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Administration Finally Releases Proposed Drug Importation Policies for Stakeholder and Public Comments

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At the end of July 2019, the U.S. Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) jointly published the Safe Importation Action Plan, which outlined the Trump Administration's two-part plan to allow foreign prescription drugs to be imported into the United States in an effort to reduce drug prices. We wrote about the release of the Safe Importation Action Plan here, and the detailed proposals made public by the Administration on December 18, 2019, follow the framework that the agencies sketched out earlier this year. Specifically, HHS and FDA have proposed two different pathways: one that is being implemented via notice-and-comment rulemaking, and one that is being implemented via an FDA guidance document. HHS Secretary Alex Azar touted the two pathways together in a same-day FDA press release as "historic actions…[that] represent the bold nature of President Trump's agenda for lowering drug costs."

Former FDA Commissioner Scott Gottlieb, who left the agency in April 2019 and previously had expressed skepticism that foreign drug importation could be done safely or generate substantial savings for American consumers, tweeted, "On close review of the 'importation' plan unveiled today, the proposed rule places stringent conditions on the importation of drugs. While it may sharply limit who can actually import Canadian drugs under this framework, it maintains critical FDA safeguards to protect consumers."

At the same time, however, the wholesale distributor trade association Healthcare Distribution Alliance (HDA) stated, "While we acknowledge that the administration and proponents of state importation plans are mindful of the safety protections offered by traceability requirements under the [Drug Supply Chain Security Act (DSCSA)], significant concerns remain about the feasibility of an importation program from an operations perspective." And leadership from both of the large trade associations representing the pharmaceutical and biopharmaceutical industries (PhRMA and BIO, respectively) issued statements that criticized the HHS/FDA proposals for putting patient safety at risk. (See here and here.)

This initial reaction from industry suggests that at least for the second pathway, to which U.S. drug companies would have to voluntarily avail themselves, there may not be as much buy-in from large manufacturers as would be needed for that program to have a noticeable impact on domestic

pharmaceutical product costs. We will be watching to see how the rulemaking and implementation phases of this significant Trump Administration agenda item proceed and whether these two programs ultimately have a measurable impact on Americans' health care costs.

Pathway One or the "Section 804 Importation Program"

The first pathway (Pathway One) for prescription drug importation is being implemented under a statutory provision in the Federal Food, Drug, and Cosmetic Act (FD&C Act) that has been in place since 2003 – Section 804 of the FD&C Act, which is codified at 21 U.S.C. § 384. However, no previous HHS Secretary has been willing to certify, as required by the law, that drug importation would "pose no additional risk to the public's health and safety" and would "result in a significant reduction in the cost of covered products to the American consumer." (And although such a certification has not yet been provided to Congress, HHS indicates that it will take that step if and when the new proposed rule is finalized.) Because of that existing law, FDA refers to the proposed programs that may be authorized by the agency as "Section 804 Importation Programs." In a press conference before the release of the two documents on December 18th, Secretary Azar indicated that states such as Colorado, Florida, Maine, New Hampshire, Vermont, and Michigan have expressed interest in setting up their own importation programs, and, indeed, we know that Florida submitted a plan to HHS in August 2019 even before the federal government had made any detailed proposals under Section 804. Colorado expects to submit its plan to HHS by January 15, 2020, and, under a state law, Maine has until May 1, 2020, to submit its importation plan for federal review.

FDA released the Notice of Proposed Rulemaking (NPRM) for Pathway One in order authorize imports of eligible prescription drugs from Canada on December 18, 2019, as noted above. The proposed rule would create a new Part 251 in Title 21 of the Code of Federal Regulations (CFR) pursuant to the authorities available in Section 804 of the FD&C Act. Accordingly, some of the requirements included in the NPRM come directly from the language of the statute, while others are being proposed pursuant to the discretion granted to the HHS Secretary to require any other elements in a foreign importation plan as he deems necessary to protect the public health. Putting aside all of the political complexities of this proposal, including that the Canada government has expressed dismay at the idea and is rightfully concerned that its own pharmaceutical supply will suffer if the U.S. plan goes forward, the NPRM describes quite a robust and highly regulated Canadian importation program. If these regulations are finalized as written after the notice-and-comment process end, they will require the use of a tightly controlled, limited supply chain, as we summarize below, and will also impose significant compliance obligations on the "Sponsor" of an authorized Section 804 Importation Program (SIP). The highly regulated nature of any FDA-authorized SIP is likely going to make this an expensive and resource-intensive proposition for everyone involved in one of these potential future programs.

SIP Participants

Section 804 expressly directs the federal government to "promulgate regulations permitting pharmacists and wholesalers to import prescription drugs from Canada." In the current proposed rule, a SIP Sponsor must be a state, tribal, or territorial governmental entity only (i.e., a non-federal agency), and FDA is proposing to allow wholesalers and pharmacists to serve as SIP co-sponsors. However, pharmacists and wholesalers are the only entities that can serve in the role of Importer under the proposed rule. FDA is also requesting comments on an alternative proposal in which a governmental entity is not required to be the SIP Sponsor and a wholesaler or pharmacist could serve in the lead Sponsor role. It further specifically requests comments "on what the division of responsibility between co-sponsors should be and whether there are certain arrangements that

should not be permitted. … [and] whether non-governmental entities other than pharmacists and wholesalers, such as group purchasing organizations, pharmacy benefit managers [PBMs], or union health and welfare benefit plans, should be permitted to co-sponsor SIPs."

In addition to defining new regulatory roles for SIP Sponsors and co-sponsors, the NPRM defines the following terms and roles for these four SIP supply chain participants:

1. The "Foreign Seller" must be a Canadian establishment licensed as a wholesaler by Health Canada and will also need to register with FDA before the agency will authorize any SIP Proposal that includes that Foreign Seller. In conjunction with the U.S.-based Importer, the Foreign Seller would be responsible for ensuring supply chain integrity under the proposed regulations by, among other things, affixing a "Section 804 Serial Identifier" that is linked to the Canadian-specific drug identification number.

2. The U.S-based "Importer" can be a licensed pharmacist or licensed wholesaler but must be the owner of the prescription drugs being imported from Canada under an authorized SIP and is responsible for submitting a "Section 804 Pre-Import Request" to FDA, for screening prescription drugs for SIP eligibility and arranging for them to be tested and relabeled before they enter U.S. commerce, and for complying with a slew of post-importation regulatory requirements like adverse event reporting. Given the substantial compliance obligations being proposed in this NPRM that go beyond what typical U.S.-licensed pharmacists and wholesalers do today, FDA is seeking comments on whether Importers should be required to have additional qualifications beyond active professional licensure. The agency is also interested in hearing stakeholder views on whether a SIP co-sponsor should also be allowed to act as the Importer under the same SIP and, if so, what safeguards a SIP Sponsor would need to include in its program when a pharmacist or wholesaler is serving in those dual roles.

3. The "Manufacturer" of the prescription drugs must have originally intended the prescriptions drugs for the Canadian market but designated them for importation under an authorized SIP. The Manufacturer will play a limited role in an authorized outside SIP outside of granting the Importer rights to proprietary product information, labeling, and information about pre-SIP supply chain integrity. Interestingly, the Manufacturer entity could either be the owner of the approved marketing application for a prescription, the owner/operator of the drug manufacturing facility, or the holder of a drug master file that contains the information needed to authenticate an imported prescription drug.

4. The "Qualifying Laboratory," as required under Section 804, is responsible for testing an imported drug for "authenticity, degradation, and to ensure that the prescription drug is in compliance with established specifications and standards" (which the NPRM collectively refers to as "Statutory Testing"). The proposal includes minimum criteria for a U.S. laboratory in order for it to be approved as a qualified lab under Section 804 – which are that the lab complies with applicable CGMP requirements, has ISO 17025 accreditation, and has an FDA inspection history and no open objectionable conditions. FDA is also seeking comments on whether there are other requirements or accreditations that should apply to labs before they can be approved for use by a SIP on a case-by-case basis.

How a Section 804 Importation Program Would Work

First, it is important to note that controlled substances, biological drug products (including insulin), intravenous drugs, drugs that are subject to FDA-approved Risk Evaluation and Mitigation Strategies (REMS) programs, and drugs injected in the spine or eye would not be eligible for inclusion in a SIP, and FDA is requesting input on whether additional categories of drugs should be excluded or if decisions should be made on a product-by-product basis. Given that many biologics and other specialty drug products have received the most public and political attention for being too expensive, we expect to see a lot of written comments to the agency about these product exclusions from the SIP proposed rule.

As envisioned in the NPRM (although in highly simplified form!), the Section 805 Importation Program regulations would work like this:

- The SIP Sponsor would submit a SIP Proposal to FDA that would need to show that the proposed importation program will pose no additional risk to the public's health and safety, as well as why the Sponsor expects its plan to result in a significant reduction in the cost to the American consumer of the prescription drug(s) sought to be imported under the SIP. As currently drafted, the SIP Sponsor would only be allowed to designate one Foreign Seller and one Importer per SIP Proposal, which would need to include a lot of other information such as (among other things) how the SIP Sponsor would ensure that its imported drugs meet the Statutory Testing requirements, all the steps the Sponsor will take to ensure that the supply chain is secure, and how the Sponsor intends to educate health care providers about the drugs imported under its SIP.

- FDA will review and authorize (or deny) the SIP Proposal, which it retains discretion not to authorize even if all of the Section 804 and (future) 21 CFR Part 251 rules are met. Among other possible reasons the agency may exercise its discretion not to authorize a SIP, in addition to safety concerns or program uncertainty, is that the agency may decide to "limit the number of authorized SIP programs so FDA can effectively and efficiently carry out its responsibilities under [Section 804] in light of the amount of resources allocated to carrying out such responsibilities." FDA's authorization of the SIP would also include approval of the Qualifying Laboratory for purposes of conducting all the Statutory Testing of eligible prescription drugs.

    - Initially, FDA's authorization for a SIP would be time-limited to two years, in order to give the SIP Sponsor time to collect the data necessary to demonstrate that its program is meeting the twin goals articulated in Section 804 – ensuring patient safety and delivering significant cost savings.

    - To obtain initial authorization from FDA, a SIP would also need to explain how it would result in a "significant reduction in cost" to American consumers of the drugs that the SIP proposes to import. A SIP would also need demonstrate that it provided significantly reduced costs to be able to continue to operate after the initial two-year period.

    - A SIP that is not extended by the Sponsor after the 2-year period ends would terminate, and FDA retains discretion to terminate an authorized SIP at any time for safety or other reasons.

- Upon SIP authorization, the approved Foreign Seller would be able to purchase covered drugs directly from the manufacturer and to prepare them for export to the U.S. in compliance

with the serialization requirements of the future Part 251.

- The approved Importer would need to submit a Section 804 Pre-Import Request to FDA before any prescription drugs are actually exported from Canada pursuant to the terms of the authorized SIP (and at least 30 days before the first shipment). Once FDA grants the Pre-Import Request, the Importer can initiate the importation process under the SIP and in compliance with the procedural requirements that will be set forth in the new SIP regulations.

- Manufacturers will need to provide the SIP Importer with the necessary information to allow the Statutory Testing to take place and provide attestations that the drugs sold to the Foreign Seller meet the conditions of the comparable FDA-approved drug marketing application. The Manufacturer would also have to authorize the Importer to use, at no cost, the FDA-approved labeling for each prescription drug covered by an authorized SIP. The agency is requesting comments on whether it should include additional provisions in the Part 251 proposed rules in order to protect the proprietary information Manufacturers will be required to give to Importers under any authorized SIP. FDA also asks for input on what should be a "timely" provision of such information by the Manufacturer in order to clarify for industry when the agency will step in and make the information available to the Importer if it is contained in the Manufacturer's FDA-approved drug application.

- Importers could either dispense the imported drugs (if a pharmacist) or sell them to another U.S. entity (if a wholesaler), after complying with the Statutory Testing requirements, coordinating the relabeling of the drugs so they meet FD&C Act and FDA regulatory requirements for prescription drugs in U.S. commerce, and listing the drugs with FDA under a different National Drug Code (NDC) number than the counterpart non-imported drug (for drug listing and proposing a new NDC, the Importer would need to secure its own Labeler Code from FDA if it does not have one already). Moreover, if the SIP-imported drugs will be further distributed and not directly dispensed to patients after importation, then they would need to have a DSCSA-compliant product identifier affixed to ensure supply chain integrity. All SIP-imported drugs would also need to bear a specific statement that: "This drug was imported from Canada under [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." FDA is requesting comments on this proposed labeling statement and on other particular aspects of the supply chain logistics after the Canadian drugs reach the United States.

- In addition to post-importation compliance obligations on Importers like adverse event reports, field alert reports, and medication error reports, SIP Sponsors would need to submit a quarterly report to FDA containing substantial information on its SIP activities and whether all of the Section 804 and regulatory criteria are being met.

Many Questions and Open Issues Remain

In addition to setting out the details of how the proposed SIP regulations will function, the NPRM requests comments and stakeholder input on multiple aspects of the proposal, as well as on a number of alternative or expansion options. Particularly interesting requests include:

- Significant Reduction in Cost. What factors should the FDA evaluate to determine if cost savings are significant? What measures could a SIP use to demonstrate cost savings? These are interesting issues to consider because of how complicated the current drug pricing system

is in the U.S. The mechanics of U.S. drug pricing make us think of many downstream implementation-related questions, such as:

    - If a SIP is authorized and the Importer begins importing covered drugs under the SIP, will health plans and PBMs negotiate rebates differently for SIP-imported drugs?
    - Will SIP-imported drugs be treated differently on a plan formulary than the same drug that is distributed in the U.S. through the traditional FDA approval processes?
    - Would a pharmacy notify its customers that it has SIP-imported drugs available at lower prices?

- SIP Compliance Plan. Among other obligations, SIP Sponsors will be responsible for ensuring that all of the other participants in a SIP – i.e., Foreign Seller, Importer, Qualifying Laboratory – comply with all of the requirements of Section 804 and the proposed regulations. Although the NPRM states that the SIP Proposal should provide a detailed description of the Sponsor's compliance plan, FDA is soliciting comments on what elements should be included in such a plan and whether alternative or additional requirements might be appropriate when the SIP includes one or more co-sponsors.

- Sampling Methods for Statutory Testing. FDA does not include specific proposals in the NPRM for how Qualifying Laboratories should conduct the required drug testing using "statistical sampling" (as required by the language of FD&C Act Section 804). It is therefore requesting comments on whether it should specify a sampling method or whether it be done according to established national standards.

The Section 804 Importation Program NPRM was officially published in the Federal Register on December 23rd and is subject to a 75-day comment period, making the deadline for all comments March 9, 2020. We strongly encourage affected or interested stakeholders to submit comments to HHS/FDA on the proposed regulations.

Pathway Two or the "MMA Products Program"

In addition to the agency's NPRM formally implementing the Canadian drug importation authority it has in FD&C Act Section 804, FDA also issued a draft guidance entitled "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" – that cited section of the Act authorizes what is commonly referred to as "manufacturer reimportation." Official notice of the draft guidance document's availability was also published in the Federal Register on December 23rd but the formal comment period on this document is only 60 days, making the deadline February 21, 2020. Building on the July 2019 Safe Importation Action Plan, the notice explains that:

"In recent years, FDA has become aware that some drug manufacturers may be interested in offering certain of their drugs at lower costs and that obtaining additional NDCs for these drugs may help them to address certain challenges in the private market. This guidance is not intended to address the applicability of the Medicaid drug rebate program for manufacturers. This guidance is intended to outline a potential pathway by which manufacturers could obtain an additional NDC for an FDA-approved drug that was originally intended to be marketed in a foreign country. This guidance specifically addresses the importation of FDA-approved drugs that were also authorized for sale in a

foreign country in which the drugs were originally intended to be marketed ("MMA product")."

"MMA" in this context stands for a "multi-market approved" product, although one of the issues for which the agency is seeking feedback from stakeholders is whether this new term is understandable or adequate as a policy matter. The Draft Guidance lists several criteria for an MMA product to be eligible for manufacturer reimportation including that the foreign product differs from the FDA-approved product only with respect to the prescription labeling. FDA is recommending that the MMA labeling be updated to include a statement in order to differentiate the MMA product from similar products not covered by the new reimportation program.

Notably, unlike the proposal under Pathway One for SIPs that excludes biologics and several other product categories from its scope, the proposed pathway outlined in the Draft Guidance would not exclude biologics, insulin, or intravenous or injectable drugs. The guidance therefore makes recommendations for sponsors of both FDA-approved New Drug Applications (NDAs) and Biologics License Applications (BLAs). One of the questions in the FDA's formal notice of availability asks whether there are any considerations for certain types of drug products with special handling, such as sterile injectables, controlled substances, and drugs with Boxed Warnings or REMS programs, that would require a different approach than what is being proposed to allow for the importation of MMA products.

The FDA Draft Guidance itself goes on to describe at length:

1. the recommended labeling for an imported MMA product;

2. the process for submitting a labeling supplement to an FDA-approved NDA or BLA for an MMA product, which is necessary to provide the agency with the alternative labeling that will be used in the U.S. for the imported MMA product and to provide the manufacturer's attestation that the MMA product meets all required criteria and is the same as an FDA-approved product;

3. the process for obtaining an additional NDC for the MMA product and FDA's recommendation that such products be listed in the electronic drug listing system under the new marketing category "multi-market approved products," which the agency intends to add to its system;

4. how MMA products are expected to comply with applicable provisions of the DSCSA; and

5. recommendations related to procedures for the authorized importation of the MMA product.

The Draft Guidance does not directly discuss drug cost other than to suggest that the availability of an additional NDC "would provide an additional avenue through which drugs could be sold at a lower cost in the U.S. market." In essence, FDA is establishing a pathway for a manufacturer to obtain additional NDCs for a foreign drug product that is imported under the guidance, and that new NDC could then potentially lead to greater price flexibility. When discussing the Draft Guidance during the press conference, Secretary Azar explained that an example of a drug that might be imported through this Section 801 reimportation pathway is a branded drug for which the manufacturer is paying high rebates to insurance plans. The idea is that by obtaining a new NDC, the manufacturer can potentially avoid rebates that would be owed on claims generated for its already established NDCs.

Just as with the proposed SIP regulations, we urge all affected or interested stakeholders to review the Draft Guidance, as well as the notice of availability that identifies multiple questions for which FDA is seeking input, and to submit comments before the February 21, 2020 deadline. For example, the agency is seeking feedback on the specific wording for the "MMA statement" that will need to be included in the labeling for these imported products. FDA is also interested in hearing about whether generic drug manufacturers face similar pricing pressures with their U.S. products that would make it appropriate for the agency to establish a similar reimportation program for generic drugs, as well as whether MMA biological products could have any impacts on the still-developing U.S. biosimilars market.

**Postscript: A correction to the notice of availability for the MMA Draft guidance was published on December 30, 2019 (see here); however, the deadline for comments and docket number have not changed.*

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