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FDA Issues Proposed Rule and Draft Guidance on Drug Importation

In late December 2019, the Food and Drug Administration (FDA), an agency operating within the Department of Health and Human Services (HHS), issued two documents—a Proposed Rule and a Draft Guidance—intended to establish two pathways for drug importation. HHS previewed these approaches in its Safe Importation Action Plan last July.

These proposed pathways are broadly, if not necessarily effectively, aimed at reducing U.S. drug prices in two different ways:

1. The Proposed Rule sets out a means by which *States and certain other non-federal governmental entities* would be permitted to import certain drugs (notably excluding biologics and many specialty pharmaceuticals) from *Canada*. Manufacturer consent is not required for importation under this "Pathway I," but many manufacturer obligations and risks flow from it.

2. The Draft Guidance creates a framework under which *manufacturers* could choose to bring their drugs that are manufactured and intended for sale outside the U.S. into the U.S. market. This "Pathway II" would permit both "domestic" National Drug Codes (NDCs) and "imported" NDCs of the same product to be marketed simultaneously.

Under Pathway I, HHS would implement much of Section 804 of the Food, Drug, and Cosmetic Act (FDCA), establishing a regulatory mechanism to oversee the importation of certain prescription drugs from Canada (and Canada only). The Proposed Rule would permit States and other governmental entities—working with wholesalers, pharmacies and other co-sponsors—to submit drug importation plans to HHS for review and approval. Approved importers would be subject to supply chain security, testing, and relabeling requirements. Manufacturers of drugs subject to the importation plans would be required to provide importers with the information necessary to conduct required FDA testing and relabeling. Personal importation (Section 804(j) of the FDCA) is not implemented in the Proposed Rule.

Pathway II would allow manufacturers to import their own drugs—those that are manufactured, approved, and intended for distribution in foreign markets (including but not limited to Canada)—into the U.S. Under this pathway, a manufacturer would market the imported version of its drug under a different NDC number than the domestic version, which might (consistent with the policy hopes of the Administration) allow the manufacturer to introduce it to the U.S. market at a lower price. HHS has noted that this pathway would offer manufacturers who are "locked into contracts with other parties in the supply chain" with an opportunity to import lower-cost versions of their drugs.

The Proposed Rule, as written, appears to fail a substantive condition necessary for implementation set out in the statute. HHS can only implement Section 804 of the FDCA if HHS certifies that the implementation of that provision will (1) "pose no additional risk" to the public health, and (2) "result in a significant reduction in the cost of covered products to the American consumer." It does not appear that HHS has established a factual predicate for the second prong of the required certification—that Pathway I will result in a reduction of costs to the American consumer. The obligations that the Proposed Rule, if finalized, would place on manufacturers and others in the supply chain are likely to limit supply and drive costs up, such that it is unclear whether cost savings for the consumer could be achieved. Moreover, even if Pathway I could withstand judicial scrutiny, it is unclear how pricing for drugs in the program would work in conjunction with federal programs like Medicaid and the Medicare Part D Prescription Drug benefits.

In addition, in our view, the utility of Pathway II, at this time, is unclear. In our benchmarking and informal conversations in the industry, we have not encountered a lot of enthusiasm about Pathway II. We do not anticipate that the guidance will create much momentum for manufacturer-lead importation. Although some have theorized that the pathway would permit manufacturers to circumvent pharmacy benefit manager (PBM) rebates and contractual arrangements, it is unclear how such products could actually be covered by a health plan on formulary, or if covered, how they could avoid rebate liability. We will have to await further clarification from the Centers for Medicare and Medicaid Services (CMS) to see if this pathway is even viable from a business operations and government price reporting perspective.

Given that drug manufacturers may not embrace the manufacturer-led importation envisioned under Pathway II, the existence of the pathway may ultimately serve more as a mechanism to shift the blame for high drug prices from the government to drug manufacturers, than as a true mechanism for meaningful change. Indeed, we suspect that Pathway II might simply be a "shaming" tool that would allow HHS to say that the government gave industry the opportunity to import their own drugs at a lower cost and that industry failed to seize it.

BACKGROUND

On July 31, 2019, in response to political pressure to take action on drug prices, HHS published its Safe Importation Action Plan. The plan outlined in broad terms two potential pathways to facilitate importation of pharmaceuticals from ex-U.S. markets, which are perceived as having lower drug costs, into the U.S. The first proposal was for HHS to implement Section 804 of the FDCA through a regulation. Section 804 is a long-dormant provision in the FDCA that gives HHS the authority to legalize the importation of certain prescription drugs from Canada. The second proposal was for HHS to issue guidance enabling drug manufacturers to import foreign versions of their drugs into the U.S. In late December 2019, FDA issued the promised Proposed Rule, implementing Section 804, and the Agency issued the Draft Guidance as well.

PATHWAY I – IMPORTATION BY STATES AND OTHER NON-FEDERAL GOVERNMENTAL ENTITIES

The Proposed Rule, if finalized, would allow a State, or a tribal or territorial entity (collectively, "Non-Federal Governmental Entity"), to submit proposals to FDA for Section 804 Importation Programs (SIPs). The SIP proposals would outline plans to import *eligible* prescription drugs from Canada. SIPs could also be *co-sponsored* by a pharmacist, wholesaler, or another State Non-Federal Governmental Entity. HHS considered allowing pharmacists or wholesalers to be SIP sponsors *without a governmental co-sponsor*, but ultimately concluded that SIPs needed at least one State or

Non-Federal Governmental Entity sponsor. States and Non-Federal Governmental Entities already license and regulate pharmacists, wholesalers, and others in the supply chain, and they would be better able to oversee the programs and provide greater accountability than pharmacists and wholesalers.

Under the Proposed Rule, FDA can authorize SIPs for two years, with the possibility of extensions for two year periods. Notably, the Proposed Rule does not propose to implement the personal importation provisions under Section 804(j) of the FDCA, given the ongoing supply chain risks posed by Canadian internet pharmacies.

Prescription Drug Eligibility

For a prescription drug to be *eligible* for importation under a SIP, it must (1) be approved by Health Canada's Health Products and Food Branch (HPFB) (*i.e.*, Canada's agency that is similar to FDA), (2) meet the conditions in an FDA-approved new drug application (NDA) or abbreviated new drug application (ANDA) other than the labeling requirements (*e.g.*, conditions related to drug substance, drug product, production process, quality controls, equipment, and facilities) such that the drug could be sold legally in the U.S. with appropriate labeling, and (3) meet the definition of "product" for the purposes of the Drug Supply Chain Security Act (DSCSA) (*i.e.*, any prescription drug in finished dosage form, subject to certain exceptions).

However, pursuant to statutory exclusions under Section 804, the proposed rule would exclude: (1) controlled substances, (2) biological products, (3) infused drugs, (4) intravenously injected drugs, (5) drugs that are inhaled during surgery, and (6) drugs that are subject to risk evaluation and mitigation strategies (REMS). In addition, the Proposed Rule proposes to categorically exclude intrathecally injected drugs and intraocularly injected drugs. It is worth noting that many of the nation's most expensive drug products fall into these excluded categories.

In the Proposed Rule, FDA also recognized that the importation of the following types of drugs poses heightened safety concerns: (1) drug-device combination products that are approved under Section 505 of the FDCA; (2) inhaled drugs; (3) modified-release drugs; (4) sterile drugs; (5) ophthalmic drugs; (6) narrow therapeutic index drugs; (7) drugs with boxed warnings; and (8) drugs requiring special storage conditions. However, rather than categorically excluding those drugs from eligibility, FDA stated that it would review proposals to import those drugs on a case-by-case basis, and authorize importation only if the drugs could be safely imported within the context of the specific SIP.

Foreign Sellers and U.S. Importers

Under the Proposed Rule, an initial SIP proposal must identify (1) one Foreign Seller—the entity in Canada that will purchase the eligible prescription drug *directly* from the manufacturer, and (2) one Importer—the entity in the U.S. that will buy the drug *directly* from the Foreign Seller. Although a supplemental proposal could add additional Foreign Sellers or Importers, once the SIP can show consistent compliance with Section 804, the supply chain for *each drug* under either an initial or supplemental proposal *would be limited to three supply chain entities*—the manufacturer, the Foreign Seller, and the Importer.

To qualify as a Foreign Seller, an entity must be licensed by Health Canada as a wholesaler and registered with FDA. To qualify as an Importer, an entity must be a wholesaler or pharmacist licensed to operate in the U.S.

Both the Foreign Seller and the Importer would be subject to supply chain security requirements from the DSCSA, as well as additional requirements imposed by the Proposed Rule, if finalized. For example, the Foreign Seller would have to ensure that a Section 804 serial identifier (SSI) unique to each package or homogenous case, is affixed to, or imprinted on, such package or homogenous case; and the Importer would have to ensure that an NDC is affixed to, or imprinted on, each package or homogenous case and it would have to maintain records linking each SSI assigned by the Foreign Seller to the corresponding NDCs.

Testing and Re-Labeling Requirements

As mentioned, prescription drugs that are eligible for SIP proposals must, among other things (1) be approved by Health Canada's HPFB, and (2) meet the requirements of an NDA or ANDA in the U.S. (except for the labeling requirements), such that they could be legally marketed in the U.S. if they were relabeled. Once FDA has authorized a SIP, Section 804 of the FDCA requires Importers to provide documentation to FDA demonstrating that "each batch of the prescription drug in the shipment was statistically sampled and tested for authenticity and degradation." *See* 21 U.S.C. § 384(d)(1)(J). Under the Proposed Rule, Importers can meet that requirement by (1) requesting that the manufacturer agree to conduct the necessary testing, or (2) conducting the testing themselves, after the manufacturer provides the requisite information.

Notably, if the manufacturer fails to provide such information "in a timely fashion," the manufacturer would be committing a Prohibited Act under Section 301(aa) of the FDCA. In that circumstance, FDA could provide such information directly to an Importer, to the extent it is contained in an NDA or an ANDA. HHS specifically seeks comments on what constitutes "a timely fashion."

Post-Importation Requirements

Under the Proposed Rule, SIP sponsors and Importers would also have importation responsibilities. For example, a *SIP sponsor* would be required to provide FDA with certain information about its SIP, including the SIP's cost savings to the American consumer, and it would be responsible for effectuating any drug recalls. In addition, the Importer would be responsible for submitting adverse event, medication error, field alert, and other reports to the drug's manufacturer and to FDA.

Enhanced Penalties Against Manufacturers for Non-Compliance

Section 804 of the FDCA has a built-in statutory enforcement mechanism. Section 301(aa) of the FDCA establishes that non-compliance with Section 804, *or the implementing regulations*, is a Prohibited Act. 21 U.S.C. § 331(aa). The FDCA also establishes enhanced criminal fines and imprisonment for manufacturers or Importers that violate Section 804(e), the provision that requires manufacturers to share testing information with Importers. The standard felony provision under the FDCA authorizes 3 years imprisonment and a $10,000 fine, but the enhanced penalty is 10 years imprisonment and a $250,000 fine. *See* 21 U.S.C. § 333(a)(2) (establishing general penalties for violations of the FDCA committed with the intent to mislead or defraud and second offenses under the FDCA); *see also* 21 U.S.C. § 333(b)(6) (establishing enhanced penalties for manufacturers and importers who knowingly fail to comply with Section 804(e)). Notably, the Proposed Rule explicitly emphasizes that "the obligations on manufacturers" are enforceable under Section 301(aa).

Comment Period

The Proposed Rule was published in the *Federal Register* on December 23, 2019, and comments are due on March 9, 2020.

PATHWAY II – *MANUFACTURER* IMPORTATION

To implement Pathway II, FDA issued a guidance document 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: Draft Guidance for Industry." The Draft Guidance addresses the steps that drug manufacturers would need to take to obtain a new NDC to import FDA-approved drugs that were manufactured and authorized for sale in a foreign country where the drugs were originally intended to be marketed ("multi-market approved products" or "MMA products")—should drug manufacturers *want* to do so. The steps manufacturers must take include:

1. **Labeling** – MMA products, like all FDA-approved prescription drugs, must be accompanied by FDA-approved labeling. Therefore, a manufacturer seeking to market an MMA product under an NDA or biologics license application (BLA) must submit a labeling supplement under 21 C.F.R. §§ 314.70 or 601.12(f). The supplements, among other things, must include an attestation by the manufacturer that the MMA product has the same quality and characteristics as the FDA-approved products.
2. **Registering, Listing and Proposing an NDC** – FDA recommends that drug manufacturers propose a new NDC for the MMA product by following the procedures set forth in 21 C.F.R. 207.33. As discussed below, this separate NDC may have significant implications for drugs used in the Part D and Medicaid programs, and possibly even in the Part B program as well. The procedures for registration and listing are the same for MMA products as for all FDA-approved drugs.
3. **Drug Supply Chain Security Act (DSCSA)** – The DSCSA requires, among other things, product tracing and verification and product identification. It also establishes authorized trading partner requirements for manufacturers, repackagers, wholesale distributors, and dispensers to facilitate the tracing of certain prescription drugs through the supply chain. Any MMA product that meets the definition of a "product" under the DSCSA, *see* 21 U.S.C. § 360eee (defining "product" as any prescription drug in finished dosage form, subject to certain exceptions), will be subject to all the applicable requirements for such "products" under Section 582 of the FDCA, including product tracing and verification and product identification requirements. With regard to product identification, FDA recommends that manufacturers affix or imprint the required product identifier to the DSCSA-covered MMA product when the FDA-approved label is applied. With regard to product tracing and verification, FDA notes that trading partners are required to provide the subsequent purchaser with product tracing information for each transaction involving a DSCSA-covered MMA product and that trading partners are also required to have appropriate verification systems in place.
4. **Importation of MMA Products** – FDA encourages the filing of an electronic entry in the Automated Commercial Environment (ACE), and notes that "international mail is not appropriate for the importation of MMA products." In addition, FDA notes that it must receive information that is sufficient for the Agency to verify that each shipment of MMA product has been authorized by the *manufacturer* to be marketed in the U.S. To facilitate this, FDA encourages manufacturers to submit a report via the Electronic Submissions Gateway that includes (1) the drug name, dosage form, and quantity of the drug, (2) the name, address, and telephone number of the authorized importer, and (3) any temporal or other limitations the manufacturer has placed on the authorized importation.

Comments on the Draft Guidance are due on March 5, 2020.

IMPLICATIONS AND TAKE-AWAYS REGARDING THE PROPOSED IMPORTATION PATHWAYS

- **The Legality of the Proposed Rule Is In Question** – King & Spalding (K&S) has significant concerns that FDA does not have statutory authority to implement the Proposed Rule as written because HHS cannot make the required cost reduction certification. FDA can only implement Section 804 of the FDCA if HHS certifies that the implementation of the law will (1) "pose no additional risk" to the public health, and (2) "result in a significant reduction in the cost of covered products to the American consumer." 21 U.S.C. § 384(l)(1)(A), (B). Based on our initial read of the Proposed Rule, however, we do not believe that FDA provided a sufficient factual basis for HHS to certify that the implementation of the rule will satisfy the second prong.

  Indeed, at the very start of the Proposed Rule, FDA concedes that it is "unable to estimate the volume or value of drugs that may be imported under the SIPs or the savings to U.S. consumers who may participate in such programs." 84 Fed. Reg. 70796, 70798, (Dec. 23, 2019). K&S has serious doubts that cost savings—let alone "significant" cost savings—will materialize because the importation program only applies to Health Canada-approved drugs. The Canadian government has already made clear that it will not allow U.S. demand to create drug shortages for

Canadians, and thus, the volume of drugs that Canadians can spare, at least in the short-term until manufacturers are able to ramp up operations, may be limited. Further, the testing and re-labeling requirements will increase the cost of the drugs being imported.

- **The Testing Requirements for Manufacturers Are Vague and Could Subject Them to Significant Legal Exposure** – The Proposed Rule would require Importers to provide documentation to FDA demonstrating that each batch of imported drug was statistically sampled and tested for authenticity and degradation, and it requires manufacturers to either do the testing themselves or *provide Importers with the necessary information required to do the testing.* The Proposed Rule does not explain what such necessary information may include. We can envision disputes between manufacturers and Importers over the scope of information to be produced and the timing of the production, and the Importers would have considerable leverage in these disputes given that manufacturers are exposed to criminal enforcement if they fail to comply. Given manufacturers' potential exposure, here, comments from manufacturers on this issue will be critical.
- **Government Price Reporting and Federal Reimbursement Implications** – Neither the Proposed Rule nor the Draft Guidance addresses how the importation Pathways would affect price reporting or Federal reimbursement. This is not surprising, given that the Proposed Rule and Draft Guidance were issued by FDA, not CMS. Nevertheless, manufacturers should consider how Pathways I and II would affect the sale, use, reimbursement and rebating of imported medications. A few initial thoughts:
  - *Manufacturer Price Reporting Implications of Pathway I* – Presumably, initial ex-U.S. drug sales under Pathway I would remain excluded from price reporting requirements, even if the drugs were subsequently re-imported into the U.S. (particularly if the imported units bear unique NDCs). Sales to entities in foreign countries (including Canada) have been excluded for Medicaid, Medicare and VA/FSS price points for decades. This might change if the manufacturer is itself a party to an indirect importation sales agreement through a Canadian Foreign Seller that generates a chargeback to the manufacturer. The existing pricing rules do not contemplate a "foreign direct sale, domestic indirect sale" situation. In addition, unless imported products bear a labeler code different from that of the manufacturer, U.S. dispenses of Canadian-sourced drugs may generate government and commercial insurance rebates payable by the manufacturer that will affect price reporting and revenue. Manufacturers should consider the gross-to-net effects of being pulled into a Pathway I importation scheme (low priced sales generating rebatable utilization in a way not contemplated when contracted-for).
  - *Importer Price Reporting Implications of Pathway I* – Query (1) whether importers under Pathway I that re-label with their own labeler codes would need to sign National Rebate Agreements for the products to be covered by Medicaid, (2) whether Medicaid price reporting and rebate liability under that situation would flow to the Importer, (3) whether the Importer also would be required to extend 340B discounts, and (4) whether any Importer would be willing to undertake those expensive obligations? These issues need clarification.
  - *Price Reporting Implications of Pathway II* – The price reporting implications of Pathway II are also potentially problematic. FDA might not care if the same dosage form and strength of a single drug has multiple NDCs, but CMS certainly does. The Medicaid rules and guidance regarding blending across NDC-9s are muddy at best; they are at times mandatory, and at other times permissive. The Administration's promises of a low-price second pathway via importation may be illusory if CMS requires Best Price blending across the NDCs.
  - *Reimbursement Implications* – Query whether (1) government program reimbursement will treat "domestic" and "foreign" NDCs of the same product separately, with separate reimbursement calculations, or as the same product, with a common or blended reimbursement, and (2) whether imported products will be able to be priced separately (and lower) than their domestic counterparts in the Medicare Part D and Medicaid programs, and how

that will affect rebate and discount negotiations between Plans, PBMs and manufacturers. Arguably, importing pharmacies may be able to offer lower-cost drugs at the point of purchase to Medicare and Medicaid beneficiaries, but it is unclear whether such products would be "covered" by Part D Plans or States. These issues need clarification.

- **The Utility of Pathway II Remains Unclear** – In our benchmarking and informal conversations in the industry, we have not encountered a lot of enthusiasm about Pathway II, and we do not anticipate that the guidance will create much momentum for manufacturer-lead importation. Although some have theorized the pathway would permit manufacturers to circumvent PBM rebates and contractual arrangements, it is unclear how such products could actually be covered by a health plan on formulary, or how they would effectively be carved out of PBM rebate utilization. We will have to await further clarification from the CMS to see if this pathway is even viable from a business operations and government price reporting perspective.

  Given that drug manufacturers may not embrace the manufacturer-led importation envisioned under Pathway II, the existence of the pathway may ultimately serve more as a mechanism to shift the blame for high drug prices from the government to drug manufacturers, than as a true mechanism for meaningful change. Indeed, we suspect that Pathway II might simply be a "shaming" tool that would allow HHS to say that the government gave industry the opportunity to import their own drugs at a lower cost and industry failed to seize it.

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K&S is closely tracking the developments related to the importation proposals in the Proposed Rule and the Draft Guidance. We would be happy to discuss how either may apply to specific situations. Comments on the Draft Guidance are due on *March 5, 2020.* Comments on the Proposed Rule are due on *March 9, 2020*. As always, we stand ready to assist our clients in drafting persuasive comments to the government.