Section 804 Importation Program

Colorado's Drug Importation Program

December 5, 2022

COLORADO
Department of Health Care Policy & Financing

COLORADO
Department of Health Care Policy & Financing

1570 Grant Street
Denver, CO 80203

December 5, 2022

Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Avenue
Hillandale Building, 4th Floor
Silver Spring, MD 20993

RE: Submittal of Colorado's Section 804 Importation Program Application

On behalf of the state of Colorado, I am pleased to submit this Section 804 Importation Plan (SIP) and request an approval to permit the importation of eligible prescription drugs into Colorado from Canada. This SIP complies with all federal drug importation statutes and regulations and once approved, will help address the high costs of medications impacting Colorado consumers every day. Once fully operational, we estimate that our program can save Coloradans an average of 65% on their prescriptions—totaling $53 to $88 million in savings each year.

U.S. drug prices are harming Coloradans and their employers. A RAND report sponsored by the U.S. Department of Health and Human Services in January 2021 found that brand name prescription drug prices in the U.S. are averaging two and a half times the prices paid in other nations.[1] In Colorado, prescription drugs account for 19% of total health care spending. Meanwhile, we continue to see industry practices that emphasize profits over people. Drug companies spend nearly $40 billion a year more on sales and marketing than on research and development of new drugs[2] and pharmacy benefit managers have achieved gross profits of over $28 billion in 2019.[3]

Our SIP and the federal framework for importation underscore safety. It requires compliance with all current FDA safety standards and mandates additional laboratory testing approved by the FDA before importation can occur. It also leverages the current supply chain in the

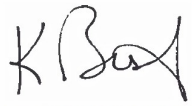
[1] RAND Corporation. (2021, January 28) Prescription Drug Prices in the United States Are 2.56 Times Those in Other Countries. https://www.rand.org/news/press/2021/01/28.html
[2] Anderson, R. (2014, November 6). Pharmaceutical industry gets high on fat profits. BBC News. https://www.bbc.com/news/business-28212223
[3] PBM Accountability Project. (2021) Understanding the Evolving Business models and Revenue of Pharmacy Benefit Managers. https://b11210f4-9a71-4e4c-a08f-cf43a83bc1df.usrfiles.com/ugd/b11210_264612f6b98e47b3a8502054f66bb2a1.pdf

U.S. which already, the FDA reports, indicates that 78% of active pharmaceutical ingredient (API) manufacturers are located outside of the U.S.[4]

The Colorado Department of Health Care Policy & Financing Drug Importation Division (HCPF DID) has built the infrastructure to effectively administer and oversee this program. We have identified experienced contractual partners to move this program forward quickly and safely, once approved, and we are confident we can create a new and innovative marketplace that disrupts the status quo to the betterment of Colorado consumers and employers.

Thank you for considering this application. Should the FDA have any questions during the review process, please contact Lauren Reveley, Colorado Department of Health Care Policy & Financing Drug Importation Program Manager, at Lauren.Reveley@state.co.us or 303-866-2718.

Sincerely,



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

[4] U.S. Food and Drug Administration. 2022. Fact Sheet: FDA at a Glance. https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance

Table of Contents

Appendices

Executive Summary

The Colorado Department of Health Care Policy & Financing (Department and SIP Sponsor) offers this Section 804 Importation Program (SIP) application to address the rising costs of prescription drugs which total almost $5 billion per year in Colorado alone.[1] Nearly one in three Coloradans do not take their prescription drugs as directed because they simply cannot afford to.[2] Colorado's SIP can offer consumers in our state an estimated 65% reduction in costs by importing prescription drugs from Canada.

Colorado's SIP is authorized by state statute signed into law in 2019 (Senate Bill 19-005)[3] and is in full compliance with the Federal Food, Drug, and Cosmetic Act (FDCA) Section 804 (21 USC § 384).[4] Since the passage of state legislation, the Department has analyzed U.S. and Canadian prescription drug markets, met with stakeholders to develop a draft SIP proposal, responded to federal regulations outlining the detailed requirements for SIP sponsors, and released an Intent to Negotiate to solicit supply chain partners. The Department has secured the partners required in the Final Rule[5] including a Canadian licensed wholesaler (Foreign Seller), a U.S. licensed wholesaler (Importer) and U.S. licensed relabeler, and an FDA-approved laboratory. All supply chain partners, in both the U.S. and Canada, have been fully vetted by the Department's Drug Importation Division (HCPF DID, or Department DID) in collaboration with our hired, expert consultants. With these partners in place, Colorado is fully prepared to implement its SIP upon approval from the FDA.

The SIP will achieve significant cost savings for the program through direct negotiation with manufacturers. Specifically, the state has identified 112 drugs that are high cost and/or high volume in Colorado and, if imported, could save on average 65% for consumers, as well as employers and other self-funded plan sponsors, municipalities, or the Colorado Department of Corrections. The state's proposed drug list targets commonly prescribed drugs, such as blood thinners and drugs used for women's health, and a variety of drugs that treat conditions such as Type 2 diabetes, asthma, cancer and HIV. For these 112 drugs, the DID estimates annual savings of $53 to $88 million, depending on market adoption.

At the time of this SIP submission, the included importation drug list is aspirational. As the state embarks on a negotiation process with drug manufacturers in Canada, we anticipate our initial list for the early years of the program to be significantly more narrow than the list presented in this SIP. In large part, this is due to likely modest participation from manufacturers in the short-term with a focus on small innovator companies and generic manufacturers. We believe, however, that with proof of the importation concept, more manufacturers will agree to participate due to market incentives that importation can offer.

---

[1] Center for Improving Value in Health Care. 2022. Affordability Dashboard. https://b11210f4-9a71-4e4c-a08f-cf43a83bc1df.usrfiles.com/ugd/b11210_264612f6b98e47b3a8502054f66bb2a1.pdf

[2] Altarum Healthcare Value Hub. 2019. Colorado Residents Worried about High Drug Costs—Support a Range of Government Solutions. https://cohealthinitiative.org/wp-content/uploads/2019/11/Colorado-Altarum-Data-Brief-Drug-Costs.pdf

[3] Colorado General Assembly. 2019. Concerning Wholesale Importation of Prescription Pharmaceutical Products from Canada for Resale to Colorado Residents. https://leg.colorado.gov/sites/default/files/2019a_005_signed.pdf

[4] 21 U.S.C.§ 384. Importation of Prescription Drugs. https://www.govinfo.gov/content/pkg/USCODE-2011-title21/html/USCODE-2011-title21-chap9-subchapVIII-sec3 84.htm

[5] U.S. Food and Drug Administration. 2020. Importation of Prescription Drugs. U.S. Department of Health and Human Services. www.hhs.gov/sites/default/files/importation-final-rule.pdf

The HCPF DID will oversee the SIP once approved and attests that the SIP will pose no additional risk to public health and safety, as required by federal law and regulation. The program's framework supports this through strong oversight and accountability in contracts with supply chain partners. All prescription drugs approved for importation through the Colorado SIP will be the same as the current FDA-approved versions, which are produced worldwide, as is the case in the U.S. market today.

Eligible drugs that have been negotiated with manufacturers and approved by the FDA for importation will be subject to the same safety protocols conducted by Canadian oversight entities today. The Foreign Seller will purchase the drug directly from the manufacturer and will be held to standards in federal rule to ensure each drug can be tracked and traced back to the manufacturer. The Foreign Seller is contracted with the Department's named Importer for purposes of importing and distributing the drug to Colorado. Before distribution can occur, the Importer must ensure that batch testing has occurred by the Department's named FDA-approved laboratory. The Importer will contract with pharmacies that have agreed to stock and dispense drugs imported from Canada under the SIP.

While the state of Colorado has great hope for its drug importation program, barriers will continue to make our effort challenging, including manufacturer resistance, health insurance carrier and PBM hesitancy, and regulatory hurdles limiting flexibility. A SIP approval will help address some of these barriers by demonstrating progress and will help our state advance its goal of reducing drug costs for consumers.

Introductory Statement & Overview of SIP Proposal (§ 251.3 (d) 1-11)

Per the Final Rule, the Colorado Department of Health Care Policy & Financing (the Department, or SIP Sponsor) is offering this SIP Proposal (named "Colorado's Drug Importation Program") to the Food and Drug Administration (FDA) for consideration. Detailed SIP Sponsor information is included in Appendix A. This introductory statement and SIP overview provides a brief history of Colorado's effort and process to bring prescription drug importation to the state.

Colorado Senate Bill 19-005

In 2019, the Colorado General Assembly passed Senate Bill 19-005, which requires the Department to develop a Canadian prescription drug importation program and pursue approval for such a program from the federal government. Senate Bill 19-005 includes detailed requirements to ensure compliance with Section 804 of the Federal Food, Drug, and Cosmetic Act (FDCA)[6] which authorizes state-led wholesale importation programs. Our state legislation reinforces requirements that testing, labeling, and recordkeeping are of the utmost importance in administering an importation program.

Senate Bill 19-005 outlines requirements for any Importer and Canadian supplier participating in the program. The legislation also provides the state with oversight authority and responsibility to ensure compliance of the SIP with state and federal policy rules and standards. This includes oversight of any vendor(s), regular monitoring of the importation drug list and suspension of importation of any drug that is in violation of the state statute or federal rules. This SIP complies with all these aspects of state statute and the process and implementation approach are outlined in further detail below.

Our Process

Since the passage of Colorado's authorizing legislation, Senate Bill 19-005, the Department has undergone a significant implementation effort to support submission of this SIP application. Launching a completely new health care initiative to establish an innovative and disruptive marketplace has been no small effort. Over the last three years, the state has primarily focused on the areas below:

Evaluation of Market Dynamics

In order to create a new marketplace, it is critical to understand systemic issues within the current prescription drug market. This has informed the Department's approach to partnerships both inside and outside of the supply chain, and the selection of drug list candidates. Through numerous engagements with stakeholders and supply chain participants and experts since the program's inception, we have grounded our SIP application in the following learnings:

1. **Supply chain innovators.**
   Large market players that benefit from the status quo were never going to be our initial partners. Smaller, nimble, innovative companies comprise our supply chain

[6] 21 U.S.C.§ 384. Importation of Prescription Drugs. https://www.govinfo.gov/content/pkg/USCODE-2011-title21/html/USCODE-2011-title21-chap9-subchapVIII-sec3 84.htm

because they support developing new strategies to bring consumers safe and effective lower priced drugs.

2. **Importance of direct negotiation with manufacturers**.
   In general, manufacturer contracts with Canadian wholesalers include language that prevents exportation of their products to the U.S. This requires a direct negotiation with manufacturers to develop agreements without such language.
3. **Rebate challenges**.
   Because of the misaligned financial incentives to carriers and pharmacy benefit managers from rebates and the concurrent reduction of rebates through the importation process, carriers will likely create pushback on all state importation plans.
4. **Pharmacy Benefit Manager (PBM) dynamics**.
   Most PBMs rely on profit-oriented or market share growth processes and strategies that are rarely transparent, such as rebates, drug price mark-ups, spread pricing, and complex fee structures; however, there are a growing number of sophisticated employer clients and responsive PBMs using pass-through, national average drug acquisition cost (NADAC) and cost-plus reimbursement approaches that provide discount transparency and direct savings to plan sponsors and their members. These are likely our best partners to bring imported drugs and their relative savings to Coloradans with coverage.

Policy Analysis

Since the launch of the Department's work on this program, the state has completed many critical policy analysis steps. Initially the Department evaluated the Canadian market's framework for drug pricing to inform the development of a preliminary drug list and operating framework. Once the FDA released its draft rule to implement Section 804 in December 2019, the Department analyzed the rule and submitted a comment letter[7] outlining concerns with its framework and highlighting the need for increased flexibility for states.

In developing and submitting a draft SIP application in early 2020, the Department analyzed the FDA's Notice of Proposed Rulemaking to assess its impact on the initial program framework and made adjustments to the proposed approach, as appropriate. Throughout these steps the Department solicited public comments, held stakeholder engagement sessions, and made program adjustments. As the work progressed to secure supply chain partners, and the FDA released a Final Rule in October 2020, the Department continued to analyze the Final Rule and identified operational challenges associated with various aspects. These policy issues have been shared with the FDA in state meetings and through requests for formal guidance.[8] Key guidance requested includes: 1) establishing a clear SIP review process and phased approval, 2) providing clarity on FDA standards for demonstrating cost savings, and 3) accepting SIP drug lists as flexible, providing opportunities to amend them. The Department has also worked diligently with other states through the National Academy of State Health Policy (NASHP) to monitor and evaluate both state and federal policy activity to inform the application approach.

Stakeholder Engagement

In advance of submitting the draft SIP application in 2020, the Department embarked on a significant stakeholder education and input gathering process to ensure the proposal would be

[7] Colorado Department of Health Care Policy & Financing. 2020. Draft Section 804 Importation Plan: Appendices. https://hcpf.colorado.gov/sites/hcpf/files/Colorado%20Draft%20SIP%20-%20Appendices.pdf

[8] Can be found in Appendix I.

responsive to the interests of our stakeholders. This process included issuance of two Requests for Information[9] to pharmacies and wholesale distributors, as well as targeted meetings with insurance carriers and PBMs in the state. The Department held three well-attended public stakeholder meetings to solicit further input and released a consumer survey[10] to over 500 stakeholders asking for their views on Canadian drug importation generally, and costs, safety and access specifically.

In addition to these efforts, the Department has continued an ongoing and open dialogue with the Canadian government through regular meetings with representatives from the Consulate General of Canada. The focus of these discussions has emphasized Colorado's commitment to not disrupting the Canadian drug supply or importing drugs on shortage in Canada. We will continue to prioritize these underlying principles.

The Department paused stakeholder engagement starting in early 2021 to focus on identifying the best supply chain partners through an active state procurement process. Now that supply chain partners have been named, the state will re-engage stakeholders in our next steps to solicit broader support for the program by pharmacies, employers, consumers, carriers and PBMs.

Partner Identification

In January 2021, the Department released an Invitation to Negotiate (ITN) to solicit supply chain partners. Through this process the Department promoted the ITN, reviewed solicitation responses, conducted site visits, all while continuing to develop the infrastructure needed to effectively operate an importation program. Each partner has been carefully vetted throughout this process, including by supply chain experts. This effort included successful site visits in both Canada and the U.S., resulting in partnerships with the following vendors:

- AdiraMedica Inc., a Canadian wholesaler located in Mississauga, Ontario, Canada, will fulfill the role of Colorado's Foreign Seller. The Foreign Seller serves as the primary conduit with Canadian manufacturers. AdiraMedica will purchase eligible drugs for Colorado's program and ensure they meet specifications for exportation to the United States. AdiraMedica has been in business for 15 years, specializing in supply chain management including import/export for global clinical trials. They are used to working with products that require the utmost care and attention to detail and are well-versed in navigating the exportation process into the United States.
- Premier Pharmaceuticals LLC, located in Boise, Idaho, will serve as Colorado's Importer and will be the primary distributor once medications come into the U.S. Premier will sell the medications to participating Colorado pharmacies as a Colorado registered wholesaler. Additionally, Premier will manage the required statutory testing and relabeling by partnering with a qualified laboratory and relabeler, respectively. Founded in 2019 by a local Boise pharmacist, Premier recognized a need to improve transparency in the wholesale distribution market. They pride themselves on transparency, innovation, and integrity.
- Q Laboratories, was selected by Premier to be the Program's Qualified Laboratory. Located in Cincinnati, Ohio, Q Laboratories is registered with FDA for pharmaceutical testing, and is cGMP/GLP Compliant and ISO/IEC 17025 Accredited. They are an independent laboratory with over 50 years of experience.

[9] Can be found in Appendix I.

[10] Can be found in Appendix I.

- Omega Tech Labs, selected by Premier to be the Program's relabeler, is a fully-integrated relabeler located in Boise, Idaho. They provide a range of relabeling support across multiple product categories. They are FDA registered and GMP compliant.
- Denver's Rocky Mountain Poison & Drug Safety (RMPDS), which has been serving the public since 1956, will be responsible for all FDA required adverse event reporting and will respond to consumer inquiries. RMPDS has decades of experience with handling medical information inquiries and safety reporting. RMPDS can fully integrate safety reporting intake processes with many different solutions for pharmacovigilance database management and reporting as required by the Final Rule. The Colorado team of pharmacists and nurses are rigorously trained to ensure they identify and capture appropriate information about any safety events or product quality complaints.

Overview of SIP Proposal

The Department, as a governmental entity of the state of Colorado, will be the SIP Sponsor and will provide oversight of the importation of FDA-approved drugs from Canada to deliver lower cost prescription drugs to Colorado consumers. The program framework establishes a robust oversight process to ensure compliance with the FDCA, including Section 804 and the provisions added by the Drug Supply Chain Security Act (DSCSA). The Department will house a Drug Importation Division (DID, or Division), which will manage the Canadian importation drug list and oversee the activities of all participants in the supply chain to ensure compliance with operational and safety requirements.

Colorado's SIP will leverage the current U.S. drug distribution system, which already relies heavily on drugs manufactured abroad. For example, the FDA estimates that 78% of active pharmaceutical ingredient (API) manufacturers are located outside the U.S.[11] Colorado's program will negotiate directly with manufacturers to arrange an agreed-to price for the purchase of prescription drugs from FDA-approved manufacturers through FDA-approved facilities. Prescription drugs approved for the program will be the same as the current FDA-approved versions. Additionally, all eligible drugs imported through Colorado's program will be trackable and traceable and in compliance with the DSCSA.[12]

The Department will work with its named Canadian Foreign Seller, AdiraMedica, to ensure all safety requirements are met, including ensuring that a Section 804 serial identifier (SSI) is assigned and affixed, if necessary, before entering the Colorado market. AdiraMedica and the Program's Importer, Premier Pharmaceuticals, will arrange for the importation of eligible prescription drugs from Mississauga, Ontario, Canada to the United States, in compliance with the requirements of the Final Rule.

Imported medications will enter the U.S. Customs and Border Patrol (CBP) port of entry in Buffalo, New York, and be shipped to the Premier Pharmaceuticals' secure distribution facility. They will be quarantined in a secured holding cage, separate from Premier's other stock. Premier will coordinate the testing of a statistically valid sample with Q Laboratories to ensure that the drug is authentic and has not degraded. The results of those tests will be submitted to the FDA for review and approval. During the testing process, the imported

[11] U.S. Food and Drug Administration. 2022. Fact Sheet: FDA at a Glance. https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance

[12] U.S. Food and Drug Administration. 2022. Drug Supply Chain Security Act (DSCSA). https://www.fda.gov/drugs/drug-supply-chain-integrity/drug-supply-chain-security-act-dscsa

prescription drugs will remain in quarantine. Once cleared for distribution by the FDA, Premier will arrange for the transport of the imported eligible drugs to Omega Tech Labs to be relabeled in accordance with the Final Rule.

Premier will contract with pharmacy providers in Colorado that have agreed to stock and dispense drugs imported from Canada under the approved SIP. Our proposed importation program will provide consumers, carriers, PBMs, hospitals and doctors in Colorado with access to drugs imported from Canada through a variety of sources, including community pharmacies and mail order pharmacies. Once relabeled, Premier will organize the secure distribution of imported drugs to participating entities.

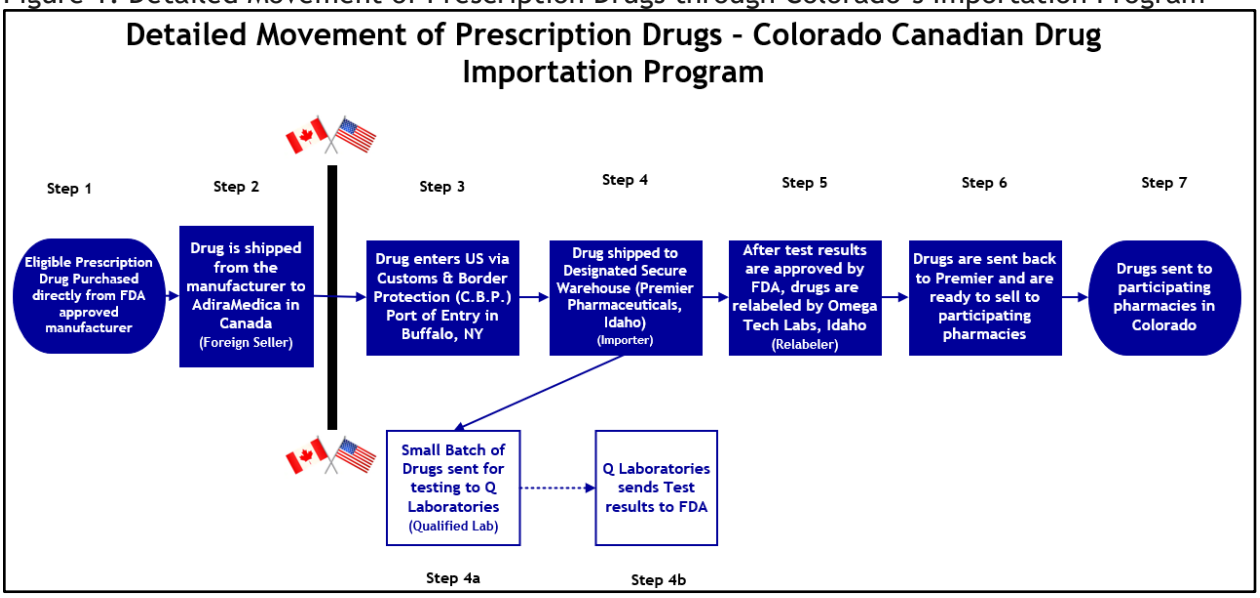
Any drug imported under the importation program and available for purchase in the state of Colorado will fall under the jurisdiction of the FDA. The Colorado State Board of Pharmacy will continue to regulate the receipt, storage, and proper dispensing of these drugs (like any other prescription drug) pursuant to valid, patient-specific orders once the drug is received by a Colorado-based, Board-registered pharmacy. In addition, as a wholesaler registered to distribute in Colorado, Premier will be subject to the same regulatory oversight as any other registered wholesaler in the state.

RMPDS, as the program's reporting partner, will support meeting compliance-related obligations by ensuring all aspects of reporting and recordkeeping for adverse events and pharmacovigilance are maintained for the program and that adequate education is provided for employees. When each eligible drug is relabeled, that label will contain contact information that consumers can use to report a safety event.

The HCPF DID will also work with Premier and RMPDS to conduct an educational outreach program to ensure pharmacists, health care providers, and patients are educated about the program. Upon SIP approval, the Department's drug importation website will be expanded to include more detailed information about the program, including information specifically for health care professionals and consumers. Consumers and providers will be able to find the names and National Drug Codes (NDC) of all drugs imported from Canada as well as a list of all participating pharmacies. There will also be information on how to report safety events and a consumer support line, hosted by RMPDS, where consumers can call for additional information on the program. A section of the website for participating pharmacies will include a link to a secure online platform hosted by Premier where pharmacies can view available drugs and place orders.

Figure 1, below, provides a process map illustrating the life cycle of a prescription drug imported to Colorado:

Figure 1. Detailed Movement of Prescription Drugs through Colorado's Importation Program



Colorado Department of Health Care Policy & Financing, 2022.

Eligible Drugs

The drug list presented in this SIP is aspirational in nature, due to the need for negotiations with drug manufacturers to secure agreements for drugs to be included in the program. That said, all drugs included are high cost or high volume drugs that Colorado consumers struggle to afford and will certainly be our starting point in future conversations with manufacturers.

The drug list includes 112 unique drugs and dosages. The HCPF DID has conducted an analysis of cost savings through the proposed importation program. All of the data is Colorado-specific, using data from the Colorado All Payer Claims Database (CO APCD) to estimate savings in the commercial market in Colorado. All of the drugs included on this list are eligible for importation per the framework laid out in the Final Rule.

Importation presents a unique opportunity to bring meaningful savings—$53 to $88 million annually and an average of 65% on drugs included on this list—to Colorado through a market-based solution.

A list identifying drugs Colorado intends to import and their associated percent savings is on page 15. A full drug list including all details specified in the Final Rule can be found in Appendix D.

Challenges and Opportunities

While the Department looks forward to receiving FDA approval for this SIP application, we are preparing to overcome barriers to success. Some parties, who enjoy the benefits of the status quo, stand ready to litigate and push back on our program through policy and other mechanisms. Also, we recognize that the Final Rule's framework may limit our ability to achieve our cost savings goals. Key areas of concern are explained below:

Lack of Federal Approval Timeframes

The Final Rule does not provide clarity around the timeline or process for review and approval of a SIP application, nor does it provide any opportunity to obtain a provisional approval from

the FDA. As the Department highlighted in its Final Rule comment letter, an indication from the FDA regarding a provisional approval would assist the state in negotiations with manufacturers and in obtaining partnership commitments from carriers and PBMs. Showing progress towards an approval will provide momentum for our program and encourage more stakeholder engagement.

Canadian Concerns
Concern among various Canadian stakeholders regarding the potential for drug shortages in Canada resulting from an approved importation program has been reported. The state of Colorado commits to monitoring current and potential shortages and will not import any drug impacted by a shortage. In addition, the state has encouraged the U.S. government to embark on a diplomatic effort to bolster importation programs to ensure that Canadian officials are hearing directly from our federal partners about the importance of protecting the Canadian drug supply.

Potential for Retaliation in a Limited Supply Chain
Per the Final Rule, a SIP may only name one Canadian Foreign Seller and one U.S. Importer. Colorado has concerns that limiting the Foreign Seller to only one entity will not only limit the number of drugs that we can access through manufacturer negotiations, but also open the Foreign Seller to retaliation from non-participating manufacturers or wholesalers that oppose our program's success.

Manufacturer Resistance
Due to manufacturer contracts with Canadian wholesalers that bar the exportation of drugs to the U.S., the HCPF DID and the program's Foreign Seller will embark on a negotiation process to identify manufacturers that agree to supply eligible drugs for Colorado's program. We have already met some initial resistance, particularly with brand name drugs. Importation programs offer a unique opportunity for pharmaceutical companies to address high costs for consumers while also sidestepping the veiled rebate and fee structure that defines the American pharmaceutical market.

Wholesale Distribution and Pharmacy Participation
While we have received some interest in our program, there are concerns from pharmacies that participation in the importation program may negatively impact current primary wholesale contracts. In most cases, primary wholesalers have volume guarantee requirements attached to discounts. While we believe that the benefit of importation savings should outweigh these concerns, pharmacy hesitancy remains a challenge to overcome. The HCPF DID is also exploring a mail order pharmacy option as a potential solution to these contractual issues.

Insurance Industry Hesitation
Carriers and PBMs have been open to conversations with the Department about the opportunities presented by importation but have generally appeared hesitant to explore partnerships or the inclusion of imported drugs in their benefit designs. The Department believes this is due to perverse incentives created by the rebate structure and the impact to their related profits. The HCPF DID has gained a commitment from the Colorado state employee program to explore the inclusion of imported drugs in future pharmacy benefits for Colorado state employees. Additionally, we are looking at how to include a requirement to cover imported drugs in the state's upcoming PBM bidding process. This partnership is a promising first step to ensuring access to Colorado consumers through a pilot with a trusted

partner. We hope carriers and PBMs will consider exploring innovative strategies with the state to achieve these lower cost options for consumers.

Final Drug List & Cost Savings (§ 251.3 (e) 1, 5-6, 9)

Colorado's final drug list contains 112 unique drugs and dosages, including medications that treat a number of conditions including respiratory illnesses, cancer, Type 2 diabetes, HIV and multiple sclerosis. To secure drug supply for Colorado's SIP, the program's Foreign Seller, in collaboration with the HCPF DID, will negotiate directly with manufacturers. These negotiations are ongoing and therefore, the list presented is aspirational and the HCPF DID will amend this SIP as we finalize manufacturer agreements. The list presents high cost, high volume drugs using Colorado-specific data from our All Payer Claims Database (APCD). All of these medications have a significant impact on affordability in the state—from employers and health plans to consumers. These drugs are integral to the everyday lives of Coloradans, representing, in many cases, lifesaving solutions if lower prices can be achieved. This section complies with all Final Rule requirements regarding submission of a drug list and demonstration of cost savings.

Methodology
The HCPF DID developed an extensive methodology to identify good candidates for importation and evaluate the estimated cost savings of Colorado's SIP. While this analysis provides a solid foundation for evaluating cost savings, the fact that imported drugs will vary based on which manufacturers, health plans, and providers participate in the program provides limitations to our findings.

The drug list was created using data from the CO All Payer Claims Database (CO APCD),[13] which is made up of claims data submitted by payers in the state. Twenty-five commercial payers currently submit pharmacy claims data to the CO APCD, representing about 1.3 million individuals across the state.[14] The Department recognizes that the CO APCD does not represent all Coloradans served by the private or commercial market. In fact, we estimate that the CO APCD does not include data for about 37% of Coloradans who are largely covered by self-funded, employer-sponsored programs that do not share data with the state's APCD.[15] The estimates for coverage were drawn from the "2021 Colorado Health Access Survey: Health Insurance Coverage" published by the Colorado Health Institute.[16]

---

[13]Center for Improving Value in Health Care. (2022) Colorado All Payer Claims Database. https://www.civhc.org/get-data/whats-in-the-co-apcd/

[14]Center for Improving Value in Health Care. (2022) Colorado All Payer Claims Database. https://www.civhc.org/get-data/co-apcd-overview/data-submission/

[15] To identify the gaps in the CO APCD, the Department started with the estimated 2021 Colorado population which is 5.81 million. The estimated number of commercially covered Colorado lives is 56.1%, which is derived from data in the 2021 CHSI survey. There are an estimated 3,259,410 commercially covered lives in Colorado (56.1% of the estimated CO population). CIVHC estimates that there are 2,069,560 individuals represented in their data which is 63% of the total commercial lives in Colorado. Therefore, 37% percent of Coloradans who are largely covered by self-funded, employer-sponsored programs are not included in the CO APCD. To account for these claims, we assumed similar utilization rates to APCD claims, but a lower cost per claim of 10% to account for the stronger negotiating power of larger self-funded employers. These assumptions are embedded in our methodology to arrive at the estimated savings.

[16] Colorado Health Institute. (2021) Colorado Health Access Survey. https://www.coloradohealthinstitute.org/research/colorado-health-access-survey-2021

As part of our savings analysis, the Department evaluated the 2,000 most expensive brand name and generic drugs for 2021. The identified drugs were compiled into a master list and checked against the Final Rule requirements and the eligible prescription drug exclusions of Section 804 to create a final list of potential prescription drugs for importation. Any drug on this list that was found to have a current Canadian shortage was excluded from further analysis.

Once the drug list was finalized, the Department compared the Colorado APCD pricing with Canadian pricing primarily using data from the July 2022 Quebec Province's "List of Medications."[17] The prices reflected on the Quebec list are the "guaranteed selling price," which is defined as the price at which it is sold by an accredited manufacturer or wholesaler to pharmacies. When Quebec data was unavailable, the Department used Ontario pricing or wholesale prices supplied by our Foreign Seller.

All Canadian prices were then converted to U.S. dollars and a 50% markup was applied to each unit price to cover estimated costs of the supply chain.

Finally, the cost savings estimate within this SIP proposal assumes that all drugs identified by the Department would be available for importation.

Our complete list, organized by drug category, is outlined below in Figure 2. The italicized listings are generic versions of the brand name drugs that precede them. In Appendix D, all drug list details are found including names, application numbers, Canadian Drug Identification Numbers (DINs) and NDCs, as well as other details required by the Final Rule.

[17] Quebec Formulary from 9/16/22, accessed September & October 2022. https://www.ramq.gouv.qc.ca/en/media/13896.

Figure 2. Final Drug List

Drug Name	Strength	Broad Category	Brand/ Generic	U.S. Price	Importation Price	Percent Savings
EpiPen Jr	0.15mg	Anaphylaxis	Brand	$224.94	$91.13	59%
epinephrine	*0.15mg*	*Anaphylaxis*	*Generic*	*$124.50*	*$91.13*	*27%*
EpiPen	0.3mg	Anaphylaxis	Brand	$264.89	$91.13	66%
epinephrine	*0.3mg*	*Anaphylaxis*	*Generic*	*$116.97*	*$91.13*	*22%*
Eliquis	2.5mg	Blood Thinner	Brand	$5.75	$1.80	69%
Eliquis	5mg	Blood Thinner	Brand	$6.22	$1.80	71%
Xarelto	2.5mg	Blood Thinner	Brand	$7.06	$1.60	77%
Xarelto	10mg	Blood Thinner	Brand	$13.73	$3.20	77%
Xarelto	15mg	Blood Thinner	Brand	$12.58	$3.20	75%
Xarelto	20mg	Blood Thinner	Brand	$12.99	$3.20	75%
Afinitor	5mg	Cancer	Brand	$496.46	$209.25	58%
everolimus	*5mg*	*Cancer*	*Generic*	*$260.92*	*$57.00*	*78%*
Afinitor Disperz	2mg	Cancer	Brand	$534.05	$238.32	55%
Afinitor Disperz	3mg	Cancer	Brand	$487.99	$238.32	51%
Afinitor Disperz	5mg	Cancer	Brand	$432.91	$238.32	45%
Cabometyx	20mg	Cancer	Brand	$586.42	$330.00	44%
Cabometyx	40mg	Cancer	Brand	$736.78	$330.00	55%
Cabometyx	60mg	Cancer	Brand	$719.57	$330.00	54%
Erleada	60mg	Cancer	Brand	$92.97	$31.88	66%
Ibrance**	100mg	Cancer	Brand	$516.16	$285.65	45%
Ibrance**	125mg	Cancer	Brand	$547.51	$285.65	48%

Ibrance**	75mg	Cancer	Brand	$524.56	$285.65	46%
Sprycel	50mg	Cancer	Brand	$262.22	$82.31	69%
Sprycel	100mg	Cancer	Brand	$476.49	$164.63	65%
Tasigna	200mg	Cancer	Brand	$144.33	$39.65	73%
Votrient	200mg	Cancer	Brand	$125.05	$38.71	69%
Xtandi	40mg	Cancer	Brand	$74.40	$31.88	57%
Zytiga	500mg	Cancer	Brand	$178.91	$63.75	64%
Xeljanz XR	11mg	Chronic Inflammatory Diseases	Brand	$145.43	$51.97	64%
Restasis	0.05%	Dry Eye	Brand	$8.28	$4.53	45%
*cyclosporin**	*0.05%*	*Dry Eye*	*Generic*	*$6.63*	*$1.54*	*77%*
Restasis Multidose	0.05%	Dry Eye	Brand	$87.79	$41.32	53%
Biktarvy*	50-200-25mg	HIV	Brand	$105.24	$44.12	58%
Cabenuva* (2mL)*	400-200mg	HIV	Brand	$4,160.48	$1,537.08	63%
Cabenuva* (3mL)*	600-300mg	HIV	Brand	$6,240.71	$3,074.14	51%
Descovy	200 -25mg	HIV	Brand	$54.36	$32.30	41%
Edurant	25mg	HIV	Brand	$41.83	$15.53	63%
Genvoya	150-150-200-10mg	HIV	Brand	$101.78	$49.28	52%
Odefsey	200-25-25mg	HIV	Brand	$92.40	$44.13	52%
Symtuza	800-150-200-10mg	HIV	Brand	$128.70	$63.24	51%
Tivicay	50mg	HIV	Brand	$50.73	$20.81	59%

Triumeq	600-50-300mg	HIV	Brand	$93.68	$45.64	51%
Xifaxan	550mg	Irritable Bowel Syndrome	Brand	$41.01	$8.64	79%
Baqsimi	3mg	Low Blood Sugar	Brand	$276.04	$148.05	46%
GlucaGen HypoKit	1mg	Low Blood Sugar	Brand	$284.88	$128.90	55%
Glucagon	1mg	Low Blood Sugar	Brand	$241.27	$86.74	64%
Latuda	20mg	Mental Health	Brand	$42.07	$4.02	90%
Latuda	40mg	Mental Health	Brand	$42.73	$4.02	91%
Latuda	60mg	Mental Health	Brand	$42.74	$4.02	91%
Latuda	80mg	Mental Health	Brand	$43.44	$4.02	91%
Copaxone	20mg	Multiple Sclerosis	Brand	$209.45	$48.60	77%
Glatopa	*20mg*	*Multiple Sclerosis*	*Generic*	*$72.88*	*$36.45*	*50%*
glatiramer	*20mg*	*Multiple Sclerosis*	*Generic*	*$127.40*	*$36.45*	*71%*
Copaxone	40mg	Multiple Sclerosis	Brand	$424.64	$138.22	67%
glatiramer	*40mg*	*Multiple Sclerosis*	*Generic*	*$213.28*	*$138.22*	*35%*
Gilenya	0.5mg	Multiple Sclerosis	Brand	$287.33	$95.81	67%
Revolade	25mg	Primary Immune Thrombocytopenia	Brand	$167.85	$59.06	65%
Revolade	50mg	Primary Immune Thrombocytopenia	Brand	$295.36	$118.13	60%
Uptravi	1400 mcg	Pulmonary Arterial Hypertension	Brand	$215.31	$72.19	66%

Ofev	100mg	Pulmonary Fibrosis	Brand	$151.57	$31.28	79%
Ofev	150mg	Pulmonary Fibrosis	Brand	$156.52	$61.16	61%
Advair Diskus	100-50mcg	Respiratory	Brand	$252.95	$85.26	66%
fluticasone & salmeterol diskus	*100-50mcg*	*Respiratory*	*Generic*	*$153.34*	*$47.71*	*69%*
Wixela Inhub	*100-50mcg*	*Respiratory*	*Generic*	*$94.47*	*$47.71*	*49%*
Advair Diskus	250-50mcg	Respiratory	Brand	$314.88	$102.03	68%
fluticasone & salmeterol diskus	*250-50mcg*	*Respiratory*	*Generic*	*$186.75*	*$57.11*	*69%*
Wixela Inhub	*250-50mcg*	*Respiratory*	*Generic*	*$103.63*	*$57.11*	*45%*
Advair Diskus	500-50mcg	Respiratory	Brand	$408.84	$102.03	75%
fluticasone & salmeterol	*500-50mcg*	*Respiratory*	*Generic*	*$209.21*	*$81.07*	*61%*
Wixela Inhub	*500-50mcg*	*Respiratory*	*Generic*	*$124.72*	*$81.07*	*35%*
Advair HFA	115-21mcg	Respiratory	Brand	$350.92	$144.83	59%
Advair HFA	230-21mcg	Respiratory	Brand	$442.56	$144.83	67%
Combivent Respimat	20-100mcg	Respiratory	Brand	$373.87	$34.14	91%
Dulera	100-5mcg	Respiratory	Brand	$298.87	$87.75	71%
Dulera	200-5mcg	Respiratory	Brand	$322.78	$108.00	67%
Flovent HFA	44mcg	Respiratory	Brand	$179.06	$25.44	86%
*Fluticasone HFA**	*44mcg*	*Respiratory*	*Generic*	*$132.95*	*$39.51*	*70%*
Flovent HFA	110mcg	Respiratory	Brand	$235.61	$42.81	82%

*Fluticasone HFA**	*110mcg*	*Respiratory*	*Generic*	*$177.99*	*$39.50*	*78%*
Flovent HFA	220mcg	Respiratory	Brand	$353.25	$85.62	76%
*Fluticasone HFA**	*220mcg*	*Respiratory*	*Generic*	*$276.46*	*$50.65*	*82%*
Pulmicort	90mcg	Respiratory	Brand	$170.01	$34.76	80%
Pulmicort	180mcg	Respiratory	Brand	$233.01	$71.06	70%
Spiriva Handihaler	18mcg	Respiratory	Brand	$377.35	$58.39	85%
Spiriva Respimat	2.5mcg	Respiratory	Brand	$324.04	$58.39	82%
Trelegy	100-62.5-25mcg	Respiratory	Brand	$237.37	$148.73	37%
Trelegy	200-62.5-25mcg	Respiratory	Brand	$255.26	$186.67	27%
Ventolin	90mcg	Respiratory	Brand	$54.00	$6.75	87%
Albuterol Inhaler	*90mcg*	*Respiratory*	*Generic*	*$25.97*	*$5.63*	*78%*
Chantix	0.5mg	Smoking Cessation	Brand	$7.88	$1.93	75%
varenicline	*0.5mg*	*Smoking Cessation*	*Generic*	*$7.69*	*$1.04*	*87%*
Chantix	1mg	Smoking Cessation	Brand	$8.35	$1.93	77%
varenicline	*1mg*	*Smoking Cessation*	*Generic*	*$7.50*	*$1.04*	*86%*
Synthroid	100mcg	Thyroid Deficiency	Brand	$0.95	$0.07	93%
Farxiga	5mg	Type 2 Diabetes	Brand	$14.09	$2.76	80%
Farxiga	10mg	Type 2 Diabetes	Brand	$14.59	$2.76	81%
Invokana	100mg	Type 2 Diabetes	Brand	$15.89	$2.94	81%

Invokana	300mg	Type 2 Diabetes	Brand	$15.78	$2.94	81%
Janumet	50/500mg	Type 2 Diabetes	Brand	$6.29	$1.54	75%
Janumet	50/1000mg	Type 2 Diabetes	Brand	$6.18	$1.54	75%
Januvia	25mg	Type 2 Diabetes	Brand	$12.87	$2.94	77%
Januvia	50mg	Type 2 Diabetes	Brand	$12.38	$2.94	76%
Januvia	100mg	Type 2 Diabetes	Brand	$12.90	$2.94	77%
Jardiance	10mg	Type 2 Diabetes	Brand	$15.78	$2.94	81%
Jardiance	25mg	Type 2 Diabetes	Brand	$15.47	$2.94	81%
Victoza	18mg/3mL	Type 2 Diabetes	Brand	$266.97	$77.05	71%
Nuvaring	2.6mg - 11.4 mg	Women's Health	Brand	$142.71	$14.11	90%
EluRyng	*2.6mg - 11.4 mg*	*Women's Health*	*Generic*	*$84.63*	*$14.11*	*83%*
ethinyl estradiol/ etonogestrel	*2.6mg - 11.4 mg*	*Women's Health*	*Generic*	*$92.01*	*$14.11*	*85%*
Estring	2mg	Women's Health	Brand	$415.69	$70.62	83%
Kyleena	19.5mg	Women's Health	Brand	$888.16	$403.50	55%
Mirena	52 mg	Women's Health	Brand	$547.62	$431.21	21%

Department of Health Care Policy & Financing, 2022.

Significant Savings

This SIP meets Final Rule requirements to demonstrate significant cost savings, providing details on uncertainties that may influence our success. Colorado has requested flexibility from the FDA in the interpretation of significant savings given the need for state-led programs to begin with narrower lists of drugs and expand over time.

Estimated Savings
Our detailed evaluation finds that the Colorado SIP has the potential to provide an estimated $53 to $88 million in annual savings, if all 112 drugs on the list were to be imported. The analysis shows an average of 65% savings across all drugs. The range of savings depends on the degree of adoption in the market. Rather than assume a 100% adoption of imported drugs across the market, Colorado conservatively estimates a 15-25% replacement within the market, as illustrated in Figure 3, below.

Figure 3. Colorado Drug Spend and Potential Savings by Market Replacement

Colorado Drug Spend and Potential Savings by Market Replacement			
Annual Drug Spend (Commercial Market)	**Estimated Annual Importation Spend**	**Potential Savings**	**Market Replacement Percent**
$134,639,802	$47,012,296	$87,627,506	25%
$80,783,881	$28,207,378	$52,576,504	15%
Colorado Department of Health Care Policy & Financing, 2022			

While we have presented cost savings estimates for all 112 drugs on our list, market adoption is dependent on manufacturer and health plan adoption and therefore these estimates serve only as a guide for estimating potential importation savings. The HCPF DID anticipates that partnerships with manufacturers will be modest in the early years, thereby limiting the number of drugs and associated volume that can be imported through the program. Further, health plan coverage of imported eligible drugs will significantly impact market adoption and access for Colorado consumers. Given these two factors, we see our initial program as a pilot— a meaningful opportunity to demonstrate Colorado's capability to administer the program and bring in cost savings, even if only modest in the early years. With this in mind, and with the lack of specific FDA guidance on how to demonstrate cost savings, Colorado's conservative approach to the early phase of this program should be considered sufficient in meeting the cost savings requirement in Section 804 and the Final Rule.

Brand and Generic Savings
We have always known that the most impactful savings through importation would be seen in the brand name drug space. Brands account for 80% of our drug list, and 92% of our SIP savings come from the importation of brand name drugs. However, through deeper analysis we found that there are opportunities for savings from generic drugs as well. U.S. generics are generally lower priced than their brand name counterparts, but our analysis finds that some Canadian generics may provide even lower pricing than U.S. generics or Canadian brands:

Figure 4. Price Comparisons for U.S. and Canadian Brands and Generics

Price Comparisons for U.S. and Canadian Brands and Generics				
Name	**U.S. Brand**	**U.S. Generic**	**Imported Brand**	**Imported Generic**

Nuvaring	$142.71	$92.01	$14.11	$14.11
Ventolin	$54.00	$25.97	$6.75	$5.63
Chantix	$8.35	$7.50	$1.93	$1.04
Colorado Department of Health Care Policy & Financing, 2022.				

Including both brand and generic versions of a drug on our drug list was intentional so that we may have broad flexibility to pursue partnerships with a variety of manufacturers. Our early research finds that generic drug manufacturers may be early adopters of the program.

Cost Savings Examples
To understand the significance of the estimated cost savings, it is important to consider the impact of importation for individual consumers across Colorado. Importation could lower costs for patients on medications that are not fully covered by insurance plans, for vulnerable populations such as children and seniors, and for those paying out-of-pocket for their medications. Colorado hopes that as the program grows, health plans will show more interest in covering imported eligible drugs. We would hope that insurers would provide reduced cost sharing or co-pays for imported drugs. Importation would greatly benefit consumers across the state through a variety of mechanisms, regardless of how they currently pay for their prescription drugs. Cost savings examples are provided below:

- **Latuda** is a staggering example of savings from Colorado's importation program with a 90% savings. For a month's supply of this highly utilized drug used to treat schizophrenia, a Coloradan without insurance coverage could expect to pay nearly $1,500. Colorado's SIP could supply an imported version to close to $120 per month. For those with insurance coverage, cost varies depending on how the drug is covered on benefit formularies, but this would account for a significant savings to the plan and could result in potential significant savings for consumers if plans were to pass the savings on to patients in the form of a zero-dollar co-pay.

- **Jardiance** is a non-insulin drug used to treat Type II diabetes. It can cost a cash paying patient more than $550 out-of-pocket for a one-month supply in the United States. For a patient who does not have insurance or who has a high deductible health plan, purchasing the same drug through Colorado's SIP would cost around $90 for a one-month supply, a savings of more than 80%, or around $460 per month.

- The cost of inhalers in the U.S. have, in general, remained stubbornly high despite generic competition—a reality that is underscored by the lower prices of their Canadian counterparts. For example, **Flovent HFA** 110mcg and its generic **fluticasone** can be imported for an average of 82% and 78% less, respectively.

Next Steps
Once this SIP is approved, we believe that our success in securing manufacturer and health plan partnerships will increase. Health plans' hesitancy has, in part, been due to skepticism that Colorado's program will receive a federal approval. Potential manufacturer partners will be seeking commitments from health plans for volume guarantees in order to justify their participation. In order to enhance the cost savings opportunity, collaboration with these two partners is of utmost importance.

Once eligible drugs are distributed to Colorado pharmacies, the program must ensure Coloradans, insured and uninsured, can access these products. Pharmacy stakeholders have told us anecdotally that more than 90% of their customers are insured patients. To adequately address access, drugs imported under this program must be covered by prescription drug benefits. To date, the HCPF DID has received soft resistance from Colorado health plans and their owned or affiliated PBMs. This is expected given that health plans and PBMs benefit too greatly from the existing rebate structure to remove even a single drug from that calculation.

This said, we believe that purchasers may be the greatest lever with health plans and PBMs to advance our program. Our efforts to pilot importation within the state employee program hold great promise. The Department has been encouraged by early discussions and collaboration with the Colorado Department of Personnel Administration (DPA) to include provisions in its upcoming PBM reverse auction that support the adoption of imported drugs on state employee formularies.

This list provided herein is a starting point. The HCPF DID looks forward to targeting many of the drugs included in the list in conversations with manufacturers. Drug importation programs present a unique opportunity for manufacturers to partner with states seeking to lower costs. Colorado's importation program aims to acquire prescription drugs at a price before rebates and inflationary practices of the supply chain. This transparent market-based solution does not aim to apply band-aids to an opaque and arduous system, but is solely focused on lowering the underlying cost of a prescription drug. The state of Colorado welcomes discussion with interested manufacturers and health plans who wish to be part of the solution.

Technical Section 804 Importation Program

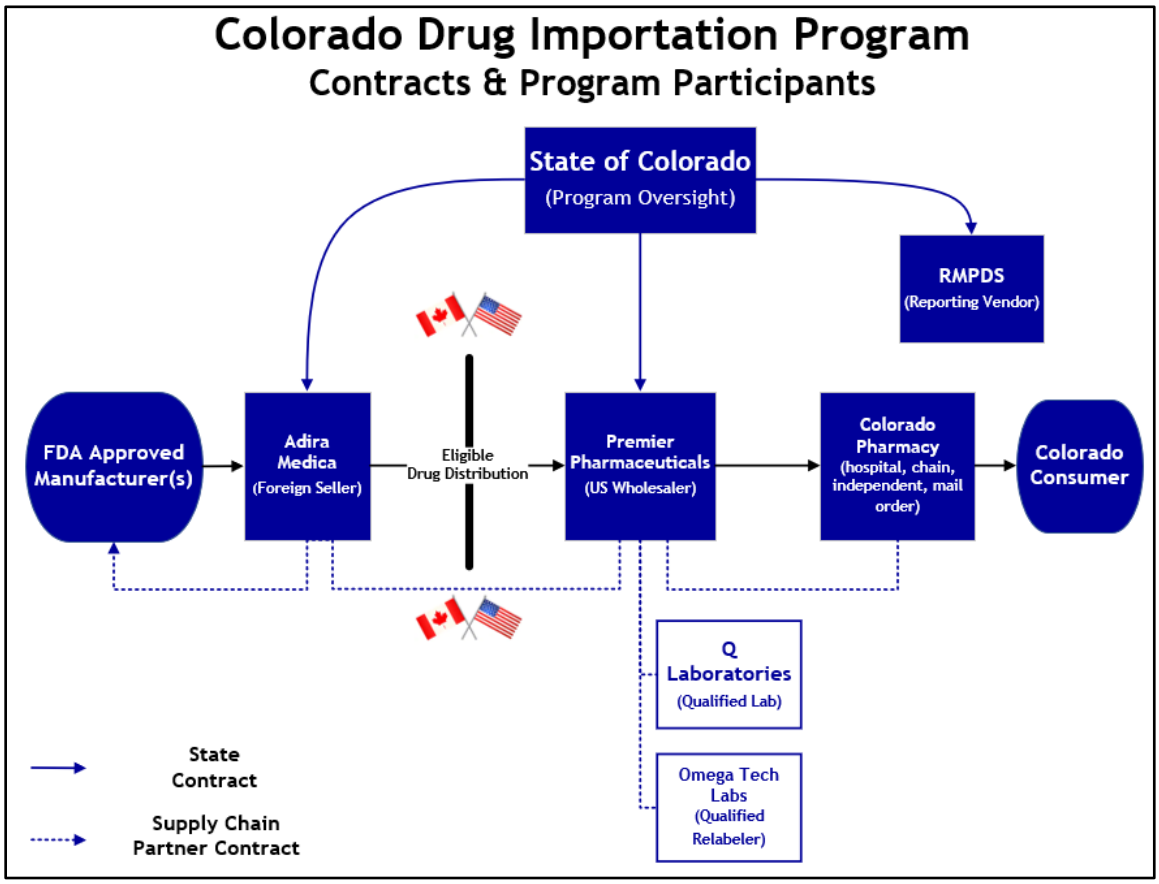
Below is Colorado's technical response to the regulatory standards set forth in the Final Rule. We have included a reference at the start of each section that outlines which regulatory requirements are addressed in the subsequent response.

Legal and Organizational Structure (§ 251.3 (e) 1-4)
The Colorado SIP is sponsored by the Colorado Department of Health Care Policy & Financing (the Department), which is the state agency that administers Health First Colorado (Colorado's Medicaid program), and is authorized to submit this SIP application and oversee an approved program. The SIP is operated by the Department's Drug Importation Division (HCPF DID) which has been fully operational since August 2019. It is important to note that Colorado's SIP is focused on the commercial market in Colorado but may explore an expansion to Health First Colorado in the future. Colorado's program does not have any co-sponsors.

The Department has executed contracts with three primary entities that make up the supply chain for the program. These entities are: the Foreign Seller (AdiraMedica), which is a U.S. licensed wholesaler with a Canadian licensed subsidiary; the Importer (Premier Pharmaceuticals), which is a U.S. and Colorado licensed wholesaler headquartered in Boise, Idaho; and the reporting partner (Rocky Mountain Poison and Drug Safety), which is a U.S.-based adverse event, pharmacovigilance, and poison control center in Denver, Colorado. The below graphic shows the contractual relationships among all parties in the SIP.

Figure 5 demonstrates the legal relationships among supply chain and other partners required per the Final Rule.

Figure 5. Legal relationships among the state of Colorado and identified partners.



Colorado Department of Health Care Policy & Financing, 2022.

Aside from Department-executed contracts, AdiraMedica and Premier Pharmaceuticals will maintain a quality agreement and contract that creates the framework for the purchase and exportation of eligible drugs. AdiraMedica will also hold contracts with participating manufacturers that detail volume and price commitments. Premier Pharmaceuticals holds a contract with a qualified laboratory and a relabler. Premier Pharmaceuticals will also execute contracts with participating pharmacies.

Colorado Department of Health Care Policy & Financing's Drug Importation Division (HCPF DID)
The Division is made up of two Full Time Equivalent (FTE) employees—a Program Manager and a Drug Importation Pharmacist. The HCPF DID has a yearly appropriation for additional FTE, should they be needed. This Division sits within the Department's Pharmacy Office and is overseen by the Director and Deputy Director of the Office. The Department's Executive Director is also involved in program implementation from a strategic perspective. The team is listed in the table below in hierarchical order.

Figure 6. SIP Sponsor Leadership and Support Team

State of Colorado	Role
Kim Bimestefer, Executive Director of the Colorado Department of Health Care Policy & Financing	Strategic guidance, program advocacy
Tom Leahey, Director of Pharmacy Office	Day to day support and advisement
Jim Leonard, Deputy Director of Pharmacy Office	Day to day support and advisement
Lauren Reveley, Drug Importation Program Manager	Program oversight, operations and communications, management, procurement and implementation
Kelly Swartzendruber, Drug Importation Pharmacist	Clinical analysis, contract management, and program oversight

Contact information and attestations for Responsible Individuals is included in Appendix A.

Outside of this oversight framework, the Division is supported by the communications and policy infrastructure within the Department as well as a hired team of expert consultants. These consultants were carefully selected for their expertise in various areas of policy and operations integral in the development of the Importation Program.

Figure 7. Colorado's SIP Consultative Team

Consultative Subject Matter Experts	Role
AgoHealth LLC	Senior Advisor and Policy Consultant
Benjamin L. England & Associates, LLC	Food, Drug, and Cosmetic Act Experts
RC Kennedy Consulting LLC	Supply Chain Security Experts
Koerber Supply Chain	Supply Chain Security Experts
Prompt Praxis Laboratories, LLC	Qualified Laboratory Experts
LDT Health Solutions, Inc.	Qualified Laboratory Capacity Experts

To identify supply chain partners, Colorado conducted numerous interviews and negotiation sessions. During these meetings, the HCPF DID included our consultants as well, to ensure the HCPF DID received expert assessments of each candidate. The HCPF DID also conducted site visits to Importer and Foreign Seller candidates, and once selected by Premier Pharmaceuticals, the qualified laboratory and relabeler. Each site visit included members of the HCPF DID and consultants with expertise specific to the type of facility visited. Each facility was assessed for:

- Good Manufacturing Practice (GMP) compliance
- Robust standard operating procedures (SOPs) for their facilities, procedures, and systems
- Physical security
- Inventory management
- Employee training programs

The Foreign Seller
AdiraMedica Inc., a Canadian wholesaler located in Mississauga, Ontario, Canada, will fulfill the role of Colorado's Foreign Seller. AdiraMedica has been in business for 15 years, specializing in supply chain management including import/export for global clinical trials.

Figure 8. Foreign Seller Key Personnel

Key Personnel	Company	Expertise
Arvind Bhandari, Founder, President and CEO	AdiraMedica Inc., Canada	More than 25 years of pharmaceutical industry experience including, but not limited to, wholesale distribution, global supply chain management and global clinical trial supply services.
Cal Baines, Director of Business Development	AdiraMedica Inc., Canada	More than 15 years of pharmaceutical industry experience including, but not limited to, wholesale distribution, global supply chain management and global clinical trial supply services.
Arvind Bhandari, U.S. Agent	AdiraMedica LLC, U.S.	U.S. parent company of AdiraMedica Inc.

AdiraMedica's attestations, licenses, full inspection history, and disciplinary actions can be found in Appendix B.

The Importer
Premier Pharmaceuticals LLC, located in Boise, Idaho, will serve as Colorado's Importer. Founded in 2019 by a local Boise pharmacist, Premier recognized a need to improve transparency in the wholesale distribution market. Premier, as the Importer, is responsible for the importation, testing, relabeling and distribution of eligible prescription drugs to the Colorado market.

Premier has a contract with a qualified laboratory, Q Laboratories, to conduct the statutory testing required by the Final Rule. Q Laboratories, a qualified laboratory located in Cincinnati, Ohio, is registered with the FDA for pharmaceutical testing, and is cGMP/GLP

Compliant and ISO/IEC 17025 Accredited. Copies of all Q Laboratories' accreditations and inspection history are included in Appendix C.

Premier has a contract with a local Boise, Idaho relabeler, Omega Tech Labs. Omega is a fully FDA registered and GMP compliant relabeler. Copies of Omega Tech Labs' registration is included in Appendix C.

Figure 9. Importer Key Personnel

Key Personnel	Company	Expertise
Jacob Fuchs, President	Premier Pharmaceuticals	Pharmacist with broad experience including retail pharmacy management, wholesale distribution management and compliance.
Adrian Constance, Executive Vice President	Premier Pharmaceuticals	Background in clinical radiology with experience in wholesale distribution management and compliance.
Tanner Wollan, Vice President of Strategy	Premier Pharmaceuticals	Background in supply chain management which includes business management and wholesale management.
Ericka Valdez, Marketing Executive	Premier Pharmaceuticals	Marketing professional with over five years of experience in external marketing and communications, production and design.
Cathleen Owen, Director of Pharmaceutical and Personal Care Services	Q Laboratories	Thirty years of manufacturer industry, regulatory, and quality experience that she applied to laboratory and pharmaceutical analysis.
Steve Shackleford, Chief Commercial Officer	Omega Tech Labs	Twenty years of experience in the pharmaceutical manufacturing industry where he worked as a process development scientist in production of therapeutic proteins.

Premier Pharmaceuticals' attestations, licenses, full inspectional history, and disciplinary actions can be found in Appendix C. All required information for Q Laboratories and Omega

Tech Labs is also included in Appendix C.

The Reporting Partner

Denver's Rocky Mountain Poison and Drug Safety (RMPDS), which has been serving the public since 1956, will be responsible for all FDA required adverse event reporting and respond to consumer inquiries. One of the premier poison control centers in the nation, RMPDS can fully integrate safety reporting intake processes with many different solutions for pharmacovigilance database management and reporting as required by the Final Rule. The Colorado team of pharmacists and nurses are rigorously trained to ensure they identify and capture appropriate information about any adverse events or product quality complaints. Additionally, RMPDS will aid the Department in operationalizing a consumer call center through which RMPDS will respond to program questions and report to the Department on the nature of these inquiries.

Figure 10. Reporting Partner Key Personnel

Key Personnel	**Company**	**Expertise**
Dr. Theresa Chua, Pharmacist Contact Center Supervisor	Rocky Mountain Poison & Drug Safety	Dr. Theresa Chua handles day to day operations for multiple contracts regarding medical information and safety report intake. She develops and implements processes to ensure regulatory compliance in everyday case handling.
Dr. Christopher Hoyte, Medical Director	Rocky Mountain Poison & Drug Safety	Dr. Christopher Hoyte is the Medical Director of the Rocky Mountain Poison Center. He is also the Fellowship Director of the Medical Toxicology Fellowship Program at RMPDS. He is an Associate Professor at the University of Colorado School of Medicine in the Department of Emergency Medicine and the Section of Medical Toxicology. He currently serves as the Medical Director of the Medical Toxicology Clinic at the University of Colorado Hospital.

Brandon Ensign, Director of Medical Information	Rocky Mountain Poison & Drug Safety	Brandon Ensign currently oversees the Drug Center, which offers services to the pharmaceutical and biopharmaceutical industries in support of FDA regulation. He is also the Operations Director within the Poison Center at RMPDS.
Dr. Andrew Monte, Medical Director	Rocky Mountain Poison & Drug Safety	Dr. Andrew Monte specializes in medical toxicology, precision medicine, and genetic testing to improve medication effectiveness and safety. As an emergency physician and medical toxicologist, Dr. Monte is well positioned to examine efficacy and safety of drugs.

Compliance & Oversight Plan (§ 251.3 (e) 10, 15)

As the SIP Sponsor, the Department will be responsible for oversight and implementation of the compliance plan and the program more broadly once the SIP is approved. Staff in the HCPF DID will be fully dedicated to SIP implementation including ensuring compliance with the requirements of Section 804 of the FD&C Act [21 U.S.C. 384], the Final Rule on Importation of Prescription drugs (as codified at 21 CFR 1.74 and Part 251), the Drug Supply Chain and Security Act (DSCSA), other applicable provisions of the FD&C Act, its implementing regulations, and any applicable state regulations.

Ensuring Compliance

The HCPF DID will ensure compliance through the state's authorizing legislation, program infrastructure, and partner contract requirements.

Legislative Requirements

The importation program's state legislation, SB 19-005, ensures there are strong state statutory requirements placed on supply chain partners in support of Section 804. SB 19-005 requires:

- Statistically sampled batch shipment testing.
- Certifications for marketing, FDA-approved labeling and ensuring no drugs are misbranded or adulterated.

- Verification that all entities participating in a SIP are in compliance with DSCSA, including track and trace rules, and
- Maintenance of qualified laboratory records, including all testing data and documentation that the testing was conducted by a qualified laboratory.

The state statute also provides the state with oversight authority and responsibility to ensure compliance with federal policy rules and standards. This includes oversight of any vendor(s), regular monitoring of the importation drug list, and suspension of importation of any drug that is in violation of state statute or federal rules. This oversight role is enforced by the Department primarily through contractual relationships with supply chain partners.

Program Infrastructure & Contracting

The Department holds direct contracts with supply chain partners and these contracts outline specific requirements placed on such partners to ensure compliance with federal statute and related regulatory requirements. Both Importer and Foreign Seller contracts require that any subcontractor partners also comply with Section 804 requirements. Any non-compliance with contract requirements will be addressed through contract remedies such as holding the vendor in breach of contract or dissolving the contract for noncompliance.

The state's contracts with AdiraMedica and Premier Pharmaceuticals are much the same in terms of standards, reporting procedures, maintenance of licensures in good standing, and audits:

Figure 11. Contract Requirements for Supply Chain Partners

Area of Compliance	Contract Requirements
Statute & rules	• Must comply with all applicable federal and state laws, rules, and regulations, regarding the development and operation of an Importation Program.
Maintenance	• Maintain proper Stand Operating Procedures (SOPs) for all processes and procedures relating to the operation of the Program. • Maintain proper physical security, storage systems and temperature controls. • Create an importation implementation work plan that outlines all steps and processes needed to successfully import drugs. • Develop education, training, and certification processes to ensure that employees and subcontractors engaged with the Program understand their compliance-related obligations that must be followed.

	• Develop a process for the handling of pre-import requests (Pre-Import Process). • Develop and implement a recall and return plan. • Develop and implement plans to ensure subcontractor compliance.
Inspection & Audit	• The Department will inspect the facility that houses imported products for the Program at least every six months. • The Department will complete site visits of subcontractors involved in integral parts of the Program. • Provide all state/federal/Canadian inspection reports to the Department upon request.
Security & Capacity	• Comply with security and capacity requirements to ensure the safe and efficient distribution of imported products.
Monitoring & Reporting	• Maintain all DSCSA records with applicable T3 data to track and trace the drug through the supply chain. • Meet every 90 days with the Department during the first year of active importation. • Submit regular quarterly and annual reports. • Maintain a process to protect the anonymity of any complainants or whistleblowers regarding any Program concerns by contractor employees.
Qualified Personnel	• Provide qualified personnel as necessary to perform the work throughout the term of the contract.
Subcontractors	• The Department reserves the right to review all contracts and subcontracts relevant to the Program. • The Department will certify each subcontractor's ability to carry out the work of the Program.
Licensure	• Maintain all required licenses, permits, and/or registrations in good standing and provide documentation to the Department.
Termination	• The Department may terminate the contract based on any noncompliance with any requirements.
Continuity	• Must have an operational continuity plan in cases of emergency.

The Colorado Department of Health Care Policy & Financing's Drug Importation Division will maintain policies and procedures that govern how the program will operate and will approve all standard operating procedures submitted by the contracted supply chain vendors. The HCPF DID will be responsible for the following compliance functions, including, but not limited to:

- Ensuring staffing in the HCPF DID and with vendors is adequately maintained to operate the SIP.
- Maintaining contracts with all supply chain vendors and holding these partners accountable to contract requirements.
    - Verifying at least annually that Foreign Seller and Importer state licenses and federal registrations are up to date and determining whether any FDA actions have been taken against partners.
    - Ensuring that all contracted entities respond to HCPF DID and FDA inquiries in a timely manner.
    - Completing annual audits of supply chain partners and additional audits as appropriate, such as for non-compliance.
    - Conducting at least annual site visits to all supply chain entities and additional parties, as identified.
    - Approving all subcontract partners, all standard operating procedures for the Program, and major staffing changes in the organizations, as they impact the Program.
- In conjunction with the Foreign Seller, maintaining, updating and consistently analyzing the importation drug list to ensure savings for Coloradans are prioritized and that importation never negatively impacts Canadian drug supply.
    - Monitoring price agreements among the Foreign Seller and manufacturers.
    - Maintaining the list of available medications through the Program on a public website.
    - Monitoring the cost savings of the program.
- Registering all entities participating in the program annually, including pharmacies, hospitals, carriers and PBMs, and listing participating entities on our public website.
    - Ensuring these entities are properly licensed to operate in Colorado and that they agree to only dispensing or reimbursing imported products for Colorado residents.
- Establishing and regularly updating written compliance policies, procedures, and protocols to ensure compliance with the FDA-approved SIP and modify as regulatory changes occur.
- Developing auditing procedures to evaluate compliance and addressing any noncompliance or misconduct.
- Providing drug importation education and training for supply chain partners. Education will include, but is not limited to:
    - Overview of relevant state and federal statute and regulations regarding the program.
    - Partner specific processes and procedures relating to the operation of the program.
    - Storage and handling of prescription drugs.
    - How to identify counterfeits or adulterated products based on visual inspections.
    - Processes for recalls and returns.
    - Regulations regarding the relabeling of imported prescription drugs.

    - Regulations regarding the laboratory testing requirements for imported prescription drugs.
- Maintaining a SIP webpage with up-to-date information related to compliance and auditing as well as education for pharmacy partners.
- Staffing a helpline for compliance reporting (including tip line for whistleblowers) and to answer program questions and provide consumer support.
- In conjunction with the Importer and the Reporting Partner, developing and implementing a recall and return plan for medications imported through the SIP.
- Submitting required FDA reports in accordance with section 804 regulations, as well as state statutory reporting requirements.
- Responding to any FDA records requests.

Supply Chain Security and Adverse Events (§ 251.3 (e) 11)

A cornerstone of Section 804 is the requirement that a SIP may only be approved if it poses no additional risk to the United States' public health and safety. Section 804 and the Final Rule provide a robust framework for the implementation of Colorado's SIP from a health and safety perspective. The FDA's proven oversight and high standards for the drug supply chain help guarantee the safety and quality of the drugs that currently enter the United States from foreign sources. Further, the provisions set forth in the Drug Supply Chain Security Act (DSCSA), once fully implemented, ensure traceability of all products in the current U.S. supply chain.

In all supply chain vendor contracts, the state requires safe storage, handling and transportation practices, as well as robust screening procedures and reporting. All of our partners are required to have approved, program specific standard operating procedures in place, as well as program specific compliance training for all employees. As a SIP Sponsor, we will leverage existing state, federal and international regulatory frameworks and agreements to ensure the drug supply is safe. Additionally, per the Final Rule and our vendor contracts, we will ensure that all eligible prescription drugs imported for distribution to Colorado are in compliance with DSCSA track and trace requirements. Our contracts ensure that all necessary data regarding the transactions and movement of eligible drugs through our program are documented, reported, and maintained for at least seven years.

Supply Chain Facilities, Standards & Reporting

All storage facilities and vehicles used to store and transport eligible prescription drugs for Colorado's program must meet state and federal standards, including the facilities in Canada, as outlined in the Department's contracts. Additionally, all facilities under the Program, both in the U.S. and Canada, will be subject to at least annual inspections by the HCPF DID.

In the Department's contracts with AdiraMedica and Premier Pharmaceuticals we have set forth standards as follows:

- The facility must have adequate space, security and environmental conditions necessary for proper storage of prescription drugs, including a designated space that is for the sole purpose of quarantining, storing, and staging eligible prescription drugs for the Program.
- The facility shall maintain:
    - SOPs for all processes and procedures relating to the operation of the Program including, but not limited to: security, product handling, log books, adverse events, environmental conditions, employee access to products, facility management, distribution processes and employee training programs.

- Standard pharmaceutical wholesale security measures such as an alarm system, an internal and external security camera system, outdoor lighting, and a keycard or locking system.
- Storage systems designed specifically for the Program that allows for eligible drugs to be kept separate from the rest of the facility's inventory.
- Temperature control for all storage areas through an environmental monitoring system.

The Colorado Department of Health Care Policy & Financing attests that standards outlined above were evaluated and deemed in compliance during site visits with both partners. The HCPF DID and supply chain facility experts conducted site visits to both supply chain vendors as part of the negotiation and procurement process. The team visited AdiraMedica's Canadian headquarters and facility once and Premier's headquarters and facility twice throughout negotiations. Our third-party consultants have certified[18] that our partners have met the standards defined above and in the Final Rule.

The Department will also approve the use of any subcontractors, such as transportation providers, for the Program and conduct any necessary site visits to ensure that they also meet all standards set forth in state and federal law and regulation.

Supply chain partners will be responsible for frequent reporting to the HCPF DID and the FDA, as required and necessary. The HCPF DID will evaluate these reports and follow up with partners if any information is incomplete or potentially out of compliance with the requirements and take corrective action, if necessary. Required reporting is outlined in Figure 12, below.

Figure 12. Required Reporting for Colorado's Importation Program

Report	Provenance	Responsible Vendor	Submitted To	Cadence
Quarterly Importation Report	Final Rule	HCPF DID will submit on behalf of Importer	FDA, Cc the HCPF DID	Quarterly
NDA and ANDA Field Alert Reports	Final Rule	Importer	FDA and manufacturers of imported medications	When quality issues are discovered
Reporting for Combination Products	Final Rule	Importer	FDA and manufacturers of imported medications	When products contain a device constituent part
Pre-Import Requests	Final Rule	Importer	FDA	At least 30 days prior to arrival or entry for

[18] Certification reports are included in Appendix E.

				consumption
Adverse Event Reports	Final Rule	Reporting partner on behalf of the Importer	FDA and manufacturers of imported medications	When adverse events occur
Drug Recall Notification	Final Rule	HCPF DID	FDA	When recalls occur
Criminal convictions, violation of law, or disciplinary actions reporting	Final Rule	HCPF DID	FDA	Within 10 calendar days of occurrence
Annual Report	CO State Statute	Foreign Seller, Importer	HCPF DID	Annually
Annual Financial Audit	CO State Statute	Foreign Seller, Importer	HCPF DID	Annually
Quarterly Financial Report	CO State Statute	Foreign Seller, Importer	HCPF DID	Quarterly

Pre-Import Requests and Importation of Eligible Drugs
Before importing an eligible drug, Premier will be required to collect and submit to the Department's DID and the FDA a Pre-Import Request for each eligible drug, as required under the Final Rule. The Importer will submit the request to the FDA via electronic format after the Department's DID has reviewed and approved a draft at least 30 calendar days prior to the scheduled date of entry for consumption. Once approved by the FDA, Premier will submit a purchase order to AdiraMedica to initiate the purchase of eligible drugs approved for importation directly from the manufacturer. The manufacturer will ship the eligible drugs to AdiraMedica's warehouse in Mississauga, where AdiraMedica staff will inspect and prepare the drugs for exportation.

Premier will facilitate the compliant importation of eligible drugs into the United States and their eventual transportation to Boise, Idaho. Premier will work with a customs-licensed customs broker to complete the required importation documentation. The customs broker, on behalf of Premier, will make an entry for consumption at a CBP port of entry. The product will be securely stored under appropriate environmental conditions to maintain the integrity of the products until the FDA issues an admissibility decision. Once the eligible drugs have cleared customs, they will be transported to Boise, Idaho, where the imported eligible drugs will be quarantined at Premier's warehouse to undergo the next steps of importation processing.

Compliance with the Drug Supply Chain Security Act

Colorado's SIP will ensure all participants and imported drugs comply with the Drug Supply Chain Security Act (DSCSA),[19] and as allowed through Final Rule exemptions. This includes requirements to hold certain registrations, licenses or permits from federal and/or state authorities, and to maintain certain records to verify the supply chain for each drug distributed so it can be traced back to the original manufacturer quickly and efficiently.

The state's Program leverages the Final Rule's equivalent set of transaction record standards and other flexibilities to ensure appropriate tracking and tracing of all imported medications. Key Final Rule exemption standards that the Colorado SIP and related supply chain partner contracts deploy include:

- Foreign Seller compliance with authorized trading partner (ATP) definitions equal to U.S. ATP standards where appropriate as well as registration with the FDA.
- Maintenance of transactional information for each eligible drug, meeting T3 data[20] requirements, including a statement that the product was purchased directly from a manufacturer.
- Permitting Importer to receive a product without:
    - A product identifier, as long as the Foreign Seller affixes a Section 804 Serial Identifier, or SSI, if necessary.
    - A standardized numerical identifier (SNI)[21] within the product identifier as long as an SSI is affixed or imprinted by the Foreign Seller.

In the Colorado Program, DSCSA compliance begins with the manufacturer. All eligible drugs in the Program will be purchased directly from manufacturers, as defined in the Final Rule. Our Foreign Seller will ensure, through purchase agreements for each eligible drug, that manufacturers supply comprehensive documentation that includes all required information to appropriately track and trace an imported drug back to its origin. Additionally, the Foreign Seller will be responsible for the addition of a Section 804 serial identifier (SSI) if the product does not already have a standard product identifier (PI) affixed by the manufacturer. Should this SSI be necessary, it will be linked to the PI subsequently affixed by the Importer and it will be crosslinked to the transaction records (described below) to ensure the data being captured is equivalent to that of the PI under DSCSA.

The Foreign Seller will also be responsible for verifying that the drug is not a suspect or illegitimate foreign product and is required to supply various applicable certifications to affirm that they received the product from the manufacturer and that the Foreign Seller did not alter the transaction history.

Both the Foreign Seller and Importer will comply with detailed documentation requirements outlined in the Final Rule, including supplying data that is comparable to DSCSA-required T3 data, or Transaction History, Transaction Information and the Transaction Statement. AdiraMedica will ensure the following data, which is equivalent to T3 data, is transferred

[19] The Drug Supply Chain and Security Act, 21 USC § 9(V) https://uscode.house.gov/view.xhtml?path=/prelim@title21/chapter9/subchapter5/partH&edition=prelim

[20] "T3 data" is a reference to an eligible drug's Transaction History (TH), Transaction Information (TI), and the Transaction Statement (TS).

[21] Title II of the Drug Quality and Security Act § 581(20) as part of the Product Identifier(14). https://www.fda.gov/drugs/drug-supply-chain-security-act-dscsa/title-ii-drug-quality-and-security-act

electronically to Premier. Figure 13 shows how the Final Rule requirements relate to their counterpart DSCSA provisions.

Figure 13. Final Rule and DSCSA Counterpart Provisions Comparison

Information	Final Rule Requirement	DSCSA Counterpart
A statement from the Foreign Seller purchased directly from the manufacturer	251.14 (c), (6) (i)	TH 25
Proprietary name of the product	251.14 (c), (6) (ii)	TI 26 A
Strength & dosage form	251.14 (c), (6) (iii)	TI 26 B
Container size	251.14 (c), (6) (iv)	TI 26 D
Number of containers	251.14 (c), (6) (v)	TI 26 E
Lot number	251.14 (c), (6) (vi)	TI 26 F
Date of transaction	251.14 (c), (6) (vii)	TI 26 G
Date of shipment if more than 24 hours after the date of transaction	251.14 (c), (6) (viii)	TI 26 H
Business name and address of the person associated with the Foreign Seller from whom ownership is being transferred	251.14 (c), (6) (ix)	TI 26 I
Business name and address of person associated with the Importer to whom ownership is transferred	251.14 (c), (6) (x)	TI 26 J
SSI for each package or homogeneous case	251.14 (c), (6) (xi)	Final Rule Specific
Canadian DIN (Drug Identification Number)	251.14 (c), (6) (xii)	(replaces TI 26 C)/Final Rule Specific
Transaction Statement Equivalent	251.14 (d), (7)	Final Rule Specific

Colorado Department of Health Care Policy & Financing, 2022.

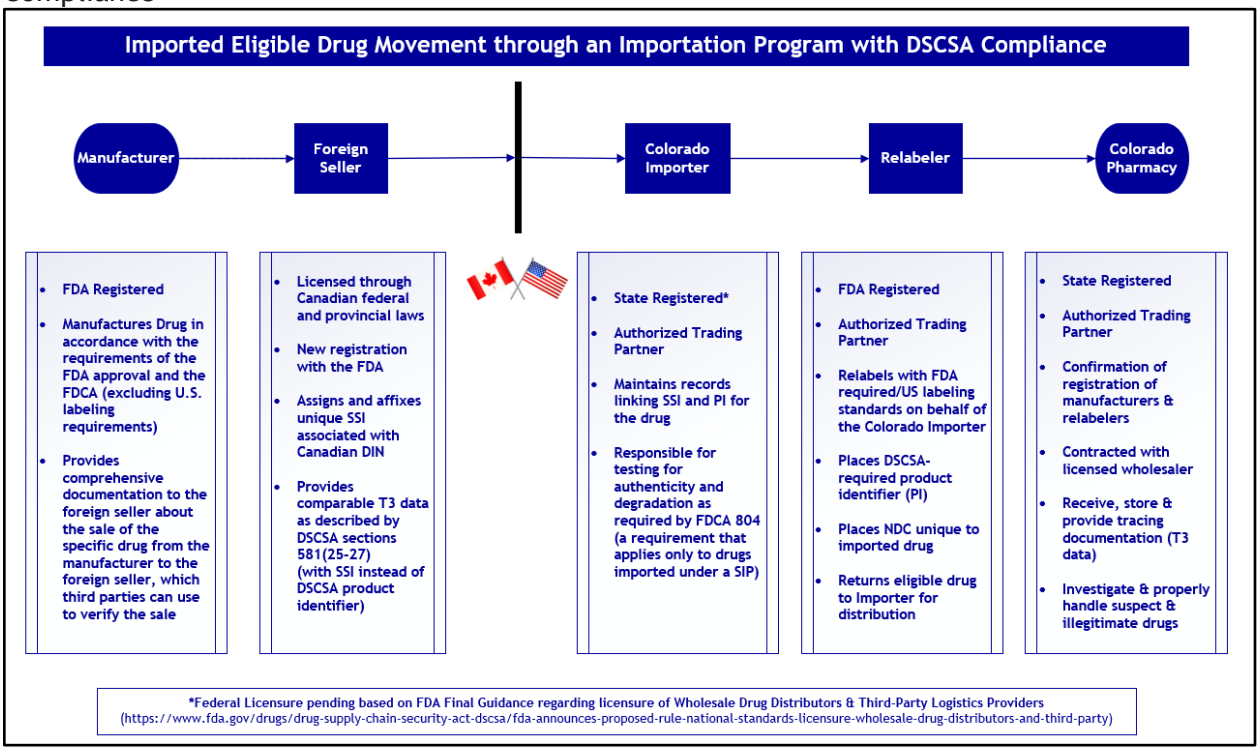
The imported eligible drugs will arrive at Premier Pharmaceuticals' secure warehouse and will be screened, according to written established SOPs, for any evidence that they may have been adulterated, are counterfeit, have been tampered with, are expired, or are a suspect foreign product or an illegitimate foreign product. This will occur prior to being moved to a specified secured and caged area within the warehouse that is designated for the program.

The drugs will remain in quarantine while a statistically valid sample is sent to the Program's qualified laboratory to undergo statutory testing. The test results, as well as three additional samples, will be sent to the FDA field lab identified by the FDA for approval. Once approved,

Premier will transport the eligible drugs to Omega Tech Labs to be relabeled including assigning the FDA-approved NDC designated for Colorado's SIP and affixing a product identifier (PI). Premier will compile and maintain all records associated with the imported products that link the SSI or previous product identifier to the newly placed product identifier. At this point, the imported eligible drug is now ready for distribution to participating Colorado pharmacies.

Once the drug is purchased by a participating pharmacy, the pharmacy will receive, store, and provide T3 documentation on any imported drug, if requested. This is no different than the drugs purchased by pharmacies in Colorado today. A summary of DSCSA requirements and how they are handled for the Colorado program is illustrated below in Figure 14.

Figure 14. Imported Eligible Drug Movement through an Importation Program with DSCSA Compliance



Colorado Department of Health Care Policy & Financing, 2022.

Between the DSCSA-equivalent transaction information, transaction statement and transaction history documentation, and the additional documentation and statutory testing required by Section 804, the documentation requirements for drugs imported under a SIP ensure the safety and transparency of the supply chain.

Adverse Events

Safety event reporting is fundamental to ensuring public safety, and industry standards for reporting were used in conjunction with the Final Rule to develop a comprehensive pharmacovigilance program which will be run by Rocky Mountain Poison and Drug Safety (RMPDS). A toll-free number and email address for safety reporting will be included in the new labeling and on the Colorado Drug Importation Program website. The line will be staffed with specialists trained in adverse event and special situation identification, collection, and

documentation. All possible safety reports will be submitted to a pharmacovigilance group for additional assessment, submission to the FDA, and follow-up.

Participating pharmacies and dispensing pharmacy staff will be trained on adverse event identification and reporting obligations upon enrollment and on an ongoing basis.

Written procedures will be developed in standard operating procedures (SOP) and work instructions to document the requirements for safety reporting and to guide relevant parties on the processes for safety report identification, collection, and submission. These documents and records of training to the documents will be retained by all relevant parties for 10 years.

Upon report of a safety event, the intake group agent will document a new report for each patient. For each safety report, an attempt will be made to collect all information required for an Individual Case Safety Report (ICSR) as outlined in 251.18 (d) 7 including:

- Patient information: patient age at time of adverse event or year of birth, patient gender, patient weight.
    - Each patient will be assigned a unique code as reports to the FDA will not include name and address of patient.
- Adverse event: outcome attributed to the event, date of adverse event, date of ICSR submission, description of adverse event (including a concise medical narrative), adverse event term(s), description of relevant tests, including dates and laboratory data, and other relevant patient history.
- Suspect medical product(s): Product name, product dose, route of administration and frequency, therapy dates, indication, whether the product is a combination product, whether adverse event abated after drug use stopped or dose reduced, whether adverse event reappeared after reintroduction of drug, lot number, expiration, NDC, and concomitant medical products and therapy dates.
- Reporter information: Reporter name, address and telephone, and whether the initial reporter is a health care professional and, if so, their occupation.
- Importer information: Name and contact office address, the date the report was received by the Importer, whether the ICSR is an expedited report, an initial report or follow-up report, and a unique case identification number that is the same as the initial report.

The pharmacovigilance group will complete and submit safety reports to the FDA and the manufacturer. Procedures completed by the pharmacovigilance group will include:

- Evaluate all reports and classify each report as an expedited ICSR, non-expedited ICSR, a follow-up to an existing ICSR, or no reportable event occurred.
- All ICSRs will be evaluated for completion of the minimum data set and all ICSR elements will include:
    - All items previously listed
    - Importer name and contact office
    - Whether the ICSR is expedited or non-expedited
    - Whether the ICSR is an initial report or follow-up report
    - All source and supporting documentation relevant to the ICSR, including if applicable:
        - Copy of the autopsy if the patient died

        - Copy of the hospital discharge paperwork if the patient was hospitalized
- Adverse event terms will be coded using standardized medical terminology (e.g., MedDRA).
- If any elements are missing from the report, attempts will be made to reach out to the reporter to gather missing information. Documentation of the attempts to gather missing information will be maintained within the case record.
- If a new reportable event is identified, a unique case identification number will be assigned. If a follow-up report is identified, the pre-existing unique case identification number will be attached to the follow-up information.
- Cases, including follow-up reports, will be submitted electronically within fifteen (15) calendar days for expedited reports and ninety (90) calendar days for non-expedited reports through the Safety Reporting Portal.
- All serious, unexpected adverse events will be submitted as expedited ICSRs regardless of whether or not the Importer believes the events are related to the imported product.

All records of safety reports will be maintained by RMPDS for 10 years. Records will be available to the FDA upon written notice.

Qualified Laboratory (§ 251.3 (e) 7)

Ensuring the purity and authenticity of imported eligible drugs is central to the design of Colorado's SIP. As required by federal and state laws and regulations, additional testing will be performed on drugs imported through Colorado's Program. In many cases, drugs imported through Colorado's Program are identical to those entering the marketplace through the traditional domestic supply chain except for their labeling. The testing described below is in accordance with the Final Rule requirements; however, the exact tests to be performed are yet to be determined pending the contents of our agreed to final drug list.

Testing & Sampling Process

Premier Pharmaceuticals has contracted with Q Laboratories, based in Cincinnati, Ohio, to conduct the statutory testing required by the Final Rule. Q Laboratories is registered with the FDA for pharmaceutical testing, and is cGMP/GLP Compliant and ISO/IEC 17025 Accredited. They are compliant with the relevant sections within Title 21 Code of Federal Regulations Sections 210 and 211, including Sections 211.160 and 211.194. Copies of all Q Laboratories' accreditations and inspection history are included in Appendix C.

Premier Pharmaceuticals will send a statistically valid sample from the lot of imported eligible drugs, based on the size of the lot. The samples, selected at random, will be pulled directly from the shipment coming from AdiraMedica. Premier will submit the sampling plan per batch of eligible drugs in a Pre-Import Request for FDA approval. The detailed sampling plan will be described in the regulatory filing for electronic Common Technical Document (eCTD) publishing. If the manufacturer completes the statistically valid testing, they will complete the same sampling techniques and process and send all paperwork directly to FDA as described by the Final Rule.

Evaluating for Authenticity

Authenticity testing discerns whether the prescription drug meets purity requirements by checking for the presence of unknown substances/toxins. Program testing will mirror the authenticity testing established by the New Drug Application (NDA) or Abbreviated New Drug Application (ANDA). This will provide confirmation that the Canadian Health Products and Food Branch (HPFB)-approved drug meets the FDA-approved drug's specifications and standards. When assessing the authenticity of a prescription drug, Q Laboratories will conduct a visual inspection as well as the required laboratory tests per drug that may include chromatography and/or spectrometry. Authenticity testing will be completed using an adequate number of tests required by the drug based on the results of multiple tests. These tests can vary by drug based on its complexity. While no single technique delivers the universal results needed for verification, there are tests that will be used on multiple drugs that will leverage the guidelines for the appropriate dosage form described within the general U.S. Pharmacopeia (USP)[22] chapters, e.g., USP <2> *Oral Drug Products, USP* <1> *Injections and Implanted Drug Products*, and USP <5>, *Inhalation and Nasal Drug Products*.

Imported medications that fail the visual inspection or laboratory test will be removed from the supply chain and dispositioned. Imported drugs that are not consistent with the U.S. counterpart, as required by the Final Rule, and/or not approved by the FDA, will be dispositioned immediately and not undergo further testing.

Q Laboratories has or can obtain the necessary equipment to perform detailed testing on the samples using spectroscopic and high-performance liquid chromatography, as applicable, based upon the methods specified by the manufacturer. They already regularly test pharmaceutical products for authenticity, degradation, and other required tests as requested by their manufacturer customers. Q Laboratories will work directly with the manufacturer to identify the proper equipment and ensure that it is used for each test required.

Testing for Degradation – Stability Testing

As required by the Final Rule, testing for degradation must include a stability-indicating assay provided by the manufacturer. Stability testing is the process for determining, through storage at defined conditions and testing at specific intervals, how long a drug substance or product remains safe and effective in particular storage conditions. Imported drugs require stability testing to determine that the medications entering Colorado have the proper standard expiration dates and will remain safe and effective while being stored. Q Laboratories regularly tests pharmaceutical products for stability and either has or can obtain the equipment to perform the necessary stability tests on samples based on the manufacturer defined methods.

In addition to testing eligible drugs following entry into the U.S., Q Laboratories will retain samples for retesting at the standard intervals based upon each product's FDA-approved

[22] United States Pharmacopeia (2022). Other USP-NF General Chapters for Compounding. https://www.usp.org/compounding/compounding-general-chapters

counterpart's shelf life. Prescription drugs that have expired or will expire before being able to be safely consumed will be designated for disposition.

Testing for Degradation – Microbial Integrity
Microbial integrity is only necessary for certain dosage forms (refer to USP <1111>) and not solid oral dosage forms. To evaluate whether a batch poses microbial or bioburden hazards, Q Laboratories will test for harmful microorganisms by following the appropriate USP monograph, e.g. USP <51>, <60>, <61> and / or <62>. Testing results will follow the allowances described in USP <1111>. If a sample presents evidence of microbial contamination, Q Laboratories will ensure Premier is aware, and the originating batch will be removed from further processing.

Submission of Testing Data to the FDA
Once all data has been generated and collected, it will be published within the relevant sections of the electronic Common Technical Document (eCTD) identifiers of the chemistry, manufacturing, and control (CMC) section of the regulatory submission and submitted through the FDA electronic submission gateway (ESG) as required by the Final Rule. The laboratory testing sections to be submitted for imported drugs include the following:

Figure 15. eCTD Section Identifier & Detailed Description

eCTD Section Identifier	**Description of Content**
3.2.P.4.1 Control of Excipients	• Names and addresses of excipient suppliers • Retest periods for excipients • Specifications for each excipient • Certificates of analysis for each excipient
3.2.P.5.1 Control of Drug Products	Specification of each drug product to include identification of the test, the associated test method, and the acceptance criteria for each test.
3.2.P.5.2 Analytical Procedures	A cross reference to the appropriate USP test method or a topline outline of each method to be used for release testing.

3.2.P.5.3 Validation of Analytical Procedures	A waiver related to already validated analytical procedures provided by the A/NDA sponsor with some verification data that demonstrates that the method performs as intended in the hands of the qualified laboratory.
3.2.P.5.6 Justification of Specification	A waiver related to already approved regulatory specifications per the approval process of the A/NDA.

Manufacturer Confidentiality for Required Testing (§ 251.3 (e) 16)

The qualified laboratory and the manufacturer will create and agree to a confidentiality agreement to establish levels of permission and authorization to all sensitive information such that it is used on a "need to know" basis with appropriate document timeouts, inability to print, inability to copy, and any other necessary mechanisms to restrict access and ability to distribute the proprietary information. Each page should contain, at minimum, the following statement: "Confidential and Proprietary Information of the Manufacturer. Do not distribute." Additionally, Q Laboratories will take steps internally to ensure security of a manufacturer's confidential information through the use of secure networks, firewalls, and Virtual Private Networks (VPN) when needed to access information.

Relabeling (§ 251.3 (e) 8)

The relabeler, Omega Tech Labs, will relabel the drug in compliance with the FDCA (e.g., FDCA Sections 502, 505, 804), and applicable regulations (e.g., 21 CFR 201 and the final drug importation rule), including ensuring that:

- All wording is displayed prominently and is not false or misleading in any way.
- The PI is affixed.
- The NDC has been assigned to the drug and is affixed to the label.
- The labeling features all labeling required by the approved A/NDA and 21 CFR 201, including:
  - the proprietary and established name of the drug,
  - product strength,
  - lot number,
  - name of the manufacturer and the Importer,
  - all warnings, indications, etc., and
  - the statement: "This drug was imported from Canada without the authorization of (insert A/NDA holder name) under the state of Colorado's Section 804 Importation Program. For more information, please visit https://hcpf.colorado.gov/drug-importation."

It is imperative to note that Colorado does not agree with the Final Rule labeling requirement to state that a drug was imported without the authorization of the manufacturer. Due to the nature of state-led importation programs, manufacturer contracting practices in Canada, and

the need for direct negotiation with drug manufacturers, all eligible drugs will have the express authorization of the manufacturer to be included in Colorado's program.

Below is a copy of an example of the proposed labeling for one of the eligible drugs on our drug list. A side-by-side comparison with the current FDA-approved labeling for the FDA-approved counterpart of the eligible prescription drug imported through Colorado's program is included in Appendix F.

We have only included one relabeling example at this time and will amend the SIP with labeling examples for all drugs once confirmed that the manufacturer will agree to sell them. It is worth noting, as well, that the program statement required by the Final Rule is technically incorrect. All drugs imported through Colorado's program will have the authorization of the manufacturer.

Drug Recall Plan (§ 251.3 (e) 13 and § 251.18 (e) and 21 CFR Part 7)

Eligible prescription drugs imported under Colorado's SIP will adhere to domestic and Canadian recall policy standards already in place today. Colorado, as the SIP Sponsor, will ensure that all supply chain partners are informed when recalls must occur. Prescription drug recalls in the traditional market are initiated by the manufacturer. Manufacturers work with the FDA to conduct a recall and are responsible for notifying their customers, including participating wholesalers. In a state-led importation program there are additional ways a recall can be initiated, due to the unique nature of these programs. A recall can be mandated by the FDA, or requested by the FDA, a SIP Sponsor, the Foreign Seller, Importer, or the manufacturer.

Recall Plan

Per the Final Rule, the HCPF DID is establishing a recall plan and process to ensure that all parties are monitoring both Canadian and FDA recall alerts. All supply chain partners will be required to participate in monitoring activities including:

- The HCPF DID, Importer and Foreign Seller engage in regular monitoring of the FDA recall and market withdrawal webpage.
- The HCPF DID, Importer, and Foreign Seller subscribe to all FDA drug recall announcements and FDA's MedWatch announcements.
- The HCPF DID, Importer, and Foreign Seller will monitor the Canadian drug recall website on a weekly basis.
- Participating manufacturers will be required to notify the Foreign Seller if an imported drug needs to be recalled.

This recall plan ensures that the HCPF DID can effectuate any recall, whether it is required by the FDA or initiated by any supply chain partner. The following individuals will be responsible for Drug Recall Monitoring for each SIP entity:

- The HCPF DID Drug Importation Pharmacist
- The Director of Operations at Premier Pharmaceuticals, LLC.
- The Director of Quality Assurance and Regulatory Affairs at AdiraMedica, Inc.

The HCPF DID will require all supply chain partners to provide regular communication regarding recalls, affirming that they have monitored and evaluated information from all sources.

If the FDA mandates a recall, or the FDA or SIP Sponsor partner suggests an imported drug recall is necessary, the HCPF DID will conduct a meeting with all SIP supply chain partners, including the Foreign Seller, Importer, and reporting vendor to immediately halt the importation of the affected medication. If a supply chain partner indicates a recall may be necessary, they will immediately inform the HCPF DID via phone and in writing of the determination with the factors supporting a recall. If the HCPF DID determines a recall is necessary, the HCPF DID will conduct a meeting to update the remaining partners to immediately halt importation. The recall shall be classified based on the standard definitions of drug recalls as defined by the United States[23] and Canada,[24] which use the same levels of classification:

- Tier 1: Recalled prescription drug poses severe risks to individuals that can result in serious health complications or death.
- Tier 2: Recalled prescription drugs may cause a temporary health problem or have a slight chance of posing a serious health complication.
- Tier 3: Recalled prescription drugs in violation of labeling or manufacturing laws and do not pose a significant risk to individuals' health.

Based on the classification and specific reason for the recall, the depth of the recall (wholesale, retail, consumer level) will be determined and a distinct recall plan will be implemented, while coordinating with the FDA.

The Importer and Foreign Seller will initiate their recall plans immediately after the need for a recall has been mandated or determined. Both entities will sequester the remaining SIP drug supply in the quarantine area of their warehouse specific to the storage of program medications. They will also ensure the drug is made ineligible in the Warehouse Management System (WMS) for further distribution. Premier will communicate with all participating pharmacies via email with instructions for quarantining the drug, or discarding and/or returning it to Premier for further processing.[25] Depending on the next steps for the recall, Premier will work with a reverse distributor to ensure all recalled drugs are appropriately disposed of.

[23] U.S. Food and Drug Administration. (2022) Recalls Background and Definitions. https://www.fda.gov/safety/industry-guidance-recalls/recalls-background-and-definitions

[24] Health Canada. (2022) What is a Recall? https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/recalls/definitions.html

[25] Both the Importer and Foreign Seller are required to have SOPs regarding the handling and communications of program recalls.

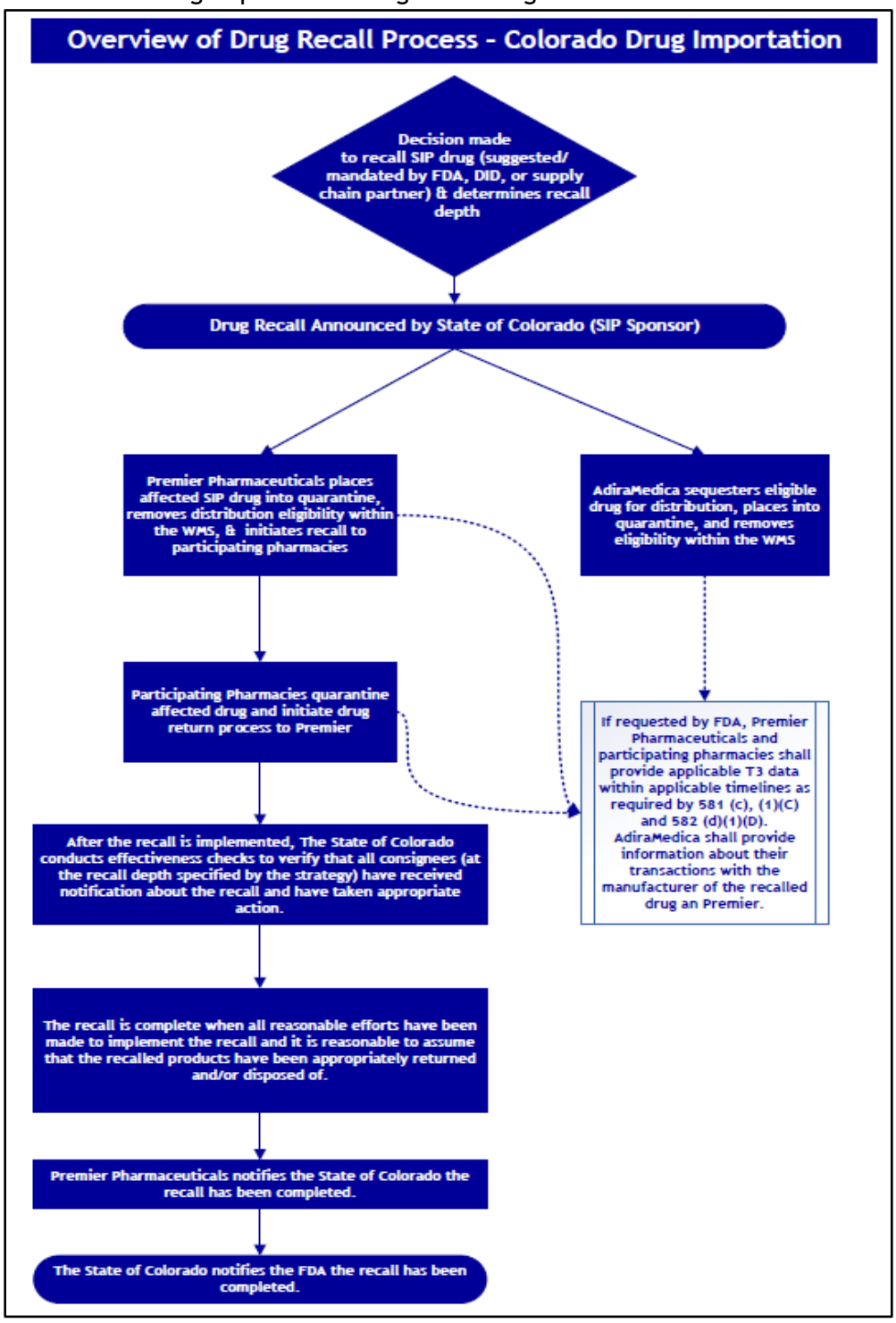
To support effectiveness checks on the recall process and to abide by DSCSA reporting requirements, within one business day of the recall initiation, Premier will submit a report to the HCPF DID with the following information:

- Quantity of drug recovered, including NDC, Section 804 serial identifier (SSI), DIN, lot, and expiration;
- Number and size of containers distributed;
- Dates of transaction and shipments between the manufacturer, AdiraMedica, and Premier and other applicable T3 data;
- The dates and quantities of the recovery;
- Unaccounted drug (if applicable); and,
- The expected amount of remaining drug to be recovered

The HCPF DID will then ensure timely periodic reporting of the recall information to the FDA.

Figure 16 shows the program's recall process:

Figure 16. Colorado's Drug Importation Program's Drug Recall Process



Colorado Department of Health Care Policy & Financing, 2022.

Recall Communications
The HCPF DID shall immediately notify the FDA in writing of the recall initiation and steps that will be followed. The HCPF DID will publish recall information on the program website. For Tier 1 and 2 recalls, the HCPF DID will notify the public about any hazard(s) presented by the recalled drug, utilizing the HCPF DID's Importation website, support from RMPDS and, if necessary, local media outlets and newspapers. The HCPF DID, with support from Premier, will inform additional stakeholders, including health plans, hospitals, or state-run facilities (e.g., prisons, clinics) with detailed return or disposal instructions.

Recall Reporting
If requested by the FDA, Premier shall provide applicable T3 data as defined in the DSCSA, to the FDA, within 2 business days or other requested timeline of the recall initiation. AdiraMedica shall provide to the HCPF DID information about its transactions of the recalled drug with the manufacturer and Premier.

Patient Level Recall Plan
In the event that a recalled imported drug has been dispensed to patients, the HCPF DID will work with its reporting partner, RMPDS to facilitate a patient level recall. This process is standard in the market today. First, RMPDS will work with the HCPF DID to compile a list of affected lot numbers and identify which pharmacies received them. RMPDS will then work with the identified pharmacies to compile a list of patients, including their contact information, who have received recalled medication. RMPDS will send communication(s), either via phone or email, to the identified patients notifying them that a recall has been issued for a product they purchased. This communication will also include details of any potential concerns presented by the recalled drug. Once contact is made, RMPDS will provide patients with instructions on how to return the recalled product for proper disposal. As part of this process, RMPDS will document all communications with the identified patients and submit records to the HCPF DID and the Importer. RMPDS will also maintain all documentation pertaining to the recall for a minimum of six years, as required by the DSCSA and the Final Rule. Any reportable safety events that are discovered during this process will be captured and reported as outlined in the Adverse Event Reporting Section.

Return Plan (§ 251.3 (e) 14)
The HCPF DID has established a robust return plan, following standard industry practices, establishing a clear return process and ensuring the safe handling of such drugs, including preventing non-saleable products from re-entering any market. The plan also provides clear standards for the assessment of medications to determine if they are saleable. For pharmacy returns or recalled medications that must go through a return process, the Department will require Premier, through its contract, to ensure that all returned products remain in the original supply chain (i.e., using existing contracted transporters, including program participating pharmacies, and stored in the Colorado program designated storage area within the Premier warehouse.) Premier will also ensure returned imported drugs remain separated from other returned Premier products.

If a participating pharmacy needs to return an imported product, they will initiate the standard return process as directed by Premier. Once the drug has been received at Premier, staff will inspect the drug for evidence of tampering or damage based on a 15 point inspection process to determine whether the product is re-saleable. As part of this inspection process, Premier will ensure each participating pharmacy completed an Ongoing Assurance Form which verifies that the entity has handled the product appropriately in accordance with state and federal regulations.

A previously recalled product may be eligible to be returned to the market for sale in a participating Colorado pharmacy if it was classified as a Tier 3 recall, such as a mistake in labeling or other minor issue that does not have clinical impact. In this case, the HCPF DID will work with Premier to have the affected batch relabeled. If retesting is deemed necessary, Premier will randomly select new samples for testing at Q Laboratories to evaluate for authenticity and degradation. Once such testing is completed, if it is determined the product can be resold to a Colorado pharmacy, its T3 data will be updated with the additional information required and it will be returned to the saleable Colorado product section of the Premier warehouse. If it is determined that the imported drug is not eligible for resale, it will be placed in the designated quarantine area, ineligible for resale.

The HCPF DID will regularly review Premier's recall and return reports to assess whether imported prescription drugs are missing from the list of received return shipments. The HCPF DID will work with Premier to resolve any discrepancies. If a discrepancy can't be resolved, the HCPF DID and Premier will communicate to all affected parties and contact law enforcement if theft is suspected.

Education and Communications Plan (§ 251.3 (e) 12)

The Department's DID has maintained a website to educate interested stakeholders and connect stakeholders with resources during the early phases of program implementation. Once operational, the nature of this website will change to allow for stakeholders to review the importation drug list, identify participating pharmacies, access other informational resources, and connect with the Program's call center. The website will also direct pharmacies to the Importer's website where orders for imported drugs under the Program can be placed. As new drugs are approved and added to the negotiated FDA-approved list, the HCPF DID will share this information on the website and via email with interested parties. The HCPF DID will also maintain an email inbox for stakeholders to share program input.

The Department's DID will also support several targeted initiatives to educate stakeholders in the state about the opportunities associated with the Program once the SIP application is approved:

Purchaser Road Show & Outreach

In order to ensure equitable access to imported drugs throughout Colorado, the Department's DID will host a series of informational sessions across the state to educate pharmacists, hospitals, and other providers that may have an interest in purchasing drugs through the program. The focus of this outreach will be to: educate about the program framework, share information about specific drugs selected for importation and their pricing, and to answer any questions about safety and compliance protocols. Urban, rural and frontier regions will all be targeted for these education sessions. Premier will also participate to answer questions about the purchasing process.

Premier will also be responsible for conducting outreach and marketing to Colorado pharmacies to increase program participation and ensure a favorable geographic spread for access. Premier will develop a Memorandum of Understanding (MOU), specific to the Importation Program, that participating pharmacies will need to review and agree to. This MOU will lay out requirements for participation, such as

- Ensuring a good faith effort is made to dispense imported prescription drugs only to Coloradans.
- Ensuring basic annual reporting to help the program track volume and consumer savings.
- Including program-specific adverse event reporting in their employee training regimens.

Ensuring Access to Imported Prescription Drugs

While the Department has conducted outreach to health plans and PBMs earlier in our program development, many indicated that until there is a clear approval from the FDA they are not able to focus attention on state partnerships to cover imported drugs. Once the FDA has provided an approval (or provisional approval) for our SIP application, the HCPF DID will work in earnest with these potential partners to obtain coverage for drugs approved under the SIP. As we await approval, the HCPF DID will offer continued opportunities for health plans, PBMs and their trade associations to meet and learn about our program and its benefits. As mentioned earlier, we do believe that smaller, more nimble PBMs that use carve-out strategies to reduce drug prices are likely our best initial partners, so we will continue to outreach these PBMs.

The HCPF DID will seek to pilot programs with specific stakeholders in the Colorado market such as the Colorado State Employee Health Benefits Program.

Consumer Outreach & Support

Once approved, the HCPF DID will host several consumer-focused sessions, both virtually and in person, to reach as many people in the state as possible. The focus of these sessions will be to educate consumers on the choices available to them, direct them to resources and answer any questions they have about the Importation Program.

Once the Colorado program is actively importing prescription drugs from Canada, the HCPF DID has contracted with Rocky Mountain Poison & Drug Safety to implement a patient education and support call center. Additionally, there will be an opportunity for patients to submit questions and concerns via email and a web portal. The support center will provide information about the program, such as:

- A list of all drugs imported from Canada, along with their NDCs and prices
- A list of participating pharmacies
- Information for consumers, including:
    - Overview of the drug importation program
    - Overview of the measures taken to ensure health and safety
    - Information regarding the recall process including additional information on any active recall
    - Information about state and federal program regulations
- Information for health care professionals, including:
    - Overview of the drug importation program
    - Overview of the measures taken to ensure health and safety

- Information regarding the recall process including additional information on any active recall
- Information on how to become a program participant
  Information about state and federal program regulations

Additionally, callers' inquiries will be screened for any possible reportable events (e.g., adverse events, product quality complaints, etc.) and if a reportable event is identified during the call, information will be collected and shared as appropriate with the Department's DID and FDA.

Conclusion

As the FDA reviews the state of Colorado's SIP application, the Department's DID will continue its work to prepare the market to fully implement the program once approved, with a focus on addressing the challenges and barriers outlined throughout this document. The Department's DID will hold a stakeholder meeting in January 2023 to educate interested parties and provide an avenue for deeper discussions with the partners needed to achieve the greatest cost savings possible, including health plans, PBMs, and pharmacies. We will continue to engage employers and consumers to highlight the value of Canadian importation and seek their feedback on the drug list and other aspects of the program. As we conduct this outreach, we will be actively pursuing negotiations with drug manufacturers and welcome opportunities to have direct conversations with such entities, not only for manufacturers represented on the drug list, but any others that may have an interest in our program. Finally, our work with supply chain partners will continue to move forward, further developing processes, procedures, and oversight protocols, so that we may quickly advance the program once the FDA approves the SIP application. Colorado looks forward to working with all parties in the coming months and stands ready to collaborate with the FDA to make this program a reality to the benefit of Colorado consumers and employers.