DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

National Standards for the Licensure of Wholesale Drug Distributors and Third-Party Logistics Providers

Docket No. FDA-2020-N-1663

Preliminary Regulatory Impact Analysis
Initial Regulatory Flexibility Analysis
Unfunded Mandates Reform Act Analysis

Economics Staff
Office of Economics and Analysis
Office of Policy, Legislation, and International Affairs
Office of the Commissioner

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I. Introduction and Summary

A. Introduction

We have examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct us to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). We believe that this proposed rule is a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the proposed rule could impose significant, although uncertain, new economic burdens on small entities, we find that the proposed rule will have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $158 million, using the most current (2020) Implicit Price Deflator for the Gross Domestic Product. This proposed rule would not result in an expenditure in any year that meets or exceeds this amount.

B. Summary of Costs and Benefits

In this rulemaking, we propose new national standards for the licensing of prescription drug wholesale distributors (WDDs) and third-party logistics providers (3PLs) as directed under the Drug Supply Chain Security Act (DSCSA), Title II of the Drug Quality and Security Act. If finalized, the rule would also establish a federal licensing system for wholesale drug distributors and third-party logistics providers to use in the absence of a state licensure program that is consistent with the proposed national standards.

We summarize the benefits and costs of the proposed rule in Table 1. The standards for prescription drug wholesale distribution in the proposed rule would result in public health benefits to consumers and benefits to distributors from reducing the diversion of prescription drugs. Other monetized benefits include cost savings from reducing the frequency and quantity of licensure applications and cost savings from reducing state licensing standards in some states. We estimate that the annualized benefits over 10 years would range from $1.25 million to $31.50 million at a 7 percent discount rate, with a primary estimate of $10.66 million. We estimate that the annualized benefits would range from $1.26 million to $32.18 million at a 3 percent discount rate, with a primary estimate of $10.89 million.

We also expect that the proposed rule, if finalized, would impose costs on wholesale drug distributors, third-party logistics providers, states, approved organizations, and the Food and Drug Administration (FDA). Costs to wholesale drug distributors and third-party logistics

providers include costs of learning about the rule, reporting to FDA, undergoing routine inspections, writing and revising standard operating procedures, and conducting background checks. Wholesale-drug distributors would also incur costs to furnish surety bonds to their state licensing authority to obtain or renew their licenses.

Costs to states include the time spent reading and understanding the rule, passing or revising the laws and regulations governing their licensure programs, and inspecting WDD and 3PL facilities. Approved organizations would incur legal, application, and training costs, as well as costs to inspect WDD and 3PL facilities. FDA costs include the costs to establish and operate a reporting database and a licensure program for wholesale drug distributors and third-party logistics providers and the costs to establish and operate an approval program for approved organizations.

As states reduce their frequency of licensure, licensure fees would transfer from states to WDD and 3PL facilities. Furthermore, to the extent that FDA would license facilities in certain states, licensure fees would transfer from states to FDA. We intend to publish this rulemaking in conjunction with the proposed rule entitled "Certain Requirements Regarding Prescription Drug Marketing; Proposed Rule" (or Part 203). We include the benefits and costs of Part 203 in this economic analysis.

We estimate that the annualized costs over 10 years would range from $13.21 million to $20.63 million at a 7 percent discount rate, with a primary estimate of $16.92 million. We estimate that the annualized costs over 10 years at a 3 percent discount rate would range from $12.83 million to $20.10 million, with a primary estimate of $16.47 million.

Table 1. Summary of Benefits, Costs, and Distributional Effects of the Proposed Rule

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Benefits	Annualized Monetized ($ millions/year)	$10.66	$1.25	$31.50	2020	7%	10 years	There is a high degree of uncertainty in the magnitude of benefits.
		$10.89	$1.26	$32.18	2020	3%	10 years	
	Qualitative							
Costs	Annualized Monetized ($ millions/year)	$16.92	$13.21	$20.63	2020	7%	10 years	
		$16.47	$12.83	$20.10	2020	3%	10 years	
	Qualitative							
Transfers	Federal Annualized Monetized ($ millions/year)	$0.12	$0.09	$0.14	2020	7%	10 years	
		$0.11	$0.08	$0.14	2020	3%	10 years	
		From: States			To: Firms			
	Other Annualized Monetized ($ millions/year)							
		From:			To:			

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Effects	State, Local, or Tribal Government: Annualized net costs to states over 10 years ranging from $0.62 million to $1.44 million at a 7 percent discount and from $0.58 million to $1.38 million at a 3 percent discount rate. Small Business: Quantified effects of more than 1 percent of average annual revenues for small 3PL firms. Unquantified effects are uncertain. Wages: No estimated effect. Growth: No estimated effect.							

C. Definitions

In Table 2, we provide definitions for several terms we use in this document. These definitions only apply to this document and not to the content of the proposed rule. For definitions applicable to the proposed rule, please refer to section 581 of the Federal Food, Drug, and Cosmetic Act and the proposed rule.

Table 2. Definitions of Terms and Abbreviations Used in this Analysis

Term	Abbreviation	Definition
We, us, our		We use these terms to refer to the FDA.
Wholesale Drug Distributor	WDD	Entities that warehouse prescription drug products and take ownership of those products. We use this term to refer to domestic facilities only.
Third-Party Logistics Provider	3PL	Entities that warehouse prescription drug products on behalf of a manufacturer. 3PLs do not take ownership of the products. We use this term to refer to domestic facilities only. DSCSA established the term "third party of logistics provider" or "3PL", but for convenience we refer to 3PL entities, including those existing before DSCSA, as 3PLs.
Drug Supply Chain Security Act	DSCSA	A law passed in 2013 that required us to establish national standards for the licensure of WDDs and 3PLs and required WDDs and 3PLs to report certain information to FDA.
Prescription Drug Marketing Act	PDMA	Pre-DSCSA law passed in 1987 on prescription drug distribution that required WDDs to obtain licenses from states.
States		We use this term to refer to any jurisdiction impacted by this proposed rule. These jurisdictions include all 50 states, the District of Columbia, Puerto Rico, Guam, and other U.S. territories.
Designated Representative		A representative of the facility manager who is responsible for managing the daily operations of a WDD or 3PL facility.
Facility		The permanent, physical location used for warehousing of prescription drug products, distribution of prescription drug products, or both warehousing and distribution of prescription drug products.
Approved Organization	AO	Entity approved by FDA that may review a facility's qualifications for licensure and may conduct facility inspections.

Term	Abbreviation	Definition
Criminal Background Check		A search for and compilation of criminal records of an employee or prospective employee.
Surety Bond		A contract between a facility and a surety company guaranteeing a payment of any administrative fines or penalties imposed on a facility.
Standard Operating Procedure	SOP	A written procedure that a firm or facility maintains and follows.
In-State License		A license obtained by a WDD or 3PL in the state in which the facility is located.
Ship-To License		A licensed obtained by a WDD or 3PL in states in which the facility is not located, but that the WDD or 3PL ships to.

II. Preliminary Regulatory Impact Analysis

A. Background

WDDs and 3PLs are the primary entities that move prescription drugs in the supply chain at the wholesale level in the United States. WDDs receive products from drug manufacturers and distribute them to dispensers. 3PLs receive products from drug manufacturers and provide warehousing and logistics services on behalf of trading partners. WDDs purchase and take ownership of the products that they distribute, while 3PLs provide warehousing and logistics services without taking ownership of the products that they warehouse.

One of the challenges of prescription drug distribution is keeping illegitimate products out of the legitimate supply chain. Such illegitimate products include, among other things, counterfeit drugs, drugs manufactured outside the legitimate U.S. supply chain and diverted or transferred into the legitimate supply chain through an illicit channel during distribution, as well as drugs that may have originated in the legitimate U.S. supply chain but that may have been diverted or transferred outside that supply chain before reentry. Drug diversion may result in contamination, deterioration, or mislabeling of the prescription drug. Counterfeit products may contain unsafe ingredients or may be ineffective. Consequently, drug diversion and counterfeiting may increase a patient's risk of receiving an ineffective, unsafe, or incorrect drug. Diverted or counterfeit drugs pose a serious public health issue (Ref. [1]). Patients may not receive life-saving treatment if a diverted or counterfeit drug is ineffective. Patients may also suffer adverse events from unsafe drugs. Because these diverted or counterfeit drugs enter the supply chain unlawfully and their origin may be unknown, consumers may purchase and use a diverted or counterfeit drug product believing that it is a legitimate drug product.

Another challenge in prescription drug distribution is ensuring that products remain safe and effective. Proper storage, transportation, and equipment maintenance can prevent drug deterioration or contamination. To address these issues, the PDMA of 1987 required WDDs to implement certain minimum wholesaling standards. When states adopted these standards for WDDs, some states also imposed standards on 3PLs.[1]

[1] While states imposed standards on the entities we refer to as "3PLs", they did not use that term.

Since the passage of PDMA, drug diversion and counterfeiting have persisted. Some states have implemented stricter standards, while other states continue to require only the minimum national standards under PDMA. Drug diverters and counterfeiters can often more easily infiltrate the supply chain by operating in states with the weakest standards for drug distributors. Rigorous national standards for WDDs and 3PLs can reduce this opportunity for drug diversion and counterfeiting.

B. Need for Federal Regulatory Action

Private markets may fail to provide the socially optimal level of security in the prescription drug supply chain. WDDs and 3PLs can reduce the likelihood of drug diversion and counterfeiting by investing in facility security and using good storage practices. WDDs and 3PLs benefit privately from storing prescription drugs with care, as it protects them against theft and spoilage of drugs. WDDs and 3PLs would have adequate incentive to invest in the security of the supply chain if the marginal cost of mitigation were less than the marginal private benefit. However, because WDDs and 3PLs do not face the same risks of drug diversion and counterfeiting as consumers, they may invest less than the socially optimal amount needed to adequately protect the supply chain. As a result of this potential underinvestment, consumers face greater risk of purchasing diverted drugs than they would with socially optimal investment.

Consumers can also suffer losses from drug diversion and counterfeiting. Consumers who unknowingly purchase diverted or counterfeit drugs through the legitimate supply chain believe that they are purchasing legitimate drugs. The price they pay reflects their willingness to pay[2] for a legitimate drug when they have received a diverted or counterfeit drug that they value much less. Consumers' willingness-to-pay for a legitimate drug likely captures expectations that a drug is safe, effective, and manufactured and distributed in accordance with all applicable laws and regulations.

It is difficult for consumers to coordinate and compensate WDDs and 3PLs for their efforts to protect against diversion. It is costly for consumers to try to avoid diverted drugs by verifying the security of the supply chain or the authenticity of drugs they purchase. Therefore, it is unlikely consumers could demand an optimal amount of security in the drug supply chain through market mechanisms. Additionally, consumers may not suspect drug diversion or counterfeiting if they suffer an adverse outcome because of a diverted or counterfeit drug and may instead incorrectly attribute the adverse outcome to other factors.

Regulation of WDDs and 3PLs varies across states, and drug diverters and counterfeiters may operate in states with weaker oversight. By creating rigorous national standards for WDD and 3PL licensure, this proposed rule, if finalized, would support a minimum level of supply chain security that may reduce the social costs associated with drug diversion and counterfeiting.

C. Purpose of the Proposed Rule

As required by statute, the proposed rule, if finalized, would create national standards for licensure of WDDs and 3PLs. We expect that harmonizing standards would improve product safety and efficacy by helping to minimize risks that arise in the supply chain. The rule would

[2] Per HHS guidelines for regulatory impact analysis, willingness-to-pay is the "maximum amount of money an individual would voluntarily exchange" for a good or service, "given his or her budget constraints" (Ref. [27]).

also streamline compliance for drug distributors by standardizing state standards. To establish uniform standards, the rule proposes stronger national licensing standards for WDDs and 3PLs than the PDMA. We summarize the new standards in Table 3.

Table 3. Summary of New Standards for WDDs and 3PLs

Standard	Description[a]	Applies to WDDs?	Applies to 3PLs?
Criminal Background Checks	All designated representatives and facility managers must pass criminal background checks.	Yes	Yes
Fingerprinting	All designated representatives and facility managers must undergo a criminal background check involving fingerprinting.	Yes	No
Routine Facility Inspections	Facilities must undergo routine inspections at least once every 3 years. If available, state licensing authorities or AOs would conduct these inspections. Otherwise, we would conduct inspections.	Yes	Yes
SOPs for Equipment Maintenance, Personnel, and Transportation	Facilities must establish, maintain, and follow written procedures for equipment maintenance, personnel qualifications, and safe transportation of products.	Yes	Yes
SOPs for Authorized Trading Partners	Facilities must establish, maintain, and follow written procedures to ensure they only engage in activities on behalf of authorized trading partners.	Yes	No[b]
Furnish Bond	Firms with annual revenue greater than $10 million must furnish a bond of $100,000 or other equivalent means of security acceptable to the state. Firms with annual revenue less than or equal to $10 million must furnish a bond of $25,000.	Yes	No

[a] The preamble to this proposed rule discusses these standards in more detail.
[b] Proposed "best practice" not but a requirement.

Either state or federal licensing authorities would enforce WDD and 3PL compliance with the above standards. States with licensure standards that conform to the standards in the proposed rule could continue to license and regulate WDDs and could establish separate programs to license and regulate 3PLs. Absent a state licensing program, we would establish a licensing program for facilities located in that state.

1. Effective Dates and Discounting

The DSCSA specifies that the effective date of the 3PL licensure standards is one year after we issue the final regulations and that the effective date of the WDD licensure standards is two years after the final regulation issues. However, as described in the proposed rule, we do not intend to enforce the national standards for licensure of 3PLs until 2 years after we issue the final regulations. Throughout our analysis, we use "year 1" to represent the year in which we would begin to enforce the national standards for licensure. Therefore, "year 1" refers to the 12-month period beginning 2 years after the regulation is finalized, i.e. the effective date for WDD licensure standards and the year after the effective date for 3PL licensure standards.

D. Baseline Conditions

The DSCSA was published in 2013, and firms are very likely to have proactively changed their practices to meet the requirements described in the DSCSA. Therefore, we adopt the pre-statute baseline for this analysis and consider impacts beginning in 2013.

1. Number of WDD and 3PL Facilities

To estimate the number of affected facilities, we use data from every facility that reported to us as a WDD or 3PL as of July 2019. We match these data to information from the Dun & Bradstreet database.[3] Dun & Bradstreet data contain information on each company's sales, number of employees, and its parent company. To measure individual facility size, we use the number of employees associated with the facility's parent company, assuming that subsidiary facilities would have access to parent company resources.

In Table 4, we report the number of WDD and 3PL facilities by employee size. We estimate that there are 1,951 WDD facilities and 459 3PL facilities. Furthermore, we estimate that there are 1,560 unique firms operating the facilities, including 1,427 firms that operate WDD facilities and 292 firms that operate 3PL facilities.[4]

Table 4. Total Number of WDD and 3PL Facilities by Employee Size

Employee Size	Number of WDD Facilities	Number of 3PL Facilities
1–19 Employees	1,056	164
20–99 Employees	423	141
100–499 Employees	309	94
500 or more Employees	163	60
Total Number of Facilities	1,951	459

2. Baseline Practices at WDD and 3PL Facilities

The rule's impact would depend upon how many facilities would need to adopt each standard to comply with the proposed rule, if finalized. We base our estimate on available data on the number of WDD and 3PL facilities and their baseline practices in each state. We use state standards that were in place around the time that Congress passed the DSCSA as a proxy for baseline practices at WDD and 3PL facilities.

Equating baseline practices with licensure standards could underestimate overall baseline practices. We expect that facilities proactively implement stricter standards when the benefits of the stricter standards outweigh their costs. We welcome any comments that estimate how many facilities practice stricter standards than those required by the states in which these facilities operate, and which stricter standards they practice.

[3] https://www.dnb.com/

[4] These numbers do not sum to the total number of firms, as several firms operate more than one facility, and some firms operate both WDD and 3PL facilities.

Using the Westlaw database, we assess state standards for WDD and 3PL licensure around the time when Congress passed the DSCSA (Ref. [2]). This database contains every state licensing standard that was applied to WDDs in 2014. We assume that states with WDD licensing standards worded similarly to the standards in this proposed rule have already adopted the proposed provisions in this rule. As of 2014, all states license WDDs. However, most states either did not license 3PLs or licensed them using the same licensure program as for WDDs. We assume that 3PLs follow the same licensure standards as WDDs and request comment on this assumption.

Licensing standards vary across states. Eighteen states, Puerto Rico, and other U.S. territories have adopted the minimum national provisions required under PDMA. We find, for example, that some states already require criminal background checks (27 states), routine inspections (4 states), and surety bonds (17 states). In Table 5, we estimate the number of WDD facilities licensed in states that do not already require these provisions proposed under this rule. In Table 6, we estimate the number of 3PL facilities licensed in states that do not already require two of these provisions proposed under this rule. We also find that no states currently have standards for written SOPs related to equipment maintenance, personnel, transportation, or authorized trading partners.

Table 5. Number of WDD Facilities Licensed in States that Do Not Require Criminal Background Checks, Routine Inspections, or Surety Bonds

Employee Size	Criminal Background Checks	Routine Inspections	Surety Bond
1–19 Employees	395	1,035	488
20–99 Employees	153	405	216
100–499 Employees	117	303	164
500 or More Employees	53	156	81
Total Number of Facilities	718	1,899	949

Table 6. Number of 3PL Facilities Licensed in States that Do Not Require Criminal Background Checks or Routine Inspections

Employee Size	Criminal Background Checks	Routine Inspections
1–19 Employees	55	162
20–99 Employees	52	134
100–499 Employees	24	92
500 or More Employees	14	58
Total Number of Facilities	145	446

3. The Cost of Labor

In Table 7, we present the estimates we use to value the cost of labor in this analysis. To estimate labor costs, we use an employee's hourly cost of labor (mean hourly wages plus benefits and overhead). Following the Department of Health and Human Services (HHS) guidance, we assume that benefits and overhead equal 100 percent of the mean wage. For private firms and states, we use data from the Bureau of Labor Statistic's 2020 National Occupational

Employment and Wage database to estimate the mean hourly wages for different occupations.[5] For our labor costs, we use internal data from our Fully Loaded Full Time Employee Cost Model.

Table 7. Labor Cost Values Used in This Analysis

Entity	Employee Category	Hourly Wage	Hourly Labor Cost
WDDs[a]	Designated Representatives[e]	$70.18	$140.36
WDDs[a]	Lawyers	$87.22	$174.44
WDDs[a]	Supervisors[f]	$31.92	$63.84
3PLs[b]	Designated Representatives[e]	$62.15	$124.30
3PLs[b]	Lawyers	$85.03	$170.06
3PLs[b]	Supervisors	$28.92	$57.84
States[c]	Lawyers	$46.85	$93.70
States[c]	Legislative Staffers[g]	$24.80	$49.60
States[c]	Compliance Officers	$29.28	$58.56
AOs[d]	Compliance Officers	$40.16	$80.32
AOs[d]	Managers	$64.13	$128.26
FDA	CDER Employees	$71.10	$142.20

[a] NAICS Code 4240A2, "Merchant Wholesalers, Nondurable Goods."
[b] NAICS Code 488500, "Freight Transportation Arrangement."
[c] NAICS Code 999200, "State Government, Excluding Schools and Hospitals."
[d] NAICS Code 813900, "Business, Professional, Labor, Political, and Similar Organizations"
[e] We use the occupation "General and Other Operations Managers" to estimate the wage for designated representatives.
[f] We use the occupation "First-Line Supervisors of Production and Operating Workers" to estimate the wage for supervisors.
[g] We use the occupation "Legal Support Workers" to estimate the wage for legislative staffers.

E. Benefits of the Proposed Rule

1. Benefits

a. Quantifying Benefits Using Cargo Theft Data

Uniform licensing standards for WDDs and 3PLs could generate public health benefits by reducing drug diversion or counterfeiting. Many drugs require strict environmental conditions to ensure their safety and efficacy. Exposing drugs to adverse conditions can change their chemical structure, potentially reducing their therapeutic benefit and thus their ability to treat the end user's underlying health condition. Diverted drugs may also spoil, potentially resulting in adverse events for patients.

We expect that the proposed rule's standards for inspections, maintenance of equipment, and standard operating procedures would reduce the diversion of illegitimate drugs into the legitimate supply chain.[6] For the purposes of our analysis, we assume that rulemaking would

[5] Available at https://www.bls.gov/oes/2020/may/oessrci.htm.
[6] Distributors already have some incentives to prevent drug diversion, as they would likely incur product losses from any spoiled drugs they discover and could incur losses if subject to enforcement actions by licensing authorities or sued by consumers affected by a spoiled drug. Any potential benefit of preventing diversion would only occur for

eliminate drug diversion, though we expect that this overestimates the effectiveness of the rule. We request comment on the impacts of the proposed rule on the amount of drug diversion.

The benefits of reducing drug diversion equals the difference between the total willingness-to-pay for the diverted drugs *had they not been diverted* minus the total willingness-to-pay for the diverted drugs *once they have been diverted*. The willingness-to-pay for a diverted drug *had it not been diverted* reflects the maximum price that a consumer would pay if they did not know the drug was diverted, while the willingness-to-pay for a diverted drug *once it has been diverted* reflects the maximum price that a consumer would pay if they know the drug was diverted. Both values are difficult to estimate and likely vary by age, gender, education, and other socioeconomic characteristics.

The willingness-to-pay for a diverted drug once it has been diverted may be positive, zero, or negative. If diversion reduces the therapeutic benefit of a drug but does not render it ineffective, the willingness-to-pay for the diverted drug may be positive. If diversion eliminates the therapeutic benefit of a drug and causes no adverse events, then the willingness-to-pay for the diverted drug may be zero. If diversion reduces the therapeutic benefit of a drug and leads to adverse events, then the willingness-to-pay for the diverted drug may be negative. In the absence of better information about the willingness-to-pay for diverted drugs, we assume that the willingness-to-pay is zero. We welcome comments on this assumption.

To approximate the willingness-to-pay for diverted drugs had they not been diverted, we use the market price of diverted drugs. Because patients would only use a drug if the therapeutic benefit is greater than or equal to the price of the drug, the market price represents a lower bound on the willingness-to-pay. We estimate the total willingness-to-pay for diverted drugs had they not been diverted using data on one form of drug diversion: cargo theft.

Cargo theft, in which drugs are stolen from warehouses or carriers, generally involves large quantities of drugs. Large quantities of drugs may be difficult for thieves to resell individually, so they may seek to sell them in bulk to wholesalers in the legitimate supply chain. Diverted drugs may be obtained through other channels, such as from individual patients or through prescription fraud, but these channels are more likely to yield smaller quantities of drugs which drug diverters could more easily sell outside the legitimate supply chain.

Based on proprietary data from the Pharmaceutical Cargo Security Coalition, we estimate that the annual replacement cost for prescription drugs lost to cargo theft ranges from $0.19 million to $5.02 million, with a primary estimate of $1.60 million. We convert these estimates to the retail value of diverted prescription drugs by dividing by the average ratio of cost of sales to revenue from two major domestic drug manufacturers, which ranges from 0.18 to 0.25, with a primary estimate of 0.21. Then, we estimate that the annual retail value of diverted prescription drugs ranges from $0.76 million to $27.96 million, with a primary estimate of $7.78 million.

Based on our assumptions that the willingness-to-pay for diverted drugs once they are diverted is zero and that the willingness-to-pay for diverted drugs had they not been diverted equals the market price, the annual retail value of diverted prescription drugs represents the

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standards of the proposed rule that both (a) decrease the risk of drug diversion and spoilage and (b) distributors currently consider costlier than their private expected benefit of the reduction in diversion risk.

benefits of the proposed rule. We assume that these benefits begin in year 1. We request comment on this approach to valuing the benefits of the proposed rule.

These estimates likely underestimate the total benefits of reduced drug diversion for two reasons (though, as noted above, we likely overestimate the effectiveness of the rule, and thus benefits). First, by using cargo theft data, we only capture one form of drug diversion. Reducing other forms of drug diversion and counterfeiting would produce additional benefits to consumers. Second, the willingness-to-pay for diverted drugs may be negative if consumers experience adverse events. We discuss this possibility in more detail in the next section.

b. Potential Public Health Benefits from Reduced Morbidity and Mortality

In our quantification of the public health benefits of diverted drugs based on cargo theft data, we assume that consumers' willingness-to-pay for diverted drugs is zero. If drug diversion reduces the therapeutic benefit of a drug and leads to adverse events, then the willingness-to-pay for the diverted drug may be negative.

Drug diversion or counterfeiting could result in adverse public health outcomes in users in the following ways:

- **Drug spoilage:** Exposing drugs to adverse conditions can change their chemical structure, potentially reducing their therapeutic benefit and thus their ability to treat the end user's underlying health condition.
- **Drug contamination:** Drug diverters may remove labels from the containers of diverted drug to help them appear legitimate before reintroducing them to the supply chain; this may involve toxic solvents such as lighter fluid, which could contaminate the drug bottle or the drug itself.
- **Interrupted drug therapy:** If drug diversion or counterfeiting results in an ineffective product or a product with missing active ingredients, consumers that unknowingly consume these drugs would experience an interruption in drug therapy, possibly leading to withdrawal symptoms, symptom reoccurrence, or worsening health.
- **Undeclared ingredients:** Counterfeit drugs containing undeclared ingredients could result in allergic reactions or toxic poisonings in patients.[7]

Because we have limited information on the frequency of these types of events, is difficult to quantify any public health benefits of the proposed rule, if finalized, resulting from reduced morbidity and mortality in patients. In an appendix in Section IV, we provide examples of adverse events resulting from drug diversion or counterfeiting that the uniform licensing standards for WDDs and 3PLs that we are proposing potentially could have prevented.

2. Cost Savings from Reduction in Frequency of Licensure Application

The proposed rule sets the license terms at two years for WDDs and three years for 3PLs. Currently, one state (New York) requires license application renewal every three years, 21 require renewal every two years, and 31 require annual renewal. The proposed standards would

[7] Worldwide, investigators have identified counterfeit drugs and devices that contain heavy metals; poisons; household materials such as floor wax, sheet rock, and paint thinner; salt or sugar; undeclared medications; and missing active ingredients (Ref. [25],[26]).

generate cost savings for WDDs and 3PLs in states that require renewal more frequently than the license terms in the proposed rule. Industry would save time to prepare and submit these applications and state governments would save time to review and process these applications. The proposed standards would generate costs for New York.

To estimate the cost savings related to a reduction in frequency of licensure application, we calculate the total number of pages in the forms and instructions for licensure in each state. We assume that a designated representative would take about 0.2 hours to review and complete each page of an application, including any forms and instructions. We base this estimate on the Paperwork Reduction Act estimate for Form FDA 3911, which has five total pages of forms and instructions and an estimated total response time of one hour. Form 3911 collects some of the same information that state licensure applications require but does not match any state's application exactly. To incorporate uncertainty in our estimates, we use a low estimate of 0.1 hours per page and a high estimate of 0.3 hours per page. We assume that 3PLs complete the same application as WDDs and request comment on this assumption.

Facilities apply for a license to operate in the state where they are located. For our lower bound, we estimate the cost savings of reduced frequency of application for in-state licenses only. This estimate only accounts for the license applications that facilities submit to their home state. In practice, facilities also apply for licenses in most states where they do business. If facilities complete the same applications for ship-to licensure as they do for in-state licensure, this would result in larger cost savings. Therefore, for our upper bound estimates, we estimate the cost savings of reduced frequency of application for both in-state and out-of-state licenses.

In Table 8, we estimate the annual cost savings from reduced frequency of licensure for WDDs. WDDs licensed in states with annual licensure frequency would experience cost savings. We estimate that annual cost savings for WDDs would range from $0.38 million to $6.21 million.

Table 8. Annual Cost Savings for WDDs from Reduced Frequency of Licensure

Value	Annual Licensure (Low)	Annual Licensure (High)
Number of Licenses	1,107	15,944
Pages per License[a,b]	49	18
Hours per Page	0.1	0.3
Hours per License	5	6
Cost per License[c]	$690	$779
Annual Cost per License (Baseline)[d]	$690	$779
Annual Cost per License (Rulemaking)[e]	$345	$389
Total Annual Cost Savings[f] ($ millions)	$0.38	$6.21

[a] Average over the set of licenses included in the estimate.
[b] The average number of pages over the set of applications for in-state and out-of-state licenses (high estimate) is less than the average number of pages over the set applications for in-state licenses (low estimate).
[c] Cost per license equals hours per license × the cost of labor for a WDD designated representative from Table 7.
[d] Baseline annual cost per license equals the cost per license ÷ the baseline licensure frequency (1 year).
[e] Annual cost per license with rulemaking equals the cost per license ÷ the new licensure frequency (2 years).
[f] Total annual cost savings equals the change in the annual cost per license × the number of licenses.

In Table 9, we estimate the annual cost savings from reduced frequency of licensure for 3PLs. Those 3PLs with licenses in states with annual licensure frequency or 2-year licensure frequency would experience cost savings. We estimate that annual cost savings for 3PLs would range from $0.08 million to $1.27 million. Total annual cost savings for WDDs and 3PLs would range from $0.47 million to $7.47 million. We expect that these cost savings would begin in year 1.

Table 9. Annual Cost Savings for 3PLs from Reduced Frequency of Licensure

Value	Annual Licensure (Low)	Annual Licensure (High)	2-Year Licensure (Low)	2-Year Licensure (High)
Number of Licenses	268	2,294	177	1,126
Pages per License[a,b]	35	20	19	14
Hours per Page	0.1	0.3	0.1	0.3
Hours per License	4	6	2	4
Cost per License[c]	$435	$763	$235	$533
Annual Cost per License (Baseline)[d]	$435	$763	$118	$266
Annual Cost per License (Rulemaking)[e]	$145	$254	$78	$178
Total Annual Cost Savings[f] ($ millions)	$0.08	$1.17	$0.01	$0.10

[a] Average over the set of licenses included in the estimate.
[b] The average number of pages over the set of applications for in-state and out-of-state licenses (high estimates) is less than the average number of pages over the set applications for in-state licenses (low estimates).
[c] Cost per license equals hours per license × the cost of labor for a 3PL designated representative from Table 7.
[d] Baseline annual cost per license equals the cost per license ÷ the baseline licensure frequency (1 year or 2 years).
[e] Annual cost per license with rulemaking equals the cost per license ÷ the new licensure frequency (3 years).
[f] Total annual cost savings equals the change in the annual cost per license × the number of licenses.

3. Cost Savings from Fewer Ship-To Licenses for 3PLs Licensed by FDA

a. Facilities Licensed by FDA

All states currently have WDD licensure programs in place. To continue licensing, they would need to modify those programs to be consistent with the proposed rule, if finalized. Some states may adjust their programs to be consistent with national standards in time for the first cycle of licenses. However, some states may take longer to adjust their programs and some states may choose not to license. We would license WDD facilities in states without compliant WDD licensure programs.

In addition, approximately 19 states had licensure programs in place for 3PLs pre-statute.[8] States without 3PL licensure programs that choose to license would need to establish licensure programs. States may not have these licensure programs in place in time for facilities to obtain licenses in the first cycle. We would license 3PL facilities in states without compliant 3PL licensure programs.

[8] As of this analysis, 31 states have licensure programs for 3PLs. We expect that states established these additional licensure programs in response to the DSCSA, and the increase in the number of programs is an impact of this rulemaking.

In Table 10, we present our assumptions about the number of states without compliant WDD licensure programs and the number of states without compliant 3PL licensure programs over time.

Table 10. States without Compliant Licensure Programs over Time

Year	States without Compliant WDD Licensure Programs (Low)	States without Compliant WDD Licensure Programs (High)	States without Compliant 3PL Licensure Programs (Low)	States without Compliant 3PL Licensure Programs (High)
1	10	15	22	27
2	10	15	22	27
3	4	8	22	27
4	4	8	10	13
5	1	4	10	13
6	1	4	10	13
7+	1	4	1	4

We assume that WDD facilities would begin to submit license applications to us in year 1 and would then renew their licenses every 2 years thereafter. We also assume that 3PL facilities would begin to submit license applications to us in year 1 and would then renew their licenses every 3 years thereafter. Based on these assumptions, we estimate the number of facilities that we would license each year over 10 years in Table 11.

Table 11. Facilities Licensed by FDA over Time

Year	WDDs[a] (Low)	WDDs[a] (High)	3PLs[b] (Low)	3PLs[b] (High)	Total (Low)	Total (High)
1	383	574	246	302	629	876
2	383	574	246	302	629	876
3	153	306	246	302	399	608
4	153	306	112	146	265	452
5	38	153	112	146	150	299
6	38	153	112	146	150	299
7+	38	153	11	45	49	198

[a] Number of WDD facilities equals the number of states without a WDD licensure program × the total number of WDD facilities (1,951) ÷ the number of states with WDD facilities (49 plus Guam and Puerto Rico).
[b] Number of 3PL facilities equals the number of states without a 3PL licensure program × the total number of 3PL facilities (459) ÷ the number of states with 3PL facilities (40 plus Puerto Rico).

b. Cost Savings to 3PLs Licensed by FDA

Under the proposed rule, 3PLs we license would need a single license per facility and would not need to apply for ship-to licenses. 3PLs would experience cost savings from having to apply for fewer licenses. In Table 11, we estimated the number of 3PL facilities that we would license over time. Those facilities would need only one license each and would avoid applying for ship-to licenses.

Based on our 3PL registration data, we estimate that 3PL facilities have an average of 7.5 licenses each. Each 3PL we license would need one license, so we estimate that the average 3PL

facility we license would avoid completing 6.5 applications, or 2.2 applications per year in a three-year licensure cycle. Using the same assumptions we used to estimate the cost per license application in Section E2, we estimate that the average cost of a 3PL license application ranges from $230 to $689. Given these estimates, we estimate the annual cost savings per cycle in Table 12.

Table 12. Average Annual Cost Savings for 3PLs Licensed by FDA

Year	Avoided Ship-To Licenses (Low)[a]	Avoided Ship-To Licenses (High)[a]	Cost Savings (Low, $ millions)[b]	Cost Savings (High, $ millions)[b]
1	536	658	$0.12	$0.45
2	536	658	$0.12	$0.45
3	536	658	$0.12	$0.45
4	244	317	$0.06	$0.22
5	244	317	$0.06	$0.22
6	244	317	$0.06	$0.22
7+	24	97	$0.01	$0.07

[a] Annual avoided ship-to licenses equals 2.2 avoided licenses per year × the number of facilities licensed by FDA from Table 11.
[b] Annual cost savings equals annual avoided ship-to licenses × the average cost per 3PL license application.

The annualized cost savings to 3PLs licensed by FDA over 10 years would range from $0.06 million to $0.24 million at a 7 percent discount rate and from $0.06 million to $0.23 million at a 3 percent discount rate.

4. Cost Savings from State Standards Not Included in the Proposed Rule

To identify state standards that are not part of the proposed rule, we reviewed regulations in thirty states with legislative activity regarding wholesale distribution as reported by the Food and Drug Law Institute (Ref. [3]). We also reviewed regulations for Washington, D.C. We reviewed state regulations current as of 2014 to exclude regulations that states may have enacted in response to the DSCSA. We assume that 3PLs are subject to the same state standards as WDDs. Based on the information and data currently available to us, we quantified and qualitatively described some of the cost savings to WDDs and 3PLs that would result from states no longer enforcing standards that would be not be included in this rule, if finalized.

a. Examinations

At least one state, Florida, requires that designated representatives pass an examination. Based on information from commercially-available test prep courses,[9] we estimate that a designated representative spends between 14 and 18 hours preparing for the examination. Furthermore, we assume that a designated representative spends between 3 and 4 hours traveling to and taking the examination. Using the fully loaded wage for a designated representative (Table 7), this total time cost ranges from $2,386 to $3,088 per designated representative. If we include the $50.50 exam fee[10], the total cost per designated representative ranges from $2,437 to $3,138.

[9] http://www.skillsplusinc.com/florida.htm
[10] http://www.pearsonvue.com/vouchers/pricelist/fldbpr.asp

We use the number of facilities in Florida (124) as the lower bound number of affected facilities and we use the number of facilities with Florida licenses (468) as the upper bound number of facilities. Using information from the Bureau of Labor Statistics Job Openings and Labor Turnover Survey, we assume that designated representatives have a turnover rate of 2.6 percent per year.[11] We therefore estimate that between 3 and 12 designated representatives would no longer take the exam each year. Given these estimates, the total annual cost savings would range from $0.01 million to $0.04 million. We assume that these cost savings would begin in year 1.

b. Self-Assessments

Currently, California requires that designated representatives complete a self-assessment with 22 pages every two years, for an average of 11 pages per year. Oregon requires a self-assessment with 4 pages annually. Under the proposed rule, designated representatives would no longer spend time completing these self-assessments. Following our assumption for licensure applications, we assume that it takes representatives between 0.1 hours and 0.3 hours to complete each page of the self-assessment. Then, we estimate that the California assessment takes between 1.1 and 3.3 hours to complete each year and that the Oregon self-assessment takes between 0.4 and 1.2 hours to complete each year.

For our lower bound, we assume that all facilities located in California and Oregon currently comply with these standards. For our upper bound, we assume that all facilities with California and Oregon licenses comply with these standards. Given these assumptions, we estimate the total annual cost of self-assessments to WDDs and 3PLs in California and Oregon in Table 13. Based on Table 13, the total annual cost savings from ending self-assessments in these two states would range from $0.03 million to $0.43 million. We assume that these cost savings would begin in year 1.

Table 13. Annual Cost of Self-Assessments in California and Oregon

Value	California (Low)	California (High)	Oregon (Low)	Oregon (High)
Annual Time per Assessment (Hours)	1.1	3.3	0.4	1.2
Number of WDDs Complying	173	641	9	465
Number of 3PLs Complying	27	104	1	90
Total Annual Time for Assessments (Hours)[a]	220	2,459	4	666
Total Annual Cost of Assessments ($ millions)[b]	$0.03	$0.34	$0.00	$0.09

[a] Equals the total number of facilities complying (WDDs and 3PLs) × the annual time per assessment.
[b] Equals the annual time per assessment × the average wage for WDDs and 3PLs (Table 7), weighted by the number of facilities of each type complying.

c. Other Cost Savings from Changes in State Standards

We identified several other state standards that are not part of the proposed rule. We summarize these standards in Table 14. To the extent that the proposed standards would create

[11] https://www.bls.gov/news.release/jolts.htm

cost savings for WDDs or 3PLs, we underestimate the cost savings of the rule. We request data and detailed comment on any cost savings due to the elimination of these standards.

Table 14. Additional Examples of State Standards for Licensure that are Not Included in the Proposed Rule and Would Result in Cost Savings to Industry

States	State Standard	Proposed Standard
Colorado	Minimum age for designated representative: 21	Minimum age for designated representative: 18
Idaho	Continuing education	No specific standard
Louisiana	Perpetual inventories of all transactions regarding the receipt and distribution or other disposition	Would retain records for 3 to 6 years
Nebraska, New Mexico, Wyoming	Must submit photograph of designated representative	No standard
New Mexico	Designated representative must complete training program	No specific standard
North Dakota, Nevada	Provisions for temporary or provisional licensure	No such provisions
Oklahoma	Wholesale facility shall not be in the same facility as a retail pharmacy	No standard
Oregon	Background checks for principals, owners, officers, and designated representatives	Background checks for facility managers and designated representatives
South Dakota	Out-of-state licensure exemption in emergencies	No such provisions

5. Cost Savings to States from Fewer State Licenses

We expect that some states would not set up a 3PL licensure program or a conforming WDD licensure program by year 1. Instead, we would license WDD and 3PL facilities in those states. State licensing authorities currently incur costs when they license facilities. States would incur cost savings from any facilities that they would no longer license under the proposed rule; they would also incur a reduction in licensure fee revenues. In Table 11, we estimate the number of facilities in states without compliant WDD or 3PL programs over time. We would license these facilities, and states would incur cost savings related to licensing these facilities.

States charge an average annual fee of $341 for licensure. We assume that this fee reflects the cost to states to license a facility. Given this assumption, we estimate the annual cost savings (and the reduction of fee revenues) over time to states from issuing fewer WDD and 3PL licenses in Table 15.

Table 15. Cost Savings to States from Fewer WDD and 3PL Licenses over Time ($ millions)

Year	Total Cost Savings (Low)[a]	Total Cost Savings (High)[a]
1	$0.21	$0.30
2	$0.21	$0.30
3	$0.14	$0.21

Year	Total Cost Savings (Low)[a]	Total Cost Savings (High)[a]
4	$0.09	$0.15
5	$0.05	$0.10
6	$0.05	$0.10
7+	$0.02	$0.07

[a] Total cost savings equals the number of facilities licensed by FDA from Table 11 × $341, the assumed average annual cost for a state to issue a license.

The reduction in costs associated with licensure represents cost savings to states. Though we use the licensure fee as a proxy for the cost of licensure to states, reductions in the revenue collected by states from licensure fees represents a transfer from states to facilities. We discuss these transfers further in Section G.

The annualized cost savings to states would range from $0.09 million to $0.14 million at a 7 percent discount rate and from $0.08 million to $0.14 million at a 3 percent discount rate.

6. Additional Benefits and Cost Savings

The proposed rule would require each WDD firm to furnish a surety bond to the licensor (the state or FDA), even if the firm had multiple facilities and operated in multiple states. This surety bond would be intended to promote compliance with the DSCSA and increase the likelihood that any administrative penalties levied on the WDD facility by the licensor would be paid. If firms with multiple facilities or firms that operate in multiple states currently hold more than one bond, they would experience cost savings under the rule from reducing the number of bonds they hold.

WDDs and 3PLs may experience additional cost savings from uniform licensing standards, particularly those WDDs and 3PLs that operate in multiple states. These firms would review and comply with only one set of standards rather than multiple sets of standards as a result of the proposed rule, if finalized.

The benefits and cost savings of this proposed rule are highly uncertain and difficult to measure. We request comment on all the assumptions in the proceeding sections and any additional benefits or cost savings associated with this proposed rule.

7. Summary of Benefits

In Table 16, we summarize the stream of monetized benefits from the proposed rule, if finalized. Benefits quantified with the cargo-theft approach and cost savings to WDDs and 3PLs from the reduced frequency of licensure, fewer examinations, and fewer self-assessments would occur annually beginning in year 1. Cost savings from fewer ship-to licenses for some 3PLs and cost savings to states from reduced licensure costs would begin in year 1, gradually decrease until the third 3PL licensure cycle, and occur annually afterwards.

Table 16. Stream of Benefits from the Proposed Rule over 10 Years ($ millions)

Year	Low Estimate	Primary Estimate[a]	High Estimate
0	$0.00	$0.00	$0.00
1	$1.60	$12.54	$36.65
2	$1.60	$12.54	$36.65

Year	Low Estimate	Primary Estimate[a]	High Estimate
3	$1.52	$12.45	$36.56
4	$1.41	$12.26	$36.27
5	$1.37	$12.21	$36.22
6	$1.37	$12.21	$36.22
7	$1.29	$12.08	$36.03
8	$1.29	$12.08	$36.03
9	$1.29	$12.08	$36.03

[a] For any component of the benefits without a primary estimate described in this PRIA, the primary estimate is the average of the low estimate and the high estimate.

In Table 17, we estimate the discounted total benefits of the proposed rule over 10 years. Annualized benefits would range from $1.25 million to $31.50 million at a 7 percent discount rate and from $1.26 million to $32.18 million at a 3 percent discount rate. The annualized benefits to WDDs would range from $0.36 million to $5.74 million at a 7 percent discount rate and $0.37 million to $5.87 million at a 3 percent discount rate. The annualized benefits to 3PLs would range from $0.14 million to $1.38 million at a 7 percent discount rate and $0.14 million to $1.40 million at a 3 percent discount rate.

Table 17. Discounted Total Benefits of the Proposed Rule over 10 Years ($ millions)

Value	Low Estimate	Primary Estimate	High Estimate
Present Value (7%)	$9.36	$80.14	$236.76
Present Value (3%)	$11.09	$95.64	$282.76
Annualized Value (7%)	$1.25	$10.66	$31.50
Annualized Value (3%)	$1.26	$10.89	$32.18

F. Costs of the Proposed Rule

1. Costs for WDDs, 3PLs, and States to Read and Understand the Rule

We expect that WDDs and 3PLs would need to read and understand the rule.[12] We assume that lawyers at each WDD or 3PL firm would read the rule, interpret its provisions, and determine which provisions they would have to implement. We also assume that designated representatives at all WDD and 3PL facilities would also need to read and understand the rule. We also expect that a government attorney in each of the 53 jurisdictions would need to read and understand the rule. Based on these assumptions, in Table 18 we estimate the number of employees that would need to read and understand the rule and the weighted average hourly labor cost per person by entity type.

Table 18. Number of Employees Reading the Rule and Average Hourly Labor Costs

Value	WDDs	3PLs	States
Number of Designated Representatives Reading the Rule[a]	1,951	459	0
Number of Lawyers Reading the Rule[b]	1,427	133	53

[12] While we also expect that approved organizations would need to read and understand the rule, we assume that the costs of executive and legal review, discussed in Section F6, would include these costs.

Value	WDDs	3PLs	States
Weighted Average Hourly Labor Cost per Person[c]	$154.76	$134.58	$93.70

[a] Based on the number facilities in Table 4.
[b] For WDDs, this number equals the number of WDD firms. For 3PLs, it equals the total number of firms minus the number of WDD firms. For states, it equals the number of jurisdictions with WDD or 3PL facilities.
[c] Based on labor cost estimates from Table 7.

We anticipate that the definitions clarified in "Certain Requirements Regarding Prescription Drug Marketing; Proposed Rule" (or Part 203) are necessary to understand this proposed rule. We assume that only the lawyers and representatives reading this rule would also read Part 203 and account for the cost of reading and understanding Part 203 by these individuals.

This proposed rule has approximately 50,000 words and Part 203 has approximately 5,000 words, for a combined 55,000 words. Based on HHS guidance, we assume a reading speed of between 200 and 250 words per minute. We then estimate that it would take each person between 3.7 hours and 4.6 hours to read and understand the rule.

Based on the estimates in Table 18 and the average time it would take each person to read and understand the rule, the total one-time cost to read and understand the rule would range from $2.23 million to $2.78 million. We assume that WDDs, 3PLs, and states would incur these costs before year zero, in the year in which the proposed rule would finalize. We include the net present value of these costs in the year 0 costs of the proposed rule.

2. Reporting Costs

DSCSA requires that designated representatives report their facilities using our website. Using information from the Eastern Research Group (ERG), we estimate that it would take representatives 0.25 hours to report a facility each year, or $35 for WDD representatives and $31 for 3PL representatives (Ref. [4]). Based on the total number of WDD and 3PL facilities from Table 4, the total annual reporting cost would equal $0.07 million for WDDs and $0.01 million for 3PLs, or a total of $0.08 million annually.

However, representatives have reported their facilities each year since 2013. Therefore, we include the present value of costs of reporting from 2013 in the year 0 costs. Because we are uncertain when this rulemaking would finalize, we assume that year 1 is between 2024 and 2026. Given this assumption, the net present value of reporting costs in year 0 would range from $1.22 million to $1.40 million at a 7 percent discount rate and from $1.14 million to $1.21 million at a 3 percent discount rate. Annually after year 0, the cost of reporting would equal $0.08 million.

3. Costs from Increased Frequency of Licensure Application

Under the proposed rule, WDDs would have to renew their licenses every two years. Under these proposed standards, WDDs in New York would have to apply for licenses more frequently than without the standards. New York currently requires licensure every three years. To estimate the potential cost of more frequent licensure application, we follow the same method we used in the benefits section for estimating cost savings of reduced licensure frequency for other states (Section E2).

We present our estimates of the annual costs due to increased frequency of licensure application in Table 19. The annual costs for WDDs in New York would range from $0.01 million to $0.12 million. We assume that these costs would begin in year 1.

Table 19. Annual Costs for WDDs from Increased Frequency of Licensure

Value	3-Year Licensure (Low)	3-Year Licensure (High)
Number of Licenses	128	731
Pages per License[a]	23	23
Hours per Page	0.1	0.3
Hours per License	2.3	6.9
Cost per License[b]	$323	$968
Annual Cost per License (Baseline)[c]	$108	$323
Annual Cost per License (Rulemaking)[d]	$161	$484
Total Annual Costs[e] ($ millions)	$0.01	$0.12

[a] Average over the set of licenses included in the estimate.
[b] Cost per license equals hours per license × the cost of labor for a WDD designated representative from Table 7.
[c] Baseline annual cost per license equals the cost per license ÷ the baseline licensure frequency (3 years).
[d] Annual cost per license with rulemaking equals the cost per license ÷ the new licensure frequency (2 years).
[e] Total annual costs equal the change in the annual cost per license × the number of licenses.

4. Cost of New Standards for WDDs and 3PLs

a. Costs to Conduct Criminal Background Checks

The rule would require designated representatives and facility managers at WDDs and 3PLs to undergo a one-time criminal background check. We would additionally require designated representatives and facility managers at WDDs to undergo fingerprinting during this background check. Facility managers are managers that supervise employees that operate and handle prescription drugs. Implementing a background check would impose an initial one-time cost to check current designated representatives and facility managers and annual costs to perform background checks when facilities hire new designated representatives and facility managers.

In Table 20 we estimate the number of employees requiring criminal background checks in year 1 and annually after year 1. Based on information from ERG, we assume that each facility employs one designated representative and that the number of facility managers depends on the size of the facility. Specifically, we assume that facilities of fewer than 100 workers employ two facility managers, facilities with between 100 and 500 workers employ six facility managers, and facilities with 500 or more workers employ eight facility managers (Ref. [5]).

In year 1, all 3,555 designated representatives and facility managers in states that do not already require criminal background checks would require a background check. Following our assumption about employee turnover in Section E4a, we estimate that 92 new employees (3,555 employees × 2.6 percent turnover) would require a background check annually after year 1.

Table 20. Number of Employees Requiring Criminal Background Checks under the Proposed Rule

Value	1–19 Employees	20–99 Employees	100–499 Employees	500 or more Employees	Total
WDD Facilities with New Standards[a]	395	153	117	53	718
3PL Facilities with New Standards[a]	55	52	24	14	145
Background Checks in Year 1[b]	1,350	615	987	603	3,555
Background Checks Annually After Year 1[c]	35	16	26	16	92

[a] The number of facilities with new standards equals the number of facilities of that size category from Table 4 minus the number of facilities in states that already conduct criminal background checks (Table 5 for WDDs and Table 6 for 3PLs).
[b] The number of background checks in year 1 equals the total number of designated representatives and facility managers at all WDD and 3PL facilities.
[c] The number of background checks annually after year 1 equals the total number of background checks in year 1 × the average employee turnover rate of 2.6 percent.

We estimate that a single criminal background check costs approximately $100. For WDDs, a designated representative also would spend approximately 15 minutes per employee collecting and submitting fingerprints at a cost of $35 per background check. Then, the estimated cost to conduct a single background check would equal $129 on average for WDDs and 3PLs.[13]

Based on the average cost of a single background check and the number of background checks in Table 20, we estimate that the costs of conducting criminal background checks would equal $0.46 million in year 1 and $0.01 million annually after year 1.

b. Costs of Establishing Written Standard Operating Procedures (SOPs)

The rule would require facilities to establish four types of written standard operating procedures. First, WDD facilities[14] would need to establish procedures to ensure that facilities only conduct business with authorized trading partners. Second, both 3PL and WDD facilities would need to establish procedures to ensure products are transported under conditions that prevent the compromise of product identity, strength, quality, integrity, or purity. In addition, these procedures would need to include methods to ensure the identification, investigation, documentation, correction, and reporting of deviation from the above are identified, investigated, documented, corrected, and reported to authorized trading partners. Third, facilities would need to establish procedures to document regular calibration and validation of equipment in the

[13] The cost of a background check for a WDD employee would equal $135 ($100 fee + 0.25 hours × $140.36 per hour) and the cost of a background check for a 3PL employee would equal the $100 fee. The average cost to conduct a background check, weighted by the number of affected WDD and 3PL facilities in Table 4, is $129.
[14] The rule would not require that 3PL facilities establish procedures to ensure that facilities only conducting business with authorized trading partners. However, we do regard this as best practice for 3PLs. To the extent that some 3PLs would adopt these recommendations in response to the proposed rule, we would underestimate the costs to 3PLs. We request comment on this assumption.

facility. Fourth, facilities would need to establish procedures to ensure the qualifications of all personnel are met, maintained, and documented.

In this section, we estimate the one-time costs to establish written SOPs, the recurring costs to annually update SOPs, and the recurring costs to review SOPs.

One-Time Cost to Establish Written SOPs

We estimate the burden associated with establishing written SOPs from a report by ERG (Ref. [5]). We expect that the number of hours required to establish an SOP depends on the size of the facility. In Table 21, we estimate the total time required to establish SOPs per facility by facility size.

Table 21. Estimated Time to Establish SOPs per Facility (Hours)

Type of SOPs	1–19 Employees	20–99 Employees	100–499 Employees	500 or more Employees
Transportation	14	14	25	36
Authorized Trading Partners	13	13	21	32
Equipment Maintenance	8	8	14	22
Personnel	8	8	13	18
Total Time per Facility	43	43	73	108

We assume that all WDD and 3PL facilities would need to establish written SOPs in response to this rulemaking (see Table 4). Based on this assumption and the estimates in Table 21, we expect that it would take the average WDD facility 53 hours to establish written SOPs, while it would take the average 3PL facility 58 hours to establish written SOPs.[15] To incorporate uncertainty in our estimates, we assume an uncertainty range of 25 percent around these estimates, for a range of 40 hours to 66 hours for WDDs and a range of 43 hours to 72 hours for 3PLs.

We assume that designated representatives would write up these procedures. Given this assumption, the cost of labor for designated representatives (Table 7), the range of hours required to establish written SOPs, and the total number of WDD and 3PL facilities, the one-time cost to establish written SOPs would range from $10.92 million to $18.20 million for WDDs and from $2.47 million to $4.11 million for 3PLs. We assume that facilities would incur these costs in year 1.

Recurring Costs to Revise SOPs

We use the same data, methods, and assumptions to estimate the recurring costs to revise SOPs that we used to estimate the one-time costs to establish SOPs. In Table 22, we estimate the total annual time required to revise SOPs per facility by facility size.

[15] These estimates are the average time per facility across all facility size groups, weighted by the number of facilities of the given size.

Table 22. Estimated Annual Time to Revise SOPs per Facility (Hours)

Type of SOPs	1–19 Employees	20–99 Employees	100–499 Employees	500 or more Employees
Transportation	4	4	8	11
Authorized Trading Partners	3	3	5	8
Equipment Maintenance	3	3	5	7
Personnel	2	2	4	6
Total Time per Facility	12	12	22	32

Based on our assumptions and the information in Table 22, we estimate that it would take the average WDD facility between 11 and 19 hours to revise SOPs each year, while it would take the average 3PL facility between 12 and 21 hours to revise SOPs each year. Then, the annual costs to revise SOPs would range from $3.13 million to $5.22 million for WDDs and from $0.71 million to $1.19 million for 3PLs. We assume that facilities would incur these costs annually starting in year 2, since facilities would not need to revise SOPs in the same year that they establish SOPs.

Recurring Costs to Review SOPs

Based on information from ERG (Ref. [5]), we estimate that it would take facility managers 8 hours to review the newly established SOPs each year. The average WDD facility employs 3.1 facility managers and the average 3PL facility employs 3.6 facility managers.[16] Based on this information and assuming an uncertainty range of 25 percent, we estimate that the average WDD facility would spend between 19 hours and 31 hours reviewing SOPs each year and that the average 3PL facility would spend between 22 hours and 36 hours reviewing SOPs each year.

Based on the cost of labor for facility managers (Table 7) and the total number of WDD and 3PL facilities (Table 4), the total annual cost to review SOPs would range from $2.34 million to $3.90 million for WDDs and from $0.57 million to $0.96 million for 3PLs. We assume that facilities would incur these costs annually starting in year 1, since facility managers would need to review both the newly established SOPs and the revised SOPs.

c. Cost of Surety Bonds

Under the proposed rule, WDDs would submit a surety bond to its state licensing authority to obtain or renew their licenses or would provide evidence that it possesses equivalent surety in another state. Firms whose gross annual receipts exceed $10 million would submit a surety bond of $100,000 or equivalent means, while firms earning $10 million or less would submit a surety bond of $25,000.

17 states already require WDDs to furnish a $100,000 surety bond. To estimate the costs of surety bonds, we first identify firms without licenses in those states. We match information from WDD facility reporting data to firm information from Dun & Bradstreet to determine the number of firms without licenses in states that already require surety bonds. Dun & Bradstreet

[16] These estimates are averages of the number facility managers at facilities of different sizes, listed in Table 20, weighted by the number of facilities of each size, listed in Table 4.

data also include data on firm sales, which we use to determine the type of bond a firm would purchase. We identify 47 WDD firms with sales that exceed $10 million and 244 WDD firms with sales below $10 million that do not have licenses in states that already require a surety bond.

The annual cost to maintain a surety bond approximately equals the product of the surety bond's principal (in this case, $100,000 or $25,000) and its interest rate. We estimate that the average interest rate for surety bonds is 1.75 percent. Then, the annual cost to maintain a $100,000 surety bond is $1,750 ($100,000 principal × 1.75 percent interest rate) and the annual cost to maintain a $25,000 surety bond is $438 ($25,000 principal × 1.75 percent interest rate).

Therefore, the total annual cost to maintain surety bonds is $0.08 million ($1,750 per year × 47 firms) for firms with greater than $10 million in annual revenue and $0.11 million ($438 per year × 244 firms) for firms with less than $10 million in annual revenue. The estimated total cost of surety bonds equals $0.19 million per year, starting in year 1.

d. Recordkeeping Costs

Current law already requires recordkeeping of commercial prescription drug transactions. We request comment on how much the proposed rule, if finalized, would increase the recordkeeping burden for the 1,951 WDD facilities and 459 3PL facilities beyond current requirements. We expect that the longer record retention time for suspect and illegitimate products of six years would have minimal costs. We request comment on this assumption.

e. Cost for 3PLs to Separate Illegitimate and Legitimate Products

The proposed rule would require 3PLs to keep illegitimate products and other products unfit for distribution separate from saleable products in a clearly defined and designated area. This requirement may create additional burden for 3PLs that do not have the space to keep the product separate. We request comment on any burden associated with this requirement.

5. Cost of Routine Inspections

To ensure compliance with the rule, if finalized, we would require routine inspections of WDD and 3PL facilities every three years. The rule would allow three types of entities to inspect facilities: FDA, states, and approved organizations (AOs). If a state has a licensure program that conforms to our standards, facilities in that state would apply for licenses from that state. Then, the state would inspect facilities licensed in their state or contract out inspections to approved organizations. If a state does not have a licensure program that conforms to our standards, facilities in that state would apply for an FDA license. We expect that our licensure program would primarily rely on inspection reports that staff from approved organizations would prepare.

Though state licensing authorities and approved organizations would inspect facilities, we expect that WDDs and 3PLs would bear the costs of inspection. We request comment on this assumption.

a. One-Time Cost for States and AOs to Train New Staff

Under the proposed rule, states and AOs would need to train employees to conduct inspections. We assume that these employees would complete an 8-hour training module covering the standards in this rulemaking. Based on the wages for compliance officers in Table 7, the cost to train a new employee would range from $468 (if only state employees conduct inspections) to $643 (if only AO employees conduct inspections).

Our Office of Regulatory Affairs (ORA) estimates that our investigators conduct roughly 15 site visits per year each. We assume that AO or state employees could complete the same number of inspections each year. From Table 5 and Table 6 we estimate that 1,899 WDD facilities and 446 3PL facilities would require inspections, for a total of 2,345 inspections. To conduct these inspections, states or approved organizations would need to train approximately 156 employees (2,345 inspections ÷ 15 inspections per employee).

The total one-time cost to train new inspection staff would range from $0.07 million to $0.10 million. We expect that states and approved organizations would incur these costs in year 1.

b. Costs for WDDs and 3PLs to Participate in Inspections

Inspections would impose costs on WDD and 3PL facilities. During an inspection, designated representatives would escort investigators, AO staff, or state inspectors around the facility, answer questions and complete paperwork related to the inspection, and provide investigators, AO staff, or state inspectors with any required records. WDDs and 3PLs would have an initial inspection in year 1 prior to the issuance of their initial license. We expect these facilities would then undergo routine inspections every third year thereafter.

We use information from our ORA to estimate the time spent by designated representatives engaging in inspection-related activities in Table 23. We estimate that designated representatives at WDDs would spend 8,826 hours participating in initial inspections in year 1 and 4,413 hours participating in subsequent inspections every 3 years afterwards. We estimate that designated representatives at 3PLs would spend 2,200 hours participating in initial inspections in year 1 and 1,100 hours participating in subsequent inspections every 3 years afterwards.

Table 23. Number of Hours Spent Participating in Inspections by WDDs and 3PLs

Value	1–19 Employees	20–99 Employees	100–499 Employees	500 or more Employees	Total
Hours per Initial Inspection	4	4	6	8	
Hours per Subsequent Inspection	2	2	3	4	
Total Hours for Initial Inspections of WDDs[a]	4,140	1,620	1,818	1,248	8,826
Total Hours for Subsequent Inspections of WDDs[a]	2,070	810	909	624	4,413
Total Hours for Initial Inspections of 3PLs[b]	648	536	552	464	2,200

Value	1–19 Employees	20–99 Employees	100–499 Employees	500 or more Employees	Total
Total Hours for Subsequent Inspections of 3PLs[b]	324	268	276	232	1,100

[a] Total hours for inspections of WDDs equals the number of hours per inspection × the number of facilities requiring inspections from Table 5.
[b] Total hours for inspections of 3PLs equals the number of hours per inspection × the number of facilities requiring inspections from Table 6.

Using the cost of labor for designated representatives at WDDs from Table 7, we estimate that inspections of WDDs would cost facilities $1.24 million in year 1 and $0.62 million every 3 years afterwards. Similarly, we estimate that inspections of 3PLs would cost facilities $0.27 million in year 1 and $0.14 million every 3 years afterwards. The annualized costs of participating in inspections over 10 years would equal $0.33 million at a 7 percent discount rate and $0.31 million at a 3 percent discount rate.

c. Costs for States and AOs to Conduct Inspections

The costs for a state inspector or AO employee to conduct the inspection include the time the state inspector or AO employee spends reading and evaluating the facility's written procedures, conducting the on-site inspection, and writing up the inspection report. We estimate the time spent by state or AO compliance officers conducting inspections using information from ORA in Table 24.

Table 24. Number of Hours Spent Conducting Inspections by States and AOs

Value	1–19 Employees	20–99 Employees	100–499 Employees	500 or more Employees	Total
Hours per Initial Inspection	40	40	50	60	
Hours per Subsequent Inspection	20	20	25	30	
Total Hours for Initial Inspections[a]	47,880	21,560	19,750	12,840	102,030
Total Hours for Subsequent Inspections[a]	23,940	10,780	9,875	6,420	51,015

[a] Total hours for inspections equal the number of hours per inspection × the number of facilities requiring inspections (the sum of the number of facilities requiring inspections from Table 5 and Table 6).

Using the costs of labor for state and AO compliance officers from Table 7, we estimate that the cost to conduct initial inspections in year 1 would range from $5.97 million (if only state employees conduct inspections) to $8.20 million (if only AO employees conduct inspections). The cost to conduct subsequent inspections every three years after year 1 would range from $2.99 million to $4.10 million. The annualized cost to conduct inspections would range from $1.29 million to $1.77 million at a 7 percent discount rate and from $1.24 million to $1.70 million at a 3 percent discount rate.

While we assume that states and AOs would inspect facilities, if states and AOs are unavailable, we would inspect facilities. We estimate our cost to inspect facilities would equal

around $59,000 per inspection, which is significantly higher than the estimated costs for states or AOs. Therefore, if our assumption that states and AOs would inspect facilities is incorrect, then we underestimate the costs of inspections.

6. Approved Organization Approval Costs

We expect to use approved organizations to inspect most facilities we license. Approved organizations would not license facilities and would only assist us in determining whether facilities meet the necessary licensing standards. To receive approval, approved organizations would need to prepare and submit various materials to us, including statements containing basic background information, policies, procedures, and documentation.

At least two entities have expressed interest to us to become approved organizations. In the past, the HHS Centers for Medicare and Medicaid Services (CMS) approved 10 approved organizations meeting CMS program requirements, with respect to suppliers of durable medical equipment, prosthetics, orthotics, and supplies. We therefore assume that between 2 and 10 entities would apply for approval. We request comment on the number of organizations that would apply.

Based on assumptions about the approval process in the regulatory impact analysis of a previous rule on the Unique Device Identification System (Ref. [6]) and the hourly labor cost for managers at AOs from Table 7, we assume it would take one manager 80 hours to complete the initial approval process, for a cost of $0.01 million per organization in year 1. We also assume that each AO would incur $0.25 million in executive and legal costs in year 1. The total cost of the initial approval process would equal $0.26 million per organization.

AOs would also incur recurring executive and legal costs and reapplication costs after year 1. We assume that each AO would incur executive and legal costs of $0.03 million annually after year 1. In addition, AOs would reapply for approval every fifth year. We assume that the reapplication process would take 20 hours to complete, for a cost of $2,565 per organization that would recur every five years.

In Table 25, we estimate the stream of annual approval costs for AOs over time. The annualized approval costs to approved organizations would range from $0.10 million to $0.51 million at a 7 percent discount rate and from $0.10 million to $0.48 million at a 3 percent discount rate.

Table 25. Annual Approval Costs for Approved Organizations over Time ($ millions)

Year	Cost per AO[a]	Total Costs (Low)[b]	Total Costs (High)[c]
0	$0.00	$0.00	$0.00
1	$0.26	$0.52	$2.60
2	$0.03	$0.05	$0.25
3	$0.03	$0.05	$0.25
4	$0.03	$0.05	$0.25
5	$0.03	$0.05	$0.25
6	$0.03	$0.06	$0.28
7	$0.03	$0.05	$0.25
8	$0.03	$0.05	$0.25

Year	Cost per AO[a]	Total Costs (Low)[b]	Total Costs (High)[c]
9	$0.03	$0.05	$0.25

[a] Equals the sum of application costs and initial executive and legal costs (year 1), annual legal and executive costs (years 2–10), and reapplication costs (years 5 and 10).
[b] Equals cost per AO × 2 organizations.
[c] Equals cost per AO × 10 organizations.

Though approved organizations would apply to become FDA approved organizations, we expect that they would only do so if their expected profits from fees would be greater than their expected costs of entering and staying in business. We expect that WDDs and 3PLs would bear some of these approval costs because such costs would be passed on to them by approved organizations. We request comment on this assumption.

7. State Costs to Establish or Revise Licensure Programs

To license WDDs and 3PLs, states would implement the proposed rule's standards. Implementing these standards would require some states to revise their laws and increase communication and enforcement resources.

The proposed rule would not require that states pass new legislation or create or revise regulations. We assume, however, that states would choose to update their programs through statute or regulation so that they could continue to operate them under the proposed standards. Updating state programs would likely require a revision to statutes, regulations, or both. We do not know if states would address both WDD and 3PL licensure in the same legislation and regulation but assume that states would have separate legislative and regulatory efforts for WDDs and 3PLs. We request comment on this assumption.

In Table 26, we summarize our assumptions about the timing of legislative and regulatory activity by states in response to the proposed rule, if finalized. We assume that legislative and regulatory activity would follow the licensure schedule for WDDs (every 2 years) and 3PLs (every 3 years). For our low estimates, we assume that fewer states would publish regulations in earlier years than in later years. For our high estimates, we assume that more states would publish regulations in earlier years than in later years.

Table 26. Number of States Acting on WDD and 3PL Legislation and Regulations by Year

Year	States for WDDs (Low)	States for WDDs (High)	States for 3PLs (Low)	States for 3PLs (High)	Total States (Low)	Total States (High)
1	41	36	19	14	60	50
2	0	0	0	0	0	0
3	6	7	0	0	6	7
4	0	0	12	14	12	14
5	3	4	0	0	3	4
6	0	0	0	0	0	0
7	0	0	9	9	9	9

We assume that states act on WDD legislation and regulations at the beginning of the first three two-year licensure cycles and that states act on 3PL legislation and regulations at the beginning of the first three three-year licensure cycles.

a. State Costs of Licensure Legislation and Regulations

To create and update state licensure laws, we expect that state attorneys would first format and prepare legislation. We assume it would take an attorney from a state between 2 and 4 hours to format and prepare legislation and request comment on this assumption. Then, we expect that attorneys from the program office, the legislature, and the governor's office would review the legislation. We assume that each of these three attorneys would spend between 0.5 and 2 hours reviewing the legislation and request comment on this assumption. Using the hourly labor cost for state attorneys from Table 7, the total cost for attorneys to format, prepare, and review legislation for a single state would range from $328 to $937.

Once the legislation is drafted, we expect that at least one person from each state legislator's office would read it. Using information from the National Conference of State Legislatures, we estimate that the average state has 143 legislators. Using the hourly labor cost for legislative staffers from Table 7 and assuming that it would take each legislative staffer between 0.25 minutes to 0.75 minutes to read the legislative documents, the total cost for legislative staffers to read proposed legislation for a single state would range from $1,773 to $5,320. We request comment on our assumption regarding the time it would take legislative staffers to read legislative documents.

If legislation is passed, we expect that states would change their licensure regulations to conform to the standards under the proposed rule. State employees working on regulations in two states indicated that it would take between 100 hours and 600 hours to prepare and review state licensure regulations. Using the wage for state lawyers from Table 7, the total cost for a state to prepare and review state licensure regulations would range from $9,370 to $56,220.

Based on these estimates, the total cost for a state to act on legislation and regulations for WDDs or 3PLs in response to the proposed rule, if finalized, would range from $11,471 to $62,477. Given the number of states acting on WDD and 3PL legislation and regulations in each year from Table 26, the annualized costs of legislative and regulatory activity by states in response to the proposed rule, if finalized, would range from $0.12 million to $0.60 million at a 7 percent discount rate and from $0.11 million to $0.56 million at a 3 percent discount rate.

b. State Program Costs of a Conforming Licensure Program

We understand that some states already operate licensure programs for both WDDs and 3PLs and incur costs beyond inspection costs. We assume that states already incur overhead costs associated with operating these programs, such as invoicing, payment oversight, internal reviews, reconciling accounts, conducting internal and external communications, non-payment enforcement, standard operating procedures, regulatory support documents, and employee training. We expect that states would modify or augment these processes in response to the proposed rule. Changes to these processes would likely vary across states. We request detailed comment on the costs that states may incur to change or expand support for their licensure programs. We also request comment on the likelihood that states would choose to continue to license following the implementation of the proposed rule, and how long it would take for states to establish new licensure programs.

8. FDA Costs

a. Licensure Program Costs

As illustrated in Table 11, though we expect that states would license most WDDs and 3PLs, we would license some facilities. To license facilities, we would incur costs to create our own licensure program. The costs of a licensure program would include the costs to process applications, costs to conduct appeals of denied, suspended, or revoked licenses, costs to take compliance or enforcement actions, and costs to review inspection reports from AOs.

As reflected in tables 10 and 11, FDA estimates that most states will establish conforming licensure programs for WDDs and 3PLs by year 1 , while some states may take additional time to establish these programs. We estimate that nearly all states will eventually set up conforming licensure programs, however we recognize the possibility that it may take some states additional time.

Based on proprietary data from the National Association of Boards of Pharmacy, 2020 Survey of Pharmacy Law, every state licenses/registers WDDs, whereas 31 states had laws or pending laws to regulate 3PLs. FDA estimates that more states will be able to establish licensure programs for WDDs than 3PLs within the first licensure periods following year 1 because more states have experience with and currently license WDDs than license 3PLs. We request comment on the likelihood that states would choose to continue to license following the implementation of the proposed rule, and how long it would take for states to establish new licensure programs.

In Table 27, we summarize our assumptions about the time costs of running our licensure program. Using the hourly labor cost for employees from the FDA Center for Drug Evaluation and Research (CDER) from Table 7, we estimate that the average annual cost to FDA per license application would range from $1,386 to $2,268 for WDD licenses and from $924 to $1,512 for 3PL licenses.[17] To estimate the total costs of licensure applications to FDA in a given year, we multiply the average annual cost per license application by the number of facilities we would license in each year from Table 11.

Table 27. Time Cost to FDA per License Application

Value	Low Estimate	High Estimate
Hours to Process Application	11.5	11.5
Expected Hours to Process Appeals of Denied Licenses[a]	0	2.2
Expected Hours to Process Appeals of Revoked or Suspended Licenses[b]	0	3.6
Expected Hours Related to Compliance or Enforcement Actions[c]	0	6.6
Hours to Review Inspection Report	8	8
Expected Total Hours per Application	19.5	31.9

[a] We assume it would take 11 hours to process each appeal and that the probability that we deny a license would range from 0 percent to 20 percent.
[b] We assume it would take 72 hours to process each appeal and that the probability that we revoke or suspend a license would range from 0 percent to 5 percent.
[c] We assume it would take 33 hours to take compliance or enforcement actions on a facility and that the probability that we take compliance or enforcement actions would range from 0 percent to 20 percent.

[17] The average annual cost for FDA to review a WDD license application would equal the expected total hours per application × the wage for a CDER employee from Table 7 ÷ 2-year licensure cycle. Similarly, the average annual cost for FDA to review a 3PL license application would equal the expected total hours per application × the wage for a CDER employee from Table 7 ÷ 3-year licensure cycle.

In addition to the time costs associated with each license, we expect that establishing and operating a licensure program would also include some additional overhead costs. We use internal budget information to estimate the additional costs of the licensure program over time. In Table 28, we estimate the overhead costs of the licensure program over time. Note that we expect that we would incur some of these costs *before* year 0. We include the net present value of any costs incurred before year 0 in the total year 0 costs.

Table 28. Additional Costs to FDA Associated with the Licensure Program ($ millions)

Cost	Year 0 Costs (7%)[a]	Year 0 Costs (3%)[a]	Year 1 Costs	Year 2 Costs
Information Technology	$0.80	$0.80	$0.03	$0.03
System to Issue License Certificates	$0.13	$0.13	$0.03	None
Legal Review and Support	$0.40	$0.39	None	None
Monitoring of State Legislation and Regulations	$0.15	$0.14	$0.07	None
User Fee Infrastructure	$0.28	$0.28	$0.28	$0.28
Total Cost	$1.75	$1.74	$0.40	$0.31

[a] Year 0 costs include the net present value of all costs incurred before year 0.

We estimate that the total annualized costs of our licensure program would range from $0.82 million to $1.35 million at a 7 percent discount rate and from $0.77 million to $1.30 million at a 3 percent discount rate.

b. Approval Program Costs

We would approve organizations to conduct inspections of WDDs and 3PLs on our behalf. To approve these organizations, we would incur costs to develop guidelines for the approval program, costs to review AO applications, and costs to audit AOs.

We expect that we would incur costs related to setting up the approval program before year 0. Using internal budget information, we estimate that the net present value of these costs in year 0 would equal $0.07 million at a 7 percent discount rate and at a 3 percent discount rate. We also estimate that we would incur costs of $0.57 million in year 1 related to setting up the approval program.

Following our assumptions in Section F6, we assume that between 2 and 10 entities would apply to be approved organizations. We would review applications and conduct initial inspections of the AOs in year 1. We then would review renewal applications and audit AOs every 5 years thereafter. We assume that the time to review an application and conduct an initial inspection would range from 88 to 144 hours per AO. We also assume that the time to review a renewal application and conduct an audit would range from 64 to 84 hours per AO. Using the hourly labor cost for a CDER employee from Table 7, the total costs to review, inspect, and audit AOs would range from $0.03 million to $0.20 million in year 1 and from $0.02 million to $0.12 million every 5 years thereafter.

The total annualized costs of the approval program would range from $0.16 million to $0.21 million at a 7 percent discount rate and from $0.14 million to $0.18 million at a 3 percent discount rate.

c. Costs of Training and Outreach

We expect that we would incur costs to train our staff and AOs to conduct inspections of WDD and 3PL facilities. We also expect that we would incur costs to offer webinars and public meetings to inform stakeholders about the new licensure standards. Using internal budget information, we estimate the costs of training and outreach over time in Table 29. The total annualized costs of training and outreach would equal $0.18 million at a 7 percent discount rate and $0.16 million at a 3 percent discount rate.

Table 29. Costs to FDA of Training and Outreach over Time ($ millions)

Cost	Year 0 Costs (7%)[a]	Year 0 Costs (3%)[a]	Year 1 Costs	Year 2 Costs	Year 3 Costs
Training Cost for FDA and AO Staff	$0.50	$0.50	None	None	None
Webinars	$0.46	$0.44	$0.14	None	None
Public Meetings	$0.13	$0.13	$0.03	$0.03	$0.07
Online Training Software	$0.05	$0.05	None	None	None
Total Cost	$1.14	$1.12	$0.17	$0.03	$0.07

[a] Year 0 costs include the net present value of all costs incurred before year 0.

d. Costs of the Reporting Database

As discussed in Section F2, we established a reporting database for WDDs and 3PLs in 2013 and we assume that year 1 is between 2024 and 2026. Although we have already established this database, submitting data to the database is an explicit requirement of this proposed rule. Therefore, we include the costs of establishing and maintaining the reporting database in this analysis.

We estimate that we incurred an initial cost of $0.35 million to set up the reporting database in 2013 and that the cost to maintain the reporting database is about $0.07 million in subsequent years. Given these estimates, the annualized cost to establish and maintain the reporting database would range from $0.28 million to $0.33 million at a 7 percent discount rate and from $0.21 million to $0.23 million at a 3 percent discount rate.

9. Summary of Costs

In Table 30, we summarize the stream of monetized costs from the proposed rule. These estimates include costs to WDDs, 3PLs, AOs, states, and FDA.

Table 30. Stream of Costs from the Proposed Rule over 10 Years ($ millions)

Year	Low Estimate (7%)	High Estimate (7%)	Low Estimate (3%)	High Estimate (3%)
0[a]	$8.56	$9.64	$7.97	$8.75
1	$27.82	$46.74	$27.82	$46.74
2	$8.26	$13.97	$8.26	$13.97
3	$8.05	$13.84	$8.05	$13.84
4	$11.67	$18.83	$11.67	$18.83
5	$7.67	$13.00	$7.67	$13.00
6	$7.65	$12.90	$7.65	$12.90
7	$11.39	$18.01	$11.39	$18.01

Year	Low Estimate (7%)	High Estimate (7%)	Low Estimate (3%)	High Estimate (3%)
8	$7.54	$12.60	$7.54	$12.60
9	$7.54	$12.60	$7.54	$12.60

[a] Year 0 costs include the net present value of any costs incurred before year 0.

In Table 31, we estimate the discounted total costs of the proposed rule over 10 years. Annualized costs would range from $13.21 million to $20.63 million at a 7 percent discount rate and from $12.83 million to $20.10 million at a 3 percent discount rate. The annualized costs to WDDs would range from $8.47 million to $12.90 million at a 7 percent discount rate and $8.35 million to $12.75 million at a 3 percent discount rate. The annualized costs to 3PLs would range from $1.76 million to $2.73 million at a 7 percent discount rate and $1.74 million to $2.70 million at a 3 percent discount rate.

Table 31. Discounted Total Costs of the Proposed Rule over 10 Years ($ millions)

Value	Low Estimate	Primary Estimate	High Estimate
Present Value (7%)	$99.30	$127.17	$155.04
Present Value (3%)	$112.75	$144.68	$176.60
Annualized Value (7%)	$13.21	$16.92	$20.63
Annualized Value (3%)	$12.83	$16.47	$20.10

G. Distributional Effects

States charge application fees to facilities applying for licensure. States without conforming licensure programs would lose revenue from these application fees. This revenue would transfer from states back to facilities. Based on the average annual fee states charge for licensure, we estimate that these annualized transfers would range from $0.09 million to $0.14 million at a 7 percent discount rate and from $0.08 million to $0.14 million at a 3 percent discount rate. The transfers from states to WDDs would range from $0.05 million to $0.09 million at both a 7 percent discount rate and a 3 percent discount rate. The transfers from states to 3PLs would range from $0.04 million to $0.05 million at both a 7 percent discount rate and a 3 percent discount rate.

We also expect that we would charge fees to facilities we license. As a result, at least some, if not all, of the transfers between states and facilities would subsequently transfer to us. If we would charge higher fees for licensure than states, then we would expect additional transfers between facilities and us.

The proposed rule may also have implications for public health equity. Research suggests that low income individuals or individuals without health insurance coverage may be disproportionately impacted by diverted drugs (Ref. [1], [7]). We request comment on any health equity impacts of this proposed rule.

H. International Effects

The licensing standards of the proposed rule would apply only to WDD and 3PL facilities located in the United States. We therefore expect negligible effects, if any, on international trade

or international entities. We request comment on the effect, if any, on international trade and international entities.

I. Uncertainty and Sensitivity Analysis

In Section E1, we discuss the possible benefits of the rule using cargo theft data. . In this section, we use an alternative data source to estimate the benefits of this rule.

Our Office of Criminal Investigations releases press releases about criminal cases. We collected information from press releases from criminal cases involving wholesale distributions from 2009 and 2010.[18] These press releases give information on indictments, convictions, and sentences in criminal cases. We use this information to identify cases in which there was reason to believe a domestic WDD or 3PL participated in drug diversion. We excluded any cases involving scheduled drugs (that is, drugs with a high likelihood of abuse), because criminals could easily sell these drugs illegally without diverting them through a WDD or 3PL.

From these data, we estimate that the value of diverted product in 2020 dollars in this period ranged from $7.41 million in 2010 to $32.63 million in 2009. Following the same assumptions used in Section E1, this alternative data source implies annual benefits that would range from $29.49 million to $181.62 million. However, since press releases do not represent all diversion schemes in the United States, these estimates likely underestimate the benefits of reduced of drug diversion (while also likely overstating regulatory effectiveness and, in that regard, overestimating benefits).

J. Analysis of Regulatory Alternatives to the Proposed Rule

1. Exercising Additional Enforcement Discretion

As discussed in Section C1, we intend to exercise enforcement discretion with respect to 3PLs for one additional year after the effective date of the regulation. Alternatively, we could extend additional enforcement discretion for 3PLs and exercise enforcement discretion for WDDs. Applying additional enforcement discretion would reduce compliance costs by shifting them further in the future. It would also reduce costs if extending the compliance period would allow facilities, states, and AOs to have enough time to meet standards in the proposed rule before the first licensure cycle.

However, additional enforcement discretion would also reduce the benefits of the rule, as the benefits and cost savings related to the new standards would also shift further in the future. We present our primary estimates of the benefits and costs of exercising one additional year of enforcement discretion for WDDs and 3PLs in Table 33. With this alternative, we would begin to enforce the licensure standards in the proposed rule in year 2 (three years after we issue the final regulations). We request comment on the impacts of extending further enforcement

[18] We deliberately use pre-statutory data to inform our analysis. As we state in section D, the DSCSA was published in 2013, and firms are very likely to have proactively changed their practices to meet the requirements described in the DSCSA. It is difficult to disentangle trends that are attributable to the statute from trends that are not attributable to the statute. Therefore, we believe trend analysis would be inappropriate in this case.

discretion on the benefits and costs of the proposed rule beyond the impacts of shifting benefits and costs in time.

2. Requiring Drug Testing

In another alternative to the proposed rule, we could require designated representatives and facility managers to undergo initial, random, and for-cause drug screening tests. Implementing drug screenings would impose an initial one-time cost to test all designated representatives and facility managers and annual costs to conduct random and for-cause drug tests.

We find that some states already require designated representatives and facility managers to undergo drug testing. In Table 32, we estimate that number of WDD and 3PL facilities that would employ drug testing under this regulatory alternative. We also estimate the number of employees that would undergo drug testing initially and annually, using assumptions from Section F about the number of designated representatives and facility managers at facilities by employment size.

Table 32. Number of Facilities with New Drug Testing Standards under the Regulatory Alternatives and the Number of Drug Tests Conducted

Value	1–19 Employees	20–99 Employees	100–499 Employees	500 or More Employees
Number of WDD Facilities with New Standards	1,039	412	297	159
Number of 3PL Facilities with New Standards	157	132	90	55
Drug Tests in Year 1[a]	3,588	1,632	2,709	1,926
Drug Tests Annually After Year 1[a,b]	897	408	677	482

[a] We assume that each facility employees 1 designated representative. We also assume that facilities with fewer than 100 employees employ 2 managers, facilities with between 100 and 499 employees employ 6 managers, and facilities with 500 or more employees employ 8 managers.
[b] We assume that the probability of an employee receiving a random or for-cause drug test in a given year is 25 percent, based on recommendations from the Department of Transportation (Ref. [8]).

Using information from an internet search, we estimate that the average fee for pre-employment drug testing is $45. We also estimate that it would take approximately 0.25 hours for each employee to complete all activities involved with a drug test. Using the hourly labor costs for designated representatives and facility managers at WDDs and 3PLs from Table 7, we estimate that the average cost of drug testing would equal $79 per employee.

Given the estimates in Table 32 and the cost of drug testing per employee, we estimate that the annualized cost of drug testing would equal $0.21 million at a 7 percent discount rate and $0.20 million at a 3 percent discount rate. We present the total benefits and costs of this regulatory alternative in Table 33. However, we note that these estimates do not account for any benefits associated with drug testing.

3. Creating a Minimum Standard of Licensure

We could also consider the standards in the rule as minimum standards rather than as uniform standards. If the rule specified minimum standards, states could choose to have stricter standards than the ones in the rule. We do not expect that a minimum standard would have different costs than the proposed uniform standard.

Cost savings under a minimum standard would likely be lower than under a uniform standard. Some states could continue imposing standards that exceed national standards, including more frequent licensure renewal, examinations for designated representatives, and self-assessments for designated representatives. We expect that a minimum standard would reduce the cost savings from the proposed rule. We present our primary estimates of the benefits and costs of this regulatory alternative in Table 33.

To the extent that WDDs and 3PLs would experience cost savings from uniform national licensing standards, this alternative approach of minimum standards would diminish these cost savings. We request comment on the potential benefits of state standards not included in this rulemaking.

4. Summary of Regulatory Alternatives

In Table 33, we summarize the annualized benefits, costs, and net benefits of these alternatives to the proposed rule. These estimates only include any benefits and costs that we can quantify, and do not include any qualitative benefits or costs of the proposed rule.

Table 33. Summary of Annualized Benefits and Costs of Alternatives to the Proposed Rule ($ millions)

Alternative	Benefits (7%)	Costs (7%)	Net Benefits (7%)	Benefits (3%)	Costs (3%)	Net Benefits (3%)
Exercising Additional Enforcement Discretion[a]	$9.15	$12.93	($3.78)	$9.55	$12.85	($3.31)
Proposed Rule	$10.66	$16.92	($6.26)	$10.89	$16.47	($5.58)
Requiring Drug Testing	$10.66	$17.13	($6.47)	$10.89	$16.67	($5.78)
Creating a Minimum Standard of Licensure	$7.00	$16.92	($9.92)	$7.14	$16.47	($9.32)

a

III. Initial Small Entity Analysis

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the proposed rule could impose significant, although uncertain, new economic burdens on small entities, we find that the proposed rule will have a significant economic impact on a substantial number of small entities. This analysis, as well as other sections in this document, serves as the Initial Regulatory Flexibility Analysis, as required under the Regulatory Flexibility Act.

A. Description and Number of Affected Small Entities

We estimate the number of affected small entities using data from Dun & Bradstreet. In Table 34, we describe the small WDD firms that this proposed rule would impact. The Small

Business Administration defines a small WDD firm as a firm with fewer than 250 employees.[19] Under this definition, 90 percent of affected WDD firms are small businesses.

Table 34. Description of Small WDD Firms

Employee Size	Number of Firms	Percent of Firms	Average Annual Receipts ($ millions)	Average Number of Establishments per Firm
1–19 Employees	989	69.31%	$3.66	1.03
20–99 Employees	223	15.63%	$21.72	1.17
100–249 Employees	74	5.19%	$140.95	1.45
All Small	1,286	90.12%	$14.69	1.08

In Table 35, we describe the small 3PL firms this proposed rule would impact. The Small Business Administration defines a small 3PL firm as a firm with revenues less than $15 million.[20] Under this definition, 66 percent of affected 3PL firms are small businesses.

Table 35. Description of Small 3PL Firms

Revenue Size	Number of Firms	Percent of Firms	Average Annual Receipts ($ millions)	Average Number of Establishments per Firm
Under $1 million	122	41.78%	$0.23	1.00
$1 to $5 million	49	16.78%	$2.40	1.04
$5 to $15 million	22	7.53%	$9.62	1.09
All Small	193	66.10%	$1.85	1.02

B. Description of the Potential Impacts of the Rule on Small Entities

To calculate net costs of the proposed rule, if finalized, as it relates to small firms, we consider cost savings to WDDs and 3PLs from reduced frequency of licensure and reducing state licensing standards in some states; and cost savings to 3PLs from fewer ship-to licenses (estimated in Section II.E). We consider costs to WDDs and 3PLs from reading and understanding the rule, reporting to FDA, undergoing routine inspections, writing and revising standard operating procedures, conducting background checks, and increased frequency of licensure in one state; and costs to WDDs to furnish surety bonds to their state licensing authority to obtain or renew their licenses (estimated in Section II.F). We also consider transfers from states to WDDs and 3PLs in the form of licensure application fees (estimated in Section II.G).

We estimate that the net annualized costs[21] to WDDs would range from $7.07 million to $8.06 million at a 7 percent discount rate and from $6.80 million to $7.93 million at a 3 percent

[19] Based on NAICS Code 424210, "Drug and Druggists' Sundries Merchant Wholesalers." Note that we use this NAICS Code for our regulatory flexibility analysis and the NAICS Code 4240A2, "Merchant Wholesalers, Nondurable Goods," for our labor cost estimates because wage data is unavailable for NAICS Code 424210. We assume that the wage for NAICS Code 4240A2 is the same as the wage for NAICS Code 424210.
[20] Based on NAICS Code 488500, "Freight Transportation Arrangement."
[21] Where net annualized costs to WDDs equal annualized costs to WDDs minus annualized transfers to WDDs minus annualized cost savings to WDDs.

discount rate. We summarize the annualized cost savings, costs, and distributional effects of the proposed rule, if finalized, for WDDs in Table 36.

Table 36. Annualized Cost Savings, Costs, and Distributional Effects of the Proposed Rule for WDDs ($ millions)

Value	Low Estimate (7%)	High Estimate (7%)	Low Estimate (3%)	High Estimate (3%)
Annualized Cost Savings	$0.36	$5.74	$0.37	$5.87
Annualized Costs	$8.47	$12.90	$8.35	$12.75
Annualized Transfers	$0.05	$0.09	$0.05	$0.09
Annualized Net Costs	$8.06	$7.07	$7.93	$6.80

To estimate the average annualized net cost per firm, we divide the net annualized costs by the total number of WDD firms. Then, the average annualized net cost per WDD firm would range from $4,957 to $5,645[22] at a 7 percent discount rate. Similarly, the average annualized net cost per WDD firm would range from $4,764 to $5,558 at a 3 percent discount rate. In Table 37, we present the annualized net costs per firm as a percent of average annual revenue. We find that quantified net costs represent less than 1 percent of annual revenues for small WDDs.

Table 37. Annualized Net Costs per Firm as a Percent of Average Annual Revenue for Small WDD Businesses

Employee Size	Low Estimate (7%)	High Estimate (7%)	Low Estimate (3%)	High Estimate (3%)
1–19 Employees	0.14%	0.15%	0.13%	0.15%
20–99 Employees	0.02%	0.03%	0.02%	0.03%
100–249 Employees	0.00%	0.00%	0.00%	0.00%
All Small	0.03%	0.04%	0.03%	0.04%

Similarly, we estimate that the net annualized costs[23] to 3PLs would range from $1.29 million to $1.58 million at a 7 percent discount rate and from $1.25 million to $1.56 million at a 3 percent discount rate. We summarize the annualized cost savings, costs, and distributional effects of the proposed rule, if finalized, for 3PLs in Table 38.

Table 38. Annualized Cost Savings, Costs, and Distributional Effects of the Proposed Rule for 3PLs ($ millions)

Value	Low Estimate (7%)	High Estimate (7%)	Low Estimate (3%)	High Estimate (3%)
Annualized Cost Savings	$0.14	$1.38	$0.14	$1.40
Annualized Costs	$1.76	$2.73	$1.74	$2.70
Annualized Transfers	$0.04	$0.05	$0.04	$0.05
Annualized Net Costs	$1.58	$1.29	$1.56	$1.25

[22] These values equal $7,073,649 ÷ 1,427 and $8,055,879 ÷ 1,427, respectively.
[23] Where net annualized costs to 3PLs equal annualized costs to 3PLs minus annualized transfers to 3PLs minus annualized cost savings to 3PLs.

To estimate the average annualized net cost per firm, we divide the net annualized costs by the total number of 3PL firms. Then, the average annualized net cost per 3PL firm would range from $4,424 to $5,407[24] at a 7 percent discount rate. Similarly, the average annualized net cost per 3PL firm would range from $4,282 to $5,347 at a 3 percent discount rate. In Table 39, we present the annualized net costs per firm as a percent of average annual revenue. We find that quantified net costs represent over 1 percent of annual revenues for the smallest 3PLs and less than 1 percent for 3PLs with over $1 million in average annual revenue.

Table 39. Annualized Net Costs per Firm as a Percent of Average Annual Revenue for Small 3PL Businesses

Revenue Size	Low Estimate (7%)	High Estimate (7%)	Low Estimate (3%)	High Estimate (3%)
Under $1 million	1.91%	2.34%	1.85%	2.31%
$1 to $5 million	0.18%	0.23%	0.18%	0.22%
$5 to $15 million	0.05%	0.06%	0.04%	0.06%
All Small	0.24%	0.29%	0.23%	0.29%

These estimates only include the direct costs to WDDs and 3PLs. We expect that AOs and states would pass some of the costs of complying with this proposed rule onto WDDs and 3PLs through inspection fees or licensure fees. Our estimates in Table 37 and Table 39 likely underestimate the burden of the proposed rule on small businesses.

C. Alternatives to Minimize the Burden on Small Entities

In Section II.J, we analyze three alternative policies. According to the Small Business Administration definition, approximately 90 percent of the affected WDD firms and 66 percent of the 3PL firms are small entities. Therefore, those alternatives that minimize the burden on WDDs and 3PLs would also minimize the burden on the subset of small WDDs and 3PLs. Specifically, exercising one additional year of enforcement discretion would reduce the costs to small businesses. However, it would also reduce cost savings to small businesses.

IV. Appendix: Adverse Events from Drug Diversion or Counterfeiting

In this section, we provide examples of suspected and documented adverse events resulting from drug diversion or counterfeiting that the uniform licensing standards for WDDs and 3PLs that we are proposing potentially could have prevented. We rely on (1) reported adverse events to CDER's Office of Surveillance and Epidemiology (OSE) and (2) information from documented cases of drug diversion and counterfeiting.

A. Evidence from Suspected Cases of Drug Diversion or Counterfeiting

One approach to estimating benefits is to look at the reported adverse events that may be associated with drug diversion or counterfeiting. Each year, OSE evaluates more than 1.5 million adverse event reports associated with the use of an FDA-regulated drug, biologic, medical

[24] These values equal $1,291,875 ÷ 292 and $1,578,802 ÷ 292, respectively.

device, dietary supplement, or cosmetic submitted by health professionals and consumers to FDA's MedWatch program (Ref. [9]). By evaluating the cases of suspected prescription drug counterfeiting or tampering reported to us between 2009 and 2014, we identified 140 adverse event reports between 2009 and 2014 that could plausibly have resulted from drug diversion or counterfeiting.[25]

In Table 40, we present examples of these adverse events. We likely receive few adverse event reports relative to the actual number of adverse events consumers experience from diverted drugs. Moreover, we consider that these events might not represent the total adverse events that may have arisen due to drug diversion or counterfeit drugs.

Table 40. Suspected Adverse Events from Drug Diversion or Counterfeiting

Drug	Adverse Event	Suspected Cause	Additional Details	Year Reported to FDA
Exalgo (hydromorphone hydrochloride extended-release)	Gastrointestinal bleeding	Product tampering	Tablet appeared to be cut open	2014
Cymbalta (duloxetine)	Ineffective drug	Product tampering	Empty capsules	2012
Cymbalta (duloxetine)	Ineffective drug; illness	Product counterfeit	Unusual appearance of capsules	2011
Protonix (pantoprazole sodium)	Ineffective drug	Product counterfeit	Change in appearance of tablets	2011
Atripla (efavirenz/ emtricitabine/ tenofovir)	Ineffective drug	Product counterfeit	Change in appearance of pills	2011
Topamax (topiramate)	Ineffective drug; body rash and hives	Product counterfeit	Change in appearance of tablets	2009

B. Evidence from Documented Cases of Drug Diversion or Counterfeiting

In addition to adverse event reports, we can additionally glean information about adverse events resulting from drug diversion or counterfeiting from public sources, including news articles, press releases, and congressional testimonies.

For some of these cases, we can identify a direct link between a drug diversion or counterfeiting event and an adverse public health outcome. In Table 41, we describe notable cases of drug diversion or counterfeiting resulting in adverse events that the uniform standards we propose in the rule could potentially have prevented.

[25] The initial reporter provides a narrative describing the adverse event. We rely on these narratives to identify adverse events that potentially resulted from drug diversion or counterfeiting. We do not disclose these narratives in the publicly available FDA Adverse Event Reporting System (FAERS) Quarterly Data files or the FAERS Public Dashboard.

Table 41. Notable Cases of Drug Diversion or Counterfeiting Resulting in Adverse Events

Drug(s)	Description of Case	Adverse Event(s)	Year of Event
Avastin (bevacizumab)	Counterfeit, misbranded, and adulterated versions of Avastin from abroad entered the U.S. supply chain (Ref. [10], [11], [12])	One cancer patient became nauseated and feverish following a drug infusion containing mold (Ref. [13])	2011
Levemir (insulin detemir)	Diverters sold stolen vials of Levemir to drug wholesaler, and consumers purchased these drugs through the legitimate supply chain (Ref. [14])	Two patients reported potentially fatal blood sugar levels and others became ill	2009
Epogen (epoetin alfa)	Diverters purchased and relabeled "low-dose" Epogen as "high-dose" Epogen and reintroduced the mislabeled drugs into the legitimate supply chain (Ref. [15])	Mislabeled low dose drug did not provide effective treatment for one patient recovering from a liver transplant	2002
Serostim and Nutropin AQ (somatropin)	An unlicensed wholesale drug distributor diverted hundreds of boxes of these drugs in interstate commerce, some purchased from patients in California (Ref. [16])	One child was harmed by counterfeit Nutropin	Unknown[26]
Procrit (epoetin alfa)	Counterfeiters introduced drug that contained nonsterile tap water in place of the active ingredient into the legitimate supply chain (Ref. [15])	Counterfeit drug did not provide effective treatment for one cancer patient	1998

In Table 42, we summarize additional cases of drug diversion and counterfeiting that potentially could have contributed to adverse public health outcomes. Although we are not aware of sources that directly link these cases to adverse events, based on the details of each case, it is plausible that unreported adverse events could have occurred. We request information on any additional cases of drug diversion or counterfeiting that may have contributed to adverse events in patients.

Table 42. Other Notable Cases of Drug Diversion or Counterfeiting

Drug(s)	Description of Case	Timing of Case
Xanax (alprazolam)	A counterfeiter manufactured 4.3 million counterfeit pills (with controlled substances purchased abroad) and shipped them nationwide, earning $2.1 million in profit (Ref. [17])	2017–2018
HIV pharmaceuticals	Diverters stole drugs intended for indigent HIV patients from the Washington, D.C. Department of Health Pharmacy Warehouse; a Louisiana pharmacist purchased and dispensed some of these drugs to patients (Ref. [18])	2013

[26] This diversion scheme occurred between 2000 and 2002 (Ref. [16]).

Drug(s)	Description of Case	Timing of Case
Rx oncology drugs	A pharmacist in California purchased unapproved versions of drugs such as Avastin, Eloxatin, Gemzar, Neupogen, Rituxan, Taxotere, and Zometa from a foreign distributor and supplied the drugs to doctors (Ref. [19])	2010–2011
Oncology and cosmetic drugs	An unlicensed Virginia wholesale drug distributor purchased unapproved drugs intended for foreign markets for resale in the U.S. and distributed more than 17,000 units of these drugs to physicians nationwide; diverters did not follow refrigeration protocols for at least some of these drugs while in transit (Ref. [20], [21])	2009–2013
HIV pharmaceuticals	Pharmacists in New York purchased over $275 million in black market, “medically worthless” drugs on behalf of shell companies and resold the drugs to patients (Ref. [22], [23])	2008
Rx medications	As part of a $50 million drug diversion scheme, diverters purchased and distributed drugs from unlicensed suppliers that had unlawfully purchased the drugs from patients; pharmacies that received the drugs reported bottles containing wrong drugs, incorrect dosage information, and foreign objects (Ref. [24])	2006–2009

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