

**Comment on the Food and Drug Administration's Proposed Rule
for the Importation of Prescription Drugs**

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I. Introduction

a. Who we are.

The Duke Science Regulation Lab (SciReg Lab) is composed of graduate students from a variety of disciplines at Duke University, including science, engineering, law, ethics, and policy. The SciReg Lab was originally inspired by the traditional role of *amicus curiae*: to provide a court with unbiased information necessary to reach a binding decision. As an extension of that concept, we now provide government agencies with the scientific information necessary to undertake effective rulemaking.

Modern society requires our government to handle increasingly complex scientific issues when deciding cases or making policy. We, the Duke Science Regulation Lab, believe that the general public benefits from judgments that are based on sound scientific knowledge. To assist decision makers in understanding a scientific matter at hand, the students of the Science Regulation Lab combine their expertise to offer a non-partisan, accurate, and accessible explanatory brief or comment. The members of the Duke Science Regulation Lab vary in their academic backgrounds. The lead authors for this comment, David Yates and Scott Boisvert, are JD candidates at the Duke University School of Law.

b. Proposed Rule overview.

The proposed rule entitled “Importation of Prescription Drugs” states that its purpose is “to lower prices and reduce out of pocket costs for American patients” through the importation of certain prescription drugs from Canada.¹ However, it is unclear based on the structure of the rule whether this purpose can be achieved. To be eligible for importation, a drug would have to have been approved by Health Canada’s Health Products and Food Branch (HPFB) and meet the

¹ Importation of Prescription Drugs, 84 Fed. Reg. 246, 70797 (Dec. 23, 2019) (to be codified at 21 C.F.R. pt. 1, 251).

same conditions required for Food and Drug Administration (FDA) approval in the United States.² In order to request importation, at least one individual State, tribe, or territorial government entity would have to sponsor an importation plan.³ When creating these plans, Sponsors must identify which drug they are seeking to import and show: (1) that its importation will not create additional health or safety risks for the public, and (2) that the importation of the drug will result in savings to American consumers.⁴ In its proposal a Sponsor must also “identify the Foreign Seller in Canada that would purchase the drug directly from its manufacturer, and the Importer in the United States that would buy the drug directly from the Foreign Seller.”⁵

This Foreign Seller would also need to be “registered with the FDA as a Foreign Seller and be licensed by Health Canada” and the US as a wholesaler.⁶ The FDA then reserves broad discretion to reject a proposal, even if all requirements under the scheme are met.⁷ However, if the FDA authorizes a proposal, the FDA must assign the drug a limited port of entry and the importer must “electronically file an entry for consumption” with the FDA to ensure that the imported product is what was requested by the sponsor and approved by the FDA.⁸ Additionally, the proposed rule requires the Importer or Manufacturer to “conduct testing of drugs for authenticity, degradation, and” to ensure compliance with Statutory Testing requirements in the United States.⁹ “The Importer would also have to ensure that the drug bears the required U.S. labeling.”¹⁰ However, both the Foreign Seller and Importer would be required to ensure the security of the supply chain and Importers must provide the FDA with information regarding

² *Id.*

³ *Id.*

⁴ *Id.* at 70802.

⁵ *Id.*

⁶ *Id.*

⁷ *Id.*

⁸ *Id.*

⁹ *Id.*

¹⁰ *Id.* 70802–03.

event[s], medication error[s], field alert[s], and other reports to a drug’s manufacturer.”¹¹ Lastly, in order for the scheme to become effective, the Secretary of Health and Human Services (HHS) must certify to Congress that its implementation “will pose no additional risk to the public’s health and safety, and result in a significant reduction in the cost of covered products to the American consumer.”¹² However, even if a Secretary of HHS grants certification, this certification is conditioned on each importation request meeting the relevant requirements, and if “one or more of the provisions of” the rule becomes invalid, then the certification would become null and void.¹³

c. Proposed Rule versus the Medicine Equity and Drug Safety (MEDS) Act.

Since this is not the first time an importation scheme from Canada has been proposed, it is important to consider what makes this proposed rule different from past failed attempts. Our analysis suggests that other than some additional details aimed at addressing safety concerns with imported drugs, many other previous concerns have not been addressed in the new proposed rule. In 2000, Congress enacted the MEDS Act, which was never implemented, but “would have allowed pharmacists or wholesalers in the United States to import certain prescription drugs without the authorization of the manufacturer.”¹⁴ Before implementation, the law required the Secretary of HHS to “demonstrate that the importation of these drugs 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.”¹⁵ Yet, at the time, the Secretary of HHS sent a

¹¹ *Id.* at 70803.

¹² *Id.*

¹³ *Id.*

¹⁴ *Id.* at 70799.

¹⁵ *Id.*

letter to President Clinton discussing the serious safety concerns that prevented him from making that determination.¹⁶

Nonetheless, a similar law was implemented shortly thereafter entitled The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), which also set up a means through which the government could allow the importation of drugs from Canada.¹⁷ Under the MMA, the Secretary of HHS would have been required to make the same certification of safety and cost effectiveness that was required for implementation under the MEDS Act.¹⁸ Moreover, the MMA amended the provision that would have allowed importation under the MEDS Act by enabling the Secretary to “issue regulations permitting pharmacists and wholesalers to import certain prescription drugs from Canada.”¹⁹ Yet, like in 2000, the Secretary of HHS never made the required certification needed to put the law into action.²⁰ Part of the reason that a certification was never made the second time around was a study directed by HHS that identified “potential risks and challenges associated with” a drug importation scheme from Canada.²¹

The findings of the report laid out the following concerns:

- A policy for importing drugs from Canada would not be a practical policy approach given that any expected savings from importation would “likely be a small percentage of total drug spending” compared to the high estimated costs required to establish the program.²²

¹⁶ 147 Cong. Rec. S6906, S6910 (2002).

¹⁷ Importation of Prescription Drugs, *supra* note 1 at 70799.

¹⁸ *Id.*

¹⁹ *Id.*

²⁰ *Id.*

²¹ *Id.*

²² *Id.*

- Such a policy has the potential to negatively affect innovation and liability “for consumers, manufacturers, distributors, pharmacies, and other entities.”²³
- Most prescription drugs in the U.S. are generic, and those tend to be cheaper within the U.S. than abroad, thus making a large portion of drugs that the American public would be seeking ineligible for importation under the required cost-benefit analysis component.²⁴

While the current proposed rule focuses heavily on supply chain security, labeling requirements, and adverse reporting in an attempt to ensure consumer safety, there is no indication that all of the concerns revealed in the 2004 study have been adequately addressed in the current proposal.²⁵ Additionally, the proposed rule does not discuss how liability will be assigned if consumers were to be harmed by imported drugs, nor does the proposed rule address how intellectual property rights will be protected under this scheme.²⁶ Thus, given the multiple unanswered concerns that prevented previous Secretaries of HHS from authorizing drug importation from Canada, the current rule drafters would be wise to go back and implement features that not only ensure patient safety, but also ensure cost savings and address concerns related to potential negative effects on innovation and assignment of liability.

II. Previous and Anticipated Concerns with the Proposed Drug Importation Scheme

a. Previous FDA concerns regarding drug importation.

As was just discussed, the idea of importing drugs from Canada to alleviate drug pricing concerns in the U.S. is not new, and over the last 18 years “every head of HHS and FDA . . .

²³ *Id.*

²⁴ *Id.*

²⁵ *Id.*

²⁶ *Id.* at 70796– 839.

[has] refused to certify the safety of drug importation.”²⁷ Moreover, given the spectrum of ideologies of past FDA and HHS commissioners, this highlights that concerns regarding the viability of a safe drug importation program have been bipartisan.²⁸ To further bolster this assertion, in 2017, four former FDA commissioners wrote a letter to members of Congress describing the main issues that would arise through the implementation of a drug importation policy.²⁹ In this letter, the commissioners emphasized that any bill focused on alleviating pricing concerns through an importation policy would give rise to safety and administrability concerns and likely make little to no impact on access to drugs, all while harming innovation.³⁰ Even the most recent former FDA commissioner, Scott Gottlieb, stated that drug importation schemes would not address the main problem of individuals having health plans that “don’t provide any coverage for many important medicines.”³¹ And specifically in terms of a plan for importing drugs from Canada, former commissioner Gottlieb also noted that “Canadian drugs are no longer as cheap when they’re purchased in U.S. dollars” and even “when importation of foreign drugs is done under a regulated scheme, it really wouldn’t save money.”³²

What is even more worrisome about this new proposal is that even the current secretary of HHS, Alex M. Azar II, who recently stated his support for this proposal,³³ gave a speech less than 2 years ago explaining how a drug importation scheme from Canada would be a

²⁷ *Every head of HHS and FDA for the last 18 years refused to certify the safety of drug importation*, THE PARTNERSHIP FOR SAFEMEDICINES, <https://www.safemedicines.org/2018/07/who-opposes-drug-importation-every-head-of-the-fda-and-hhs-since-2000.html> (last visited Feb. 23, 2020).

²⁸ *Id.*

²⁹ Letter from Robert M. Califf, Margaret B. Hambrug, Mark B. McClellan, and Andrew Von Eschenbach to Members of Congress on Drug Importation (Mar. 16, 2017) (on file with the Duke-Margolis Center).

³⁰ *Id.*

³¹ Scott Gottlieb, *What Trump Should Have Said on Drug Prices*, FORBES: PHARMA & HEALTHCARE (Mar. 4, 2016, 7:43 AM), <https://www.forbes.com/sites/scottgottlieb/2016/03/04/why-trump-is-wrong-on-drug-prices/#c999b472e747>.

³² *Id.*

³³ Derek Lowe, *The Latest Drug Reimportation Idea*, SCI. TRANSLATIONAL MED.: IN THE PIPELINE (July 27, 2018), <https://blogs.sciencemag.org/pipeline/archives/2018/07/27/the-latest-drug-reimportation-idea>.

“gimmick.”³⁴ Secretary Azar even said that “the Congressional Budget Office (CBO) [assessed a similar proposal before] . . . [and] said [this proposal] would have no meaningful effect” because “Canada’s drug market is simply too small to bring down prices [in the United States].”³⁵ He also pointed out that “drug companies won’t sell Canada or Europe more [drugs] just to have them imported here,” and even cited the letter sent to Congress from the past four FDA commissioners to note that there would be serious safety concerns with a system like this.³⁶

As for the previously referenced CBO assessment that was performed for the MEDS Act in 2004, it stated that “expanded parallel trade with Canada by itself would offer sharply limited prospects for aggregate savings given the small size of the drug market in Canada.”³⁷ The report cited that its analysis had also taken into account the costs of drugs in other countries, which drugs would likely be targets for importation, and how the unique tiered buyer system in the U.S. would ultimately affect downstream costs of consumers, as well as many other factors.³⁸ Given the in-depth analysis of what the costs and savings would look like for an importation scheme from Canada and the current Secretary’s agreement with the findings of said analysis only two years ago, the lack of a detailed cost and benefit analysis in the current proposed rule to refute these points seems inappropriate.³⁹ As such, any new proposed rule should look to previous CBO reports and attempt to estimate how much this proposal would actually save the American public.

³⁴ Alex M. Azar II’s Remarks on Drug Pricing Blueprint (May 14, 2018) (on file with the U.S. Department of Health and Human Services), <https://www.hhs.gov/about/leadership/secretary/speeches/2018-speeches/remarks-on-drug-pricing-blueprint.html>.

³⁵ *Id.*

³⁶ *Id.*

³⁷ Colin Baker, Would Prescription Drug Importation Reduce U.S. Drug Spending, CBO: Economic and Budget Issue Brief 3 (Apr. 29, 2004), <https://www.cbo.gov/sites/default/files/108th-congress-2003-2004/reports/04-29-prescriptiondrugs.pdf>.

³⁸ *Id.* at 4.

³⁹ Importation of Prescription Drugs, 84 Fed. Reg. 246, 70798 (Dec. 23, 2019) (to be codified at 21 C.F.R. pt. 1, 251).

b. Current Canadian and industry concerns regarding the proposed rule.

The current rule also falls silent on how it will address resistance that is expected from both the Canadian government and the pharmaceutical industry.⁴⁰ When the proposed rule was first announced, “[t]wo drug distributors and two Canadian industry groups” that represent all potential suppliers under this scheme, “said they are not interested in participating.”⁴¹ These distributors and groups have stated that they would actively oppose this framework because they are concerned about exacerbating the product and drug shortages that many Canadian patients currently face.⁴² And because some of Canada’s major distributors are subsidiaries of U.S. companies, any plan focused on setting up a drug importation scheme that would involve these players should have some mechanism to incentivize them to voluntarily lower their prices, which the current proposal does not.⁴³

Canadian officials have expressed similar concerns as that of industry, and have stated that they will “not support actions that could adversely affect the supply of prescription drugs in Canada and potentially raise costs of prescription drugs for Canadians.”⁴⁴ Moreover, Health Canada, the Canadian analog of the FDA, has stated that they are “ready to ‘take action to ensure Canadians have uninterrupted access to prescription drugs they need.’”⁴⁵ And currently, “[m]ost of the entities that regulate Canadian pharmacists forbid filling prescriptions written by foreign doctors,” and it does not look like this will change anytime soon.⁴⁶ Because of the major impact

⁴⁰ *Id.* at 70796–839.

⁴¹ Allison Martell, *Canadian drug distributors say no to Trump import plan*, REUTERS: HEALTH NEWS (Dec. 20, 2019, 1:12 PM), <https://www.reuters.com/article/us-usa-healthcare-canada/canadian-drug-distributors-say-no-to-trump-import-plan-idUSKBN1YO24O>.

⁴² *Id.*

⁴³ *Id.*

⁴⁴ Allison Martell, *Exclusive: Canada warns U.S. against drug import plans, citing shortage concerns*, REUTERS: HEALTH NEWS (JULY 18, 2019, 1:56 PM), <https://www.reuters.com/article/us-canada-pharmaceuticals-exports-exclus/exclusive-canada-warns-us-against-drug-import-plans-citing-shortage-concerns-idUSKCN1UD2LN>.

⁴⁵ *Id.*

⁴⁶ *Id.*

the proposed rule could have on Canada, and the intense opposition that will arise from both Canadian officials and industry in the event that it passes, the framework should elaborate upon how the FDA and States plan on navigating the international blockades that are sure to arise.

III. Comparison of US and Canadian Drug Approval Processes

The proposed rule requires drugs eligible for importation to be “approved by Health Canada’s Health Products and Food Branch (HPFB) . . . [and] meet the conditions in an FDA-approved new drug application (NDA) or abbreviated new drug application (ANDA).”⁴⁷ It is therefore important to analyze whether the drug approval processes track each other, such that a drug approved by Health Canada’s HPFB would also be approved by the FDA. If the processes are too varied from one another, then many drugs may not be eligible for importation under the new regulation without a costly (unfunded) evaluation of whether it might qualify for FDA approval.⁴⁸

The following section will examine ways in which the approval processes used by both the FDA and HPFB for a standard drug product differ, which may reduce the number of drugs eligible under the proposed rule.

a. Textual differences regarding the definition of a drug.

For the most part, HPFB and FDA’s drug approval processes track each other quite closely and only really differ on two key points: (1) their statutory definitions of a drug; and (2) the factors relied upon when deciding whether to approve a new drug at the end of clinical trials.⁴⁹ This section will focus exclusively on comparing the first of those key differences. The

⁴⁷ Importation of Prescription Drugs, 84 Fed. Reg. 246, 70797 (Dec. 23, 2019) (to be codified at 21 C.F.R. pt. 1, 251).

⁴⁸ *Id.* at 70799.

⁴⁹ See Gail A. Van Norman, *Drugs, Devices, and the FDA: Part 1 An Overview of Approval Processes for Drugs*, 1 JACC: BASIC TO TRANSLATIONAL SCI. 3, 171–72 (2016); *The Drug Review & Approval Process in Canada - An E-Guide* -, SPHARM, <https://spharm-inc.com/the-drug-review-and-approval-process-in-canada-an-eguide/> (last visited Feb. 18, 2020). [hereinafter *HPFB Drug Approval Process*] (explaining that both the FDA and HPFB rely on tightly

consequences of this analysis are merely theoretical at this point because the proposed rule does not elaborate on potential importation targets. This analysis is intended to speak more to the lack of concordance between the FDA and HPFD regulatory processes for drugs, which may lead to administrability or safety issues following implementation. Under 21 U.S.C. § 321(g)(1) the Food Drug and Cosmetic Act (FD&C Act) defines “drugs” as:

- (A) articles recognized in the official United States Pharmacopœia, official Homœopathic Pharmacopœia of the United States, or official National Formulary, or any supplement to any of them; and
- (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and
- (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and
- (D) articles intended for use as a component of any article specified in clause (A), (B), or (C).⁵⁰

Conversely, under Canada’s Food and Drug Act, a drug is defined as “any substance or mixture of substances manufactured, sold or represented for use in:”

- (a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in human beings or animals,
- (b) restoring, correcting or modifying organic functions in human beings or animals, or
- (c) disinfection in premises in which food is manufactured, prepared or kept.⁵¹

controlled clinical trials processes with stepwise increasing samples sizes to establish safety of new drug products before the agencies consider whether or not to grant approval).

⁵⁰ 21 U.S.C. § 321(g)(1) (2018).

⁵¹ Food and Drugs Act, R.S.C. 1985, c F-27(2).

A simple reading of the text above reveals that the FDA and HPFB do not view drugs in an exactly equivalent manner, yet the proposed rule requires that drugs eligible for importation be such that they would have been approved by both the HPFB and the FDA.⁵² Because the FDA and HPFB definitions of what constitutes a drug differ, there is the possibility that some substances approved as drugs in Canada would not be approved in the United States. For example, the FDA's definition of a drug explicitly excludes food products, while HPFB's definition states that "any substance or mixture of substances" can potentially be a drug.⁵³ Moreover, the FDA would consider an article that is "intended to affect the structure of the body" to be a drug, while HPFB's definition does not state this as a possible category of drug.⁵⁴ Additionally, the FDA extends its definition to include components of a drug under its definition of a drug, while HPFB's definition does not.⁵⁵ These examples, through textual analysis, indicate just a few ways in which drugs considered for approval by each agency would vary at the outset and highlight discordance between the regulatory schemes.

As previously stated, this variation only serves to point out one of many ways in which disagreements between the Canadian and U.S. drug approval schemes may prevent the purpose of the bill from being carried out. This variation could mean that drugs that certain consumers are interested in importing from Canada may have never qualified for approval in the U.S. and vice versa. As such, this would preclude certain drugs at the outset from moving forward with eligibility, which in turn affects potential future cost savings. It also creates a point of tension if this scheme were to be more regularly used and states attempted to use this system as a means to import drugs that would otherwise not be approved in the U.S. by the FDA as drug products.

⁵² Importation of Prescription Drugs, *supra* note 1.

⁵³ 21 U.S.C. § 321(g)(1) (2018); Food and Drugs Act, R.S.C. 1985, c F-27(2).

⁵⁴ *Id.*

⁵⁵ *Id.*

Above all, this point illustrates that if a scheme were to go forward with importation of drugs from Canada, there is a need to look at all the ways in which FDA and HPFB regulatory processes differ and the implications of those differences. Yet, the proposed rule does not go so far as to examine the textual differences in the regulations that may pose administrability problems and create greater costs down the line.

b. Differences in the post-clinical trial approval process.

The other major point of distinction between the two systems would be the final approval and post-market review process, which in some cases may result in drugs being approved in Canada that would otherwise not be approved in the US or vice versa.

After clinical trials have been completed, the FDA requires drug sponsors to submit a New Drug Application (NDA), which provides the FDA with a summary of all pertinent data for a drug seeking approval for manufacture and sale in the United States.⁵⁶ More specifically, an NDA contains “all information about the manufacturing process and facilities, quality control, and assurance; a complete product description (chemical formula, specifications, pharmacodynamics, and pharmacokinetics); indications; labeling; and proposed risk evaluation and mitigation processes if applicable.”⁵⁷ During this review process, the FDA looks for “‘substantial evidence’ of drug safety and efficacy” which is usually interpreted as “at least 2 adequate and well-controlled Phase III trials with convincing evidence of effectiveness.”⁵⁸ Approval, may come with conditions, like the need to conduct post-market Phase IV clinical

⁵⁶ Gail A. Van Norman, *Drugs, Devices, and the FDA: Part 1 An Overview of Approval Processes for Drugs*, 1 *JACC: BASIC TO TRANSLATIONAL SCI.* 3, 176 (2016)

⁵⁷ *Id.*

⁵⁸ *Id.*

studies, “distribution restrictions, changes to labeling, or other requirements.”⁵⁹ But once approved, “the manufacturer is free to manufacture and market the drug” in the United States.⁶⁰

HPFB’s approval process provides that after all clinical trials have been completed, a manufacturer is required to submit a New Drug Submission (NDS) with the Therapeutic Product Directorate (TPD) “to be granted authorization to sell the drug in Canada.”⁶¹ After the risk benefit analysis associated with a new therapeutic is done and HPFB concludes that the expected benefit to the Canadian population outweighs the risks, the sponsor receives a Notice of Compliance (NOC) and Drug Identification Number (DIN).⁶² HPFB then “requires a sponsor to ensure that the use of its drug is done under the terms of its market authorization” through mandatory Life Cycle Management activities.⁶³ These activities include “post approval submissions to Health Canada, for new indications, new dosage forms, new strengths, manufacturing changes, etc” and continue as long as the manufacturer continues to produce the drug product.⁶⁴

Here, the main differences between the FDA and HPFB approval processes are the factors relied upon to allow a manufacturer to market their drug to the public. In Canada, the “results of all the preclinical studies and clinical trials [must] show that a drug’s potential therapeutic benefit outweighs its risks.”⁶⁵ The FDA, on the other hand, heavily focuses on whether the clinical trials have demonstrated “substantial evidence” of *both* drug safety and

⁵⁹ *Id.*

⁶⁰ *Id.* at 177.

⁶¹ *The Drug Review & Approval Process in Canada - An E-Guide* -, SPHARM, <https://spharm-inc.com/the-drug-review-and-approval-process-in-canada-an-eguide/> (last visited Feb. 18, 2020).

⁶² *Id.*

⁶³ *Id.*

⁶⁴ *Id.*

⁶⁵ *Id.*

efficacy.”⁶⁶ For the FDA, this is determined by looking to whether there were “at least 2 adequate and well-controlled Phase III trials with convincing evidence of effectiveness” and by convening advisory panels to review the data.⁶⁷ Thus, although one could say that safety and efficacy tests are a form of risk-benefit analysis that is similar to the one conducted by HPFB, it is different because a drug may not be effective for its indicated usage but merely be such that its benefits as a safe and *potentially* efficacious drug outweigh its risks.

This concern is not merely theoretical given that disconnects in approval outcomes between the agencies have occurred before. For example, domperidone was approved for use in Canada “to treat slowed movement in the gastrointestinal tract associated with diabetes and gastritis.”⁶⁸ Specifically, it helps the stomach empty faster and reduces nausea.⁶⁹ However, this same drug failed the FDA approval process due to a determination that the drug lacked the requisite efficacy to be used for patients with nausea and vomiting due to acute gastroenteritis.⁷⁰ The FDA also relied upon reports showing that use of domperidone could result in “cardiac arrhythmias, cardiac arrest, and sudden death in patients receiving an intravenous form of domperidone.”⁷¹ Yet despite this regulatory approval disconnect, many patients continue to seek the drug in the U.S. through compounding.⁷² Thus, this would be a drug that would be excluded

⁶⁶ Gail A. Van Norman, *Drugs, Devices, and the FDA: Part 1 An Overview of Approval Processes for Drugs*, 1 *JACC: BASIC TO TRANSLATIONAL SCI.* 3, 176 (2016).

⁶⁷ *Id.*

⁶⁸ *Mylan-Domperidone*, CANADA.COM:HEALTH <https://bodyandhealth.canada.com/drug/getdrug/mylan-domperidone> (last visited Mar. 6, 2020).

⁶⁹ *Id.*

⁷⁰ *A Study to Evaluate the Safety and Efficacy of Domperidone in Pediatric Participants With Nausea and Vomiting Due to Acute Gastroenteritis*, CLINICALTRIALS.GOV <https://clinicaltrials.gov/ct2/show/NCT02699385> (last visited Mar. 6, 2020).

⁷¹ U.S. Food and Drug Administration, FDA Talk Papers: FDA Warns Against Women Using Unapproved Drug, Domperidone, to Increase Milk Production, FDA.GOV (Jun. 7, 2004) <https://www.fda.gov/drugs/information-drug-class/fda-talk-paper-fda-warns-against-women-using-unapproved-drug-domperidone-increase-milk-production>.

⁷² “Compounding is the process by which a pharmacist mixes drugs, chemicals, or other products to tailor a medication to an individual patient.” Mark Flatten, Sickening: FDA Bureaucracy Blocks Common “Miracle Drug,” GOLDWATER INSTITUTE (Oct. 25, 2016) <https://goldwaterinstitute.org/article/sickening-fda-bureaucracy-blocks-common-miracle-dr/>.

by the proposed rule for importation despite being approved in Canada and evidence suggesting that U.S. consumers would want to get their hands on it.⁷³

In sum, these differences could be large enough to create ineligibility issues for certain drugs that are proposed for importation from Canada. Specifically, because some drugs that Canada approved may not have gotten through the FDA approved pathway, and vice versa. Given the potential for regulatory disconnect, Importers may be unwilling to burden the up-front costs with seeking FDA approval of potential importation products and schemes. Thus, an analysis of how many drugs that consumers and States would be seeking that would be eligible under this program should be included in the cost-benefit analysis of the rule to get a better sense of the true cost savings that would be realized to the American public. If such an analysis were conducted, and it was shown that many drugs that the American public would want to import would be eligible for the program, then this would bolster the argument that this proposed rule should be put into effect. However, an opposite showing would cut the other way.

IV. Cost Effectiveness Limitations of the Proposed Drug Importation Scheme

The proposed rule requires Foreign Sellers, Importers, and State Sponsors to identify potential importation targets and jointly submit planned importation schemes to the FDA for approval.⁷⁴ However, identifying viable importation targets is a challenging endeavor as few products would meet the stringent requirement of demonstrating a “significant reduction in the cost of covered products to the American consumer.”⁷⁵ This section will explain general features of the proposed rule and the pharmaceutical market that will combine to substantially limit the rule’s applicability due to the burden of the substantial cost savings requirement.

⁷³ *Id.* (explaining how individuals with gastric conditions want domperidone to avoid having to use a feeding tube).

⁷⁴ *Supra* § I(b).

⁷⁵ Importation of Prescription Drugs, *supra* note 1 at 70796.

a. The proposed rule does not establish clear guidelines for determining substantial cost savings.

The proposed rule fails to describe the metrics by which potential drug importation targets will be evaluated for cost effectiveness. Specifically, the rule does not set a threshold value of cost savings to American consumers that would presumptively qualify an importation target as providing a significant reduction in the cost of covered products.⁷⁶ Instead, the proposed rule vests final approval authority in the FDA to determine significant reductions “in the context of considering a specific proposal.”⁷⁷ However, the proposed rule fails to lay out an analytical framework from which a flexible standard could be applied. Additionally, the proposed rule does not elucidate specific targets that it considers viable that, if included, could be used to inform the analysis. This discretionary system is ambiguous as to the factors that the FDA will ultimately consider in its determination and may lead to disparate outcomes in application approvals. Further information as to the bounds of cost effectiveness determinations will be critical to would-be Importers and State Sponsors seeking to reduce the risk of permit denial before investing in designing and applying for a novel importation scheme.

While suggesting cost effectiveness guidelines that would be reasonable for a drug importation program is beyond the scope of this comment, the remainder of this comment requires assuming the overall formula by which cost effectiveness will be evaluated. The proposed rule’s stated purpose is “to lower prices and reduce out of pocket costs for American patients” through the importation of certain prescription drugs from Canada.⁷⁸ To satisfy this purpose, imported drugs must demonstrate substantial cost savings for American consumers if

⁷⁶ *Id.* at 70798.

⁷⁷ *Id.* at 70807.

⁷⁸ *Id.* at 70797.

sold in the US at Canadian prices, plus a markup for the Importer. Determining likely targets for importation is thus a two-variable analysis based on our suggested general formula:

cost savings = savings per use * total uses. For this formula, savings per use is defined as the difference between US list prices and the proposed imported price, which is the Canadian price plus the Importer's markup. Total uses is defined as the number of prescriptions filled in the US, up to a fixed capped of the surplus of that drug that is currently available within the Canadian market.⁷⁹ This formula allows the FDA flexibility to determine systemic savings thresholds regardless of if the benefit from importation results from high-volume drugs with modest price differentials between the US and Canada or from low-volume drugs with large differentials.

b. Expanded Importer obligations under the proposed rule will reduce potential cost effectiveness.

Regardless of the drug target, Foreign Sellers and Importers will seek to leverage the newly created drug importation market to turn a profit. Importation targets must therefore exhibit a substantial price differentiation between US and Canadian list prices in order to allow space for a commercially reasonable markup. A commercially reasonable markup in this context is not clearly defined, but must, at a minimum, cover the costs that the Foreign Seller and Importer incur when seeking and maintaining regulatory approval for the importation scheme, in addition to the normal costs associated with drug storage and distribution. Despite this dynamic, the proposed rule does not consider what a reasonable markup is. The rule instead leaves it up to Foreign Sellers, Importers, and State Sponsors to decide the correct balance between making profit and securing greater cost reductions for American consumers. However, Foreign Sellers and Importers should be expected to secure the greatest margins that the market will bear in

⁷⁹ See *supra* § II (discussing how manufacturers are unwilling to increase supply to Canada above existing levels if those drugs are simply being diverted to the US market).

fulfillment of their corporate objectives. Therefore, because the resulting markup is only constrained by the upper limit of the US drug market as it currently exists, this balancing approach may result in less-than-optimal benefits flowing through to American consumers.

The proposed rule exacerbates the likelihood of high importer markups by incentivizing Importers to require high markups as a condition of taking on the various obligations imposed on them under the proposed rule. Specifically, the proposed rule requires Importers to monitor side effects, recalls, and other treatments trends relevant to updating imported drugs' labeling.⁸⁰ Importers may not have the existing structural capacity or technical expertise to engage in this type of oversight safely and efficiently because labeling in the US context is typically overseen by manufacturers.⁸¹ In order to bridge the gap, Importers may have to invest in infrastructure relevant to the new business activities and use higher markups to fund the transition.

This outcome could further be compounded by recent litigation seeking to expand distributor liability. In the opioid crisis context, distributors are in negotiations over a substantial settlement package for their alleged role in fueling the crisis.⁸² Here, Importers may face enhanced liability compared to traditional US distributors due to the more substantial obligation imposed by the rule. Thus, Importers may be compelled to secure more insurance or other liability offsets than would be traditionally utilized by US distributors. The proposed rule does not consider the impact that imposing these obligations on Importers may have on the operational markup required to incentivize participation in the scheme. Alternative importation schemes should be evaluated for enhanced cost-effectiveness compared to this model—such as

⁸⁰ Importation of Prescription Drugs, *supra* note 1 at 70812–13.

⁸¹ See generally Title 21, Subchapter C—Drugs: General, Subpart A--General Labeling Provisions, 21 C.F.R. §§ 201.1–201.21.

⁸² Sara Randazzo, *Drug Distributors in Talks to Settle Opioid Litigation for \$18 Billion*, WALL ST. J., Oct. 15, 2019, <https://www.wsj.com/articles/drug-distributors-in-talks-to-settle-opioid-litigation-for-18-billion-11571170730>.

pinning imported drug labeling to existing FDA- or HPFB-approved materials—though elaboration on such program changes is outside of the scope of this comment.

c. Cost benefits will only be realized by individuals paying out of pocket

Currently, insured individuals pay low premiums on prescriptions.⁸³ The amount paid out of pocket is comparable or lower than Canadian list prices for the same drugs.⁸⁴ Thus, for insured individuals, purchasing within the insurer’s approved list of pharmaceutical products is often the most cost-effective route. However, Canadian imports are unlikely to be approved under pharmaceutical benefit plans. Plans often use rebates negotiated with manufacturers to offer lower prices to plan participants.⁸⁵ Manufacturers will be unwilling to negotiate on imported drugs due to their general disapproval of the proposed importation scheme.⁸⁶ Manufacturers that are especially concerned with limited price-setting capabilities under the importation model could even engage in stricter negotiating tactics to explicitly deny Canadian imported drugs under pharmacy plan benefits as a condition to offering rebates on US listed drugs. Manufacturers will likely succeed in this effort as the majority of Americans will still be getting their drugs from US listed drugs, even after the passage of the proposed rule—the Canadian market is simply too small to supply the majority of US market needs.⁸⁷

⁸³ See Aaron S. Kesselheim et al., *Prescription Drug Insurance Coverage and Patient Health Outcomes: A Systematic Review*, AM. J. PUB. HEALTH 105(2) (2015) (discussing the positive externalities of prescription insurance on health outcomes due to the increased affordability of covered drugs).

⁸⁴ Compare, e.g., *How Much Does Medicare Part D Cost?*, MY MEDICARE MATTERS; NAT’L COUNCIL ON AGING, <https://www.mymedicarematters.org/costs/part-d/> (stating that, while plans vary, Medicare part D coinsurance rates are often 25% or lower of drug list price) with Jeanne Whalen, *Why the U.S. Pays More Than Other Countries for Drugs*, WALL ST. J., Dec. 1, 2015, <https://www.wsj.com/articles/why-the-u-s-pays-more-than-other-countries-for-drugs-1448939481> (comparing various prescription drug prices in Canada and the US with expected savings in the Canadian system not being less greater than 75%).

⁸⁵ *Prescription Drug Rebates, Explained*, KAISER FAMILY FOUND. (July, 26, 2019), <https://www.kff.org/medicare/video/prescription-drug-rebates-explained/>.

⁸⁶ *Supra* § II.

⁸⁷ Brett J. Skinner, *Potential impact of U.S. demand on the Canadian supply of 46 prescription drugs*, CAN. HEALTH POL. J. (2019), <https://www.canadianhealthpolicy.com/products/potential-impact-of-u-s--demand-on-the-canadian-supply-of-46-prescription-drugs-.html>.

This limitation brings into question the extent to which cost savings demonstrated by list prices alone can adequately capture consumer out-of-pocket-cost savings. Calculating expected cost-savings could be an impossible task given the multitude of insurance products in use in the marketplace, and the lack of transparency on drug rebates and other private contractual factors contributing to a drug's list price.⁸⁸ Further, even if imported drugs were to be made available lower than list prices, such benefits would only be available to uninsured individuals because insured individual's covered products will still be cheaper. Thus, the proposed rule will only directly benefit a minority of American consumers, since most Americans are insured.⁸⁹

Instead of this individual-focused system, cost savings could be more readily recouped by State and private insurers who are able to incorporate savings stemming from drug importation into resulting insurance plans and downstream customer coverage or related spending. Allowing planned importation schemes to demonstrate system-wide benefits in addition to, or in lieu of, individual consumer gains would have the further benefit of reducing downstream costs via lowering healthcare inflation, limiting premium increases, or other market-wide gains by allowing imported drugs to outcompete US-marketed drugs at the a more robust level.

Despite this benefit of scale, systemic considerations are explicitly disallowed under the proposed rule.⁹⁰ Instead, the rule requires tangible benefits to American consumers to result directly from any importation proposal.⁹¹ This limitation expressly negates the potential for the proposed rule to reduce downstream costs to American consumers and ultimately limits the

⁸⁸ See *id.* (describing the complexity in the prescription drug insurance market through the use of insurance-specific drug rebate offers).

⁸⁹ EDWARD R. BERCHICK, EMILY HOOD, & JESSICA C. BARNETT, HEALTH INSURANCE COVERAGE IN THE UNITED STATES: 2017, US CENSUS BUREAU REPORT NUMBER P60-264 (2018) (stating that 91.2% of Americans have health insurance).

⁹⁰ Importation of Prescription Drugs, *supra* note 1 at 70807.

⁹¹ *Id.* (“the SIP Proposal would need to show that there is a significant reduction in the cost of covered products to the American consumer.”).

scope of importation plans that State Sponsors may be willing to push forward. Allowing more robust systemic benefit determinations in the FDA’s approval process could help overcome the difficulties associated with demonstrating cost savings to individual consumers as currently proposed. Additionally, allowing insurers to benefit under the proposal rather than solely individual consumers may help benefits flow more readily to currently insured Americans. Further, if State insurers were allowed to design importation schemes to benefit their bottom-line then State Sponsors would be more incentivized to design and support importation schemes. In turn, aligning the incentives for State Sponsors with insurers (state or private) may increase rollout of importation plan nationwide and make the scheme more likely to realize downstream cost reductions that require sufficient scale of importation disruption to be impactful.

d. Generic drugs are not cheaper in Canada than in the US.

In looking at price differentials, most of the large differentials that the proposed rule aims to exploit to benefit American consumers are for branded pharmaceuticals. However, 9 out of 10 prescriptions filled within the U.S. are for generic drugs.⁹² Further, 93% of these generic prescriptions cost consumers \$20 or less, with the average copay being \$6.06 in 2018.⁹³ These trends have been stable, with generic utilization in the US demonstrating steady increases despite overall rising prescription drug costs.⁹⁴ Additionally, many State and private programs have recently been focused on keeping generic drug costs low.⁹⁵ With substantially lower average costs than for branded drugs,⁹⁶ it is not clear that importing generic drugs will result in cost

⁹² Rachel Schwartz, *The Generic Drug Supply Chain*, ASSOC. FOR ACCESSIBLE MEDICINES (2017), <https://accessiblemeds.org/resources/blog/generic-drug-supply-chain>.

⁹³ *NCSL Prescription Drug Policy Resource Center*, NAT’L CONFERENCE OF STATE LEGISLATURES (2019), <https://www.ncsl.org/research/health/ncsl-prescription-drug-policy-resources-center.aspx>.

⁹⁴ *Id.*

⁹⁵ *Id.*

⁹⁶ *Id.* (stating that the average copay for branded pharmaceuticals is \$40.30, which is over six times more than the average generic copay).

savings for the average American consumer. In fact, generic drug prices in the US are on par with drug costs in Canada. The average generic drug price in the US is only 1% higher than the list price in Canada for comparable drugs.⁹⁷ Further, the gap in generic drug cost between the US and Canada has been decreasing in recent years, with Canada experience higher prices in relation to the US market than were previously observed for generics.⁹⁸

Based on this direct comparison, generic drugs will generally fail to provide a substantial cost savings to American consumers, as required under the proposed rule. Accordingly, whether or not a generic formulation is available in the US is a useful proxy for determining cost effectiveness when evaluating proposed importation targets. Moving forward, this comment will assume that if a generic is available in the US, then any negligible price difference between Canadian and US list prices will be insufficient to provide substantial cost savings to American consumer. This assumption is further bolstered by no substantial savings being found even without taking into account potential Foreign Seller and Importer markups, which would further decrease any price differential that may lead to cost savings.

V. Potential Targets for Importation are Limited

However, the analysis does not end at cost effectiveness. Importation targets must also meet a variety of safety requirements to qualify.⁹⁹ For the purposes of the following analysis, it will be assumed that relevant supply chain and general formulation safety requirements are met for proposed importation targets. Additionally, Importers must comply with FDA labeling requirements and provide regular monitoring of imported drug adverse reactions, recalls, and

⁹⁷ *Generic Drug Pricing in Canada: Closing the Gap*, GOV'T OF CANADA PATENTED MEDICINE PRICES REVIEW BOARD (2019), <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1455&lang=en>.

⁹⁸ *Compare id. with Generics360 – Generic Drugs in Canada, 2016*, GOV'T OF CANADA PATENTED MEDICINE PRICES REVIEW BOARD (2016), <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1347&lang=en> (in 2016 US generic drug prices were on average 8% higher than comparable Canadian generics versus 1% higher in 2019).

⁹⁹ Importation of Prescription Drugs, *supra* note 1 at 70804.

other safety considerations.¹⁰⁰ For the purposes of the following analysis, it is assumed that ongoing monitoring and reporting requirements can be met by importers for all importation targets. Yet even if these various safety considerations are met, the proposed rules still excludes several categories of drugs in their entirety because the latent safety concerns are too substantial for the FDA to adequately regulate under the proposed rule's current authority given FDA funding levels.¹⁰¹ While these safety concerns are well-founded, the resulting exclusions are broad, including:

- Controlled substances;
- Biological products;
- Infused drugs;
- Intravenously injected drugs;
- Drugs that are inhaled during surgery;
- Drugs that are subject to risk evaluation and mitigation strategies (REMS);
- Products that are illegitimate under Section 582 of the FD&C Act;
- Intrathecally injected drugs; and
- Intraocularly injected drugs.¹⁰²

Potential importation targets falling in additional categories are also limited.¹⁰³ While not exempted from importation entirely, these additional categories will face heightened scrutiny given similar safety concerns presented by their use.¹⁰⁴ The additional categories of drugs that will face heightened scrutiny are:

¹⁰⁰ *Supra* § I(b).

¹⁰¹ *See* Importation of Prescription Drugs, *supra* note 1 at 70804.

¹⁰² *Id.*

¹⁰³ *Id.*

¹⁰⁴ *Id.*

- Drug-device combination products that are approved under section 505 of the FD&C Act, such as:
 - Dry powder inhalers,
 - Metered-dose inhalers, and
 - Transdermal patch products;
- Inhaled drugs;
- Modified-release drugs;
- Sterile drugs;
- Ophthalmic drugs;
- Narrow therapeutic index drugs;
- Drugs with boxed warnings; and
- Drugs requiring special storage conditions.¹⁰⁵

Given the variety of outright exemptions and grounds for heightened scrutiny a majority of the most likely candidates for importation will be excluded. Combined with cost-effectiveness limitations precluding the majority of generics from suitability for importation, the pool of potential importation targets will be exceedingly narrow. This section will analyze likely importation targets for their suitability for importation under these limiting criteria to determine if the proposed rule will in fact lead to potential importation schemes or if exigent realities of the pharmaceutical market will prevent the full implementation of the rule, as seen with the MEDS Act.¹⁰⁶

¹⁰⁵ *Id.*

¹⁰⁶ *Supra* § I(c).

a. Only 4 of the top 20 grossing US drugs and none of the top 20 most prescribed drugs are suitable importation targets.

To determine likely importation targets, we turn to the cost savings formula previously discussed.¹⁰⁷ The most logical starting ground for discerning importation targets based on this formula is to isolate the drugs that represent the greatest cost burden on the US system as a whole. These drugs presumptively satisfy the requirement of sufficient market size within the US to result in a substantial cost savings to American consumers if imported from Canada at a lower price point. Thus, the highest grossing US drugs are an ideal starting ground for considering possible importation targets. To conduct this analysis, we surveyed the top 20 grossing drugs in the US, based on 2018 sales data.¹⁰⁸ We assumed that if the drugs were not exempted, available in generic form, or subject to heightened scrutiny that they would make suitable importation targets. Part of this assumption is that identified drugs would be available substantially cheaper in the Canadian market, which is not a guarantee; however, that second stage of analysis was not conducted in this case study survey. Yet even assuming that the top 20 grossing US drugs would be available substantially cheaper in Canada, only four of these drugs would be suitable for importation. TABLE 1¹⁰⁹ summarizes our analysis of the suitability for importation from Canada under the proposed rule of the top 20 highest grossing drugs in the US.

¹⁰⁷ *Supra* § IV.

¹⁰⁸ Kyle Blankenship, *The top 20 drugs by 2018 U.S. sales*, FIERCEPHARMA (June 17, 2019) <https://www.fiercepharma.com/special-report/top-20-drugs-by-2018-u-s-sales>.

¹⁰⁹ TABLE 1 presents information on exemption and heightened scrutiny status pulled from data included in currently approved FDA package inserts, prescribing information, and the DEA controlled substances list. If more than one grounds for exemption or heightened scrutiny were found, only one rationale was listed. If a drug product was included in an exemption, it was not analyzed for potential grounds for heightened scrutiny. Availability of a generic drug was determined based on purchasing descriptions found on <https://www.GoodRx.com>.

TABLE 1: Top 20 Grossing Drugs (in US) are Rarely Suitable for Importation

Top Grossing Drugs (in US)	Suitable for Importation?	Exempted?	Generic Available?	Heightened Scrutiny?
1. Humira	NO	✓ biological product	—	—
2. Revlimid	NO	✓ REMS	—	—
3. Enbrel	NO	✓ biological product	—	—
4. Rituxan	NO	✓ intravenous injection	—	—
5. Opdivo	NO	✓ intravenous injection	—	—
6. Keytruda	NO	✓ intravenous injection	—	—
7. Imbruvica	YES	—	—	—
8. Eylea	NO	✓ intraocular injection	—	—
9. Neulasta	NO	✓ biological product	—	—
10. Eliquis	NO	—	✓	✓ modified release drug
11. Remicade	NO	✓ biological product	—	—
12. Genvoya	YES	—	—	—
13. Lyrica	NO	✓ controlled substance	—	—
14. Stelara	NO	✓ biological product	—	—
15. Prevnar 13	NO	✓ biological product	—	—
16. Ibrance	YES	—	—	—
17. Herceptin	NO	✓ biological product	—	—
18. Avastin	NO	✓ biological product	—	—
19. Victoza	NO	✓ biological product	—	—
20. Truvada	YES	—	—	—

While only presenting a limited subset of drugs with substantial market size in the US, TABLE 1 demonstrates the overall trend of top grossing drugs in the US—they would not be eligible for importation under the proposed rule. This trend is likely to hold true even as the list of top grossing US drugs is extended beyond the top 20 drugs, because the majority of expensive branded drug products in the US fall within the broad exempted categories—especially the categories of biological products and intravenous injections. However, analyzing the top 20 grossing drugs is only one metric that could be used to identify potential targets for implementation. The formula also allows for high-volume drugs to qualify for substantial savings to American consumers, even if presenting smaller marginal cost savings per use.¹¹⁰

Thus, we also analyzed the top 20 most prescribed drugs in the US, also based on available 2018 sales data.¹¹¹ This analysis' general trend coincides with those presented in TABLE 1: the products most likely to be desirable importation targets are unlikely to be suitable for importation due to the constraints of the exempted categories, heightened scrutiny categories, and the prevalence of generic drugs in the US market. Here, the trend was even stronger: none of the top 20 most prescribed drugs in the US would be suitable for importation under the proposed rule TABLE 2¹¹² summarizes our analysis of the suitability for importation from Canada under the proposed rule of the top 20 most prescribed drugs in the US.

¹¹⁰ *Supra* § IV.

¹¹¹ Andrea V. Fuentes, Moises D. Pineda, & Kalyan C. Nagulapalli Venkata, *Comprehension of Top 200 Prescribed Drugs in the US as a Resource for Pharmacy Teaching, Training and Practice*, PHARMACY (2018), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6025009/>.

¹¹² TABLE 2 presents information on exemption and heightened scrutiny status pulled from data included in currently approved FDA package inserts, prescribing information, and the DEA controlled substances list. If more than one grounds for exemption or heightened scrutiny were found, only one rationale was listed. If a drug product was included in an exemption, it was not analyzed for potential grounds for heightened scrutiny. Availability of a generic drug was determined based on purchasing descriptions found on <https://www.GoodRx.com>.

TABLE 2: No Top 20 Most Prescribed Drugs (in US) are Suitable for Importation

Most Prescribed Drugs (in US)	Suitable for Importation?	Exempted?	Generic Available?	Heightened Scrutiny?
1. Lisinopril	NO	—	✓	—
2. Levothyroxine	NO	—	✓	—
3. Atorvastatin	NO	—	✓	—
4. Metformin	NO	—	✓	✓ modified release drug
5. Simvastatin	NO	—	✓	—
6. Omeprazole	NO	—	✓	✓ modified release drug
7. Amlodipine Besylate	NO	—	✓	—
8. Metoprolol	NO	—	✓	✓ modified release drug
9. Acetaminophen; Hydrocodone	NO	✓ controlled substance	✓	—
10. Albuterol	NO	—	✓	✓ inhaled drug
11. Hydrochlorothiazide	NO	—	✓	—
12. Losartan	NO	—	✓	—
13. Gabapentin	NO	—	✓	—
14. Sertraline	NO	—	✓	—
15. Furosemide	NO	✓ intravenous injection	✓	—
16. Acetaminophen; Analgesic	NO	✓ REMS	✓	—
17. Atenolol	NO	—	✓	—
18. Pravastatin	NO	—	✓	—
19. Amoxicillin	NO	—	✓	—
20. Fluoxetine	NO	—	✓	✓ modified release drug

Combined, TABLES 1 and 2 demonstrate that the proposed rule faces serious concerns that suitable importation targets will be difficult to identify at best, and nonexistent at worst. Even if suitable targets are able to be identified, this analysis suggests that the most impactful importation targets—those that represent the greatest cost burden on American consumers—will be excluded from the scheme and significantly constrain the potential impact of the proposed rule. In order to ensure that the rule will be able to achieve its lofty goal of reducing pharmaceutical costs for American consumers, more analysis to identify potential importation targets is necessary. Without expanding FDA authority and funding to effectively allow regulate exempted categories of drugs or otherwise increase the list of potential importation targets, this analysis suggests that prior CBO estimates of minimal impact of Canadian drug importation schemes are likely to be accurate as applied to this iteration of the program.¹¹³

b. Current State proposals fail to meet the requirements of the proposed rule.

Some states, including Florida, Vermont, and Colorado have introduced specific proposals for drug importation regimes or have already passed legislation authorizing State sponsorship of importation plans.¹¹⁴ These proposals represent the strongest evidence available for how drug importation authority is likely to be employed by State Sponsors under the proposed rule and can supplement the proposed rule’s lack of identified importation targets. However, only Florida has identified a list of proposed importation targets, whereas other states have merely pursued implementing legislation.¹¹⁵ Florida’s proposal was promulgated prior to the introduction of this specific rule and thus the proposed targets may not be suitable for

¹¹³ *Supra* § II(a).

¹¹⁴ Michael Olive, *With Encouragement From Trump, States Move Forward on Importing Drugs*, PEW CHARITABLE TRUSTS (2019), <https://www.pewtrusts.org/en/research-and-analysis/blogs/stateline/2019/12/18/with-encouragement-from-trump-states-move-forward-on-importing-drugs>.

¹¹⁵ FLORIDA’S CANADIAN PRESCRIPTION DRUG IMPORTATION CONCEPT PAPER, FL. DEPT. OF HEALTH (2019), https://ahca.myflorida.com/executive/communications/requested_documents/Florida_Canadian_Prescription_Drug_Importation_Concept_Paper.pdf.

importation given its restrictions.¹¹⁶ To explore the potential disconnect between State Sponsor intentions and authority under the proposed rule, this section will analyze the importation targets identified in the Florida proposal.

TABLE 3¹¹⁷ summarizes the importation targets identified by the Florida concept paper. Florida selected importation targets were chosen due to the prevalence of their prescription in State-sponsored healthcare programs, in combination with noted priced differentials between Florida and Canadian prices.¹¹⁸ TABLE 3 demonstrates that the majority of importation targets identified by Florida would be allowable targets under the proposed rule.¹¹⁹ Further, the Florida proposal outlines substantial cost savings that are achievable by pursuing the identified targets, even including a substantial markup for Importers. Thus, the concept paper demonstrates viable targets specific to the Florida market.

Despite identifying suitable targets for importation, the Florida proposal fails to properly pass on cost savings to American consumers. Under both the concept paper and the corresponding authorizing legislation passed by the Florida legislature, cost savings accrued by the State Sponsor are not explicitly passed on to consumers.¹²⁰ For this reason, the Florida proposal would ultimately be rejected under the proposed rule's current formulation—importation schemes that benefit State Sponsors or provide other systemic benefits in lieu of

¹¹⁶ *Id.*

¹¹⁷ TABLE 3 presents information on exemption and heightened scrutiny status pulled from data included in currently approved FDA package inserts, prescribing information, and the DEA controlled substances list. If more than one grounds for exemption or heightened scrutiny were found, only one rationale was listed. If a drug product was included in an exemption, it was not analyzed for potential grounds for heightened scrutiny. Unlike TABLES 1 and 2, generic options for identified drugs were not analyzed in TABLE 3. The Florida proposal includes cost effectiveness analysis that eliminates the need for to use generic availability as a proxy for cost effectiveness.

¹¹⁸ *Supra* note 115 at 16.

¹¹⁹ 16 of 20 proposed importation targets would be suitable for importation under the proposed rule.

¹²⁰ *Supra* note 115.

TABLE 3: Florida's Proposed Drug Targets are Mostly Suitable for Importation

Importation Target	Suitable for Importation?	Exempted?	Heightened Scrutiny?
Atripla	YES	—	—
Aubagio	YES	—	—
Complera	YES	—	—
Diclegis Dr	UNCLEAR	—	✓ modified release drug
Epclusa	YES	—	—
Genvoya	YES	—	—
Ibrance	YES	—	—
Isentress	YES	—	—
Nasonex	YES	—	—
Odefsey	YES	—	—
Prezista	YES	—	—
Pulmicort	UNCLEAR	—	✓ inhaled drug
Sabril	YES	—	—
Stribild Tablet	YES	—	—
Tecfidera Dr	UNCLEAR	—	✓ modified release drug
Tivicay	YES	—	—
Triumeq	YES	—	—
Truvada	YES	—	—
Vimpat	NO	✓ controlled substance	—

direct-to-consumer savings is disallowed under the proposed rule.¹²¹ The Florida proposal would need to explicitly require expansion of State insurance coverage to qualify—a step not considered under the proposal as written and likely a politically contentious topic given the current divisions between states on Medicaid expansion. Thus, the FDA should re-evaluate if this limitation is the best approach to realize consumer cost savings in light of the benefit that systemic cost savings can have through downstream impacts on individual consumers. Precluding importation schemes such as the Florida proposal may further reduce the pool of suitable importation targets to such an extent that Importers may lack sufficient targets of interest to State Sponsors to warrant the upfront investment in developing and seeking approval for novel importation networks.

VI. Conclusions

This comment has demonstrated that the proposed rule for the importation of prescription drugs from Canada has not adequately considered numerous potential concerns with drug importation schemes. Many of these concerns are not new, nor are they specific to this iteration of a drug importation rule, yet despite having advanced knowledge of the primary critiques against the suitability and impact of drug importation schemes, this proposed rule is lacking in its response to the basic critiques that are based in the scientific and economic realities of the drug market in the US.

This comment suggests that additional consideration be given to a variety of concerns with the proposed drug importation framework, including:

¹²¹ See *supra* § IV(c).

- Addressing the stated concerns of previous HHS administrators regarding importation program efficacy, safety, and international political stakeholder reality;
- Addressing the underlying differences in FDA and HPFB approval pathways that may lead to differences in targeted drug formulation or approval status;
- Addressing the limited targets suitable for importation under the proposed rule stemming from the broad exemptions and categories for heightened scrutiny, perhaps by identifying example importation targets and evaluating the resulting economic impact; and
- Addressing the rationale behind precluding importation schemes that benefit State Sponsors and other systemic payers that may be unable to demonstrate immediate pass-on savings to the American consumer.

Without further exposition on these programmatic shortcomings, this comment demonstrates that the proposed rule for the importation of prescription drugs will be limited by opposition from manufacturers and other stakeholders, few suitable importation targets, precluded importation scheme designs, and continuing issues with FDA oversight and management of the international scheme given innate differences in the FDA and HPFB approval pathways. More analysis to refute these concerns and to establish programmatic workarounds is necessary before the proposed rule for the importation of prescription drugs is likely to create a system capable of achieving the stated purpose of securing cost savings for American consumers in the face of ever-increasing pharmaceutical expenditures.