



Question 1 (§ 251.17(c) Application Clarification): Can the Agency clarify what it would like to see for Colorado to comply with §251.17(c)? Is the "application" referenced assumed to be the Pre-Import request? The SIP Application itself? If no to both of these, can the Agency define the application in context of the rule?

> *"...(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..."*

FDA Response:

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.

If you file an entry for consumption as described in 19 CFR 141.0a(f), then you would need to apply for reconditioning. Therefore, when 21 CFR 251.17(c) refers to application, it means an application to relabel or recondition as indicated in 21 CFR 1.95 and 1.96.

For more information regarding the reconditioning application process, we suggest that you consult the website Reconditioning of Imported FDA-Regulated Products and read FDA's Regulatory Procedures and Manual, Chapter 9-12 Reconditioning.

Question 2 (Admissibility Decision Clarifications): We now understand that the Agency issues an admissibility decision as listed in §251.17(b) after relabeling occurs, not after testing occurs. We understand this to mean the drugs will leave the Customs and Border Patrol (CBP) secure warehouse under the importer's control, be relabeled, and come back to the CBP warehouse. Can the Agency confirm this order of events?

FDA Response:

Although products may leave your designated secured warehouse, located within 30 miles of the CBP port of entry authorized by FDA, for relabeling, an admissibility decision will only be issued after testing and relabeling occurs. The products remain in imports status during the testing and relabeling periods and are still under the control of the importer.

Question 3 (Admissibility Decision Clarifications): How do the post-labeling admissibility requirements interact with the 30-mile rule as listed in §251.17(b)? For example, how would Agency requirements address relabeling that occurs more than 30 miles from CBP?

FDA Response:

In order to efficiently and quickly process importation, we recommend that relabeling occur within 30 miles of the authorized Port of Entry. After relabeling is complete, if relabeling did not occur within

your designated secure warehouse, the product must be returned to your designated secure warehouse until the drug product is released.

The only authorized Port of Entry is Detroit, Michigan. FDA carefully selected the Port of Entry for SIP drugs that is close to the border with Canada, located within FDA's Northern Border Division, and where sufficient infrastructure is in place to appropriately process such drugs for importation. The Detroit port met these criteria. This information was publicly released via a US Customs and Border Protection bulletin (CSMS #44743727) sent on November 9th 2020. This bulletin announced that the only authorized Port of Entry for Section 804 drugs was port 3801 located in Detroit. Furthermore, the amended ACE Supplemental guide, which is also publicly available, specifically indicates that the "Section 804 Importation Program is limited to a port authorized by FDA. At the time of implementation, the only port authorized by FDA is 3801 (Detroit)."

Determining a single port allows FDA to have personnel who are specifically trained to facilitate section 804 importation and to coordinate activities more effectively with Customs and Border Patrol. This is essential to ensure a smooth importation process for this program.

Question 4 (Admissibility Decision Clarifications): In addition to the Agency inspecting the relabeled products, what other documents or items will be required for review by the Agency to receive an admissibility decision?

FDA Response:

Importation of drugs under this program cannot occur until the Importer receives formal notification from FDA that its Pre-Import Request has been granted. The Importer or its authorized customs broker is required, if the products are not admitted through an FTZ, to electronically file an entry for consumption in the Automated Commercial Environment 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 a drug that is imported or offered for import does not comply with the final rule, the drug is subject to refusal under the FD&C Act.

The specifications and requirements for filing entries of FDA-regulated products per the FDA ACE Final Rule is located in the FDA Supplemental Guide for the Automated Commercial Environment (ACE). The Government Agency Processing Code for the SIP is 804 and the Intended Use Code (IUC) is 080.012 as identified in the ACE Supplemental Guide. In addition, New Drug Application Number or Abbreviated New Drug Application Number, Drug Listing Number, Foreign Seller Registration Number, Pre-Import Request Number, Lot or Control Number assigned by the manufacturer of the eligible prescription drug, and quantity are required elements when a SIP entry is filed in ACE.

Further, once the eligible prescription drugs are shown by testing and relabeling to meet the requirements of section 804 of the FD&C Act and 21 CFR part 251, the Importer or the manufacturer must provide to FDA the written certification described in section 804(d)(1)(K)-(N) of the FD&C Act in an electronic format to FDA. *See* 21 CFR 251.7(g).

Question 5 (Labeling Question – Blister Pack): Does the Agency agree that when relabeling a non-perforated multi-dose blister package, it is sufficient to list required information per CPG Sec 430.100, "Unit Dose Labeling for Solid and Liquid Oral Dosage Forms," once on each blister card?

FDA Response:

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. 21 CFR 251.13(c) states that "[r]epackaging the container closure of a drug is not permitted under this part." The final rule does not allow repackaging of a drug product in a manner that breaches the container closure system, such as a blister pack, because it would introduce unnecessary risk of adulteration, degradation, and fraud for drugs imported under a SIP. It would also be impermissible to affix the FDA-approved labeling to a product's external packaging in lieu of relabeling its immediate container. 21 CFR 251.13(b)(4)("the labeling of the drug must be the same as the FDA-approved labeling under the applicable NDA or ANDA").

Question 6 (Labeling Question – Company Branding): Synthroid® US is distributed by Abbvie and Synthroid® CAN is distributed by Mylan. Both products are manufactured by Abbvie. Does the Agency agree that to meet the requirements listed in § 251.14(d)(2), the relabeler should add Abbvie branding and remove Mylan branding to reflect the FDA-approved US label?

FDA Response:

Consistent with 21 CFR 251.14(d)(2) and 21 CFR 251.13(b)(4), at the time the imported drug is sold or dispensed, the imported drug's labeling must be the same as the FDA-approved drug's labeling under the applicable NDA or ANDA, with certain exceptions. Specifically, the imported drug's labeling must:

- Include the imported drug's NDC instead of the FDA-approved drug's NDC,
- Include the importer's name and place of business,
- Include the following statement: ''This drug was imported from Canada without the authorization of Abbvie under the *[insert the name of SIP Sponsor]* Section 804 Importation Program", and
- Affix or imprint a product identifier, as defined in section 581(14) of the Federal Food, Drug, and Cosmetic Act.

Given that the FDA-approved drug in the United States has the Abbvie labeling (not the Mylan labeling), the Abbvie labeling (not the Mylan labeling) must be used, including on the carton and container label(s) for imported Synthroid.

Please ensure that the design, format, and organization of the labeling is the same as the FDA-approved labeling, including the labeling for the carton and container, given that 21 CFR 251.13(b)(4) requires that the labeling be the same as the FDA-approved labeling under the applicable NDA or ANDA.