DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Amendments to 21 CFR Part 3 – Product Jurisdiction

Docket No. FDA-2004-N-0191

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

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Table of Contents

List of Tables

Table 1: List of Acronyms, Initials, and Abbreviations in the Analysis

510(k)	Premarket Notification
BLS	US Bureau of Labor Statistics
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CFR	Code of Federal Regulations
FDA	US Food and Drug Administration
FTE	Full-Time Equivalent
MDUFMA	Medical Device User Fee and Modernization Act of 2002
NAICS	North American Industrial Classification System
OC	Office of the Commissioner
OCC	Office of the Chief Counsel
OCP	Office of Combination Products
PMA	Premarket Approval Application
RFD	Request for Designation
SOC	Standard Occupational Classification

I. Introduction and Summary

A. Introduction

We have examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, Executive Order 13771, 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). Executive Order 13771 requires that the costs associated with significant new regulations "shall, to the extent permitted by law, be offset by the elimination of existing costs associated with at least two prior regulations." We believe that this proposed rule is not 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 this rule imposes no new burdens, we propose to certify that the proposed rule will not 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 $148 million, using the most current (2016) 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

The objective of this proposed rule is to amend the regulations concerning requests for designations (RFDs) of the classification of products as biological products, devices, drugs, or combination products, or their assignment to Food and Drug Administration (FDA or Agency) components for premarket review and regulation. The proposed rule is intended to clarify the scope of the regulations, reflect changes in statutory provisions, simplify the process for appealing classification and assignment determinations, remove advisory content that is incomplete or out of date, and otherwise to clarify Title 21 of the Code of Federal Regulations (CFR) Part 3, including updating it to reflect Agency practices and policies.

Many provisions of this proposed rule codify current practices, and may not result in estimated costs, benefits, or savings. However, we do expect a few provisions to lead to changes that may generate additional public health benefits and cost savings to society. A summary of the quantified costs and benefits of the proposed rule are presented in Table 2. The lower and upper estimates given in Table 2 are at the 5 and 95 percent interval, respectively.

Table 2: Summary of Benefits, Costs, and Distributional Effects of the Proposed Rule[a,b]

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Costs	Annualized Monetized $/year	$17,000	$12,000	$27,000	2016	7%	10 years	
		$15,000	$10,000	$23,000	2016	3%	10 years	
	Annualized Quantified					7%		
						3%		
	Qualitative							
Benefits	Annualized Monetized $/year	$28,000	$25,000	$89,000	2016	7%	10 years	
		$28,000	$25,000	$89,000	2016	3%	10 years	
	Annualized Quantified					7%		
						3%		
	Qualitative	Firms and FDA may realize savings from sponsors choosing to submit electronic RFDs.						
Transfers	Federal Annualized Monetized $millions/year					7%		
						3%		
	From/ To	From:			To:			
	Other Annualized Monetized $millions/year					7%		
						3%		
	From/To	From:			To:			
Effects	State, Local or Tribal Government: Small Business: Will not have a significant impact on a substantial number of small entities. Wages: Growth:							

[a] We use a 10-year time horizon for this rule with payments occurring at the end of each period.
[b] All dollar values are rounded to the nearest $1,000.

The estimated primary costs of the proposed rule include the additional one-time costs incurred by industry to read and understand the regulation. We expect only a subset of firms currently producing medical products will incur this cost. Our primary estimate of the total up-front cost to industry is approximately $131,000. Annualizing these costs over a ten year period, we estimate total annualized costs to be $15,000 at a 3 percent discount rate, and $17,000 at a 7 percent discount rate. The present value of these costs over ten years is $127,000 at a 3 percent discount rate, and $122,000 at a 7 percent discount rate.

The primary public health benefit from adoption of the proposed rule would be the value of the illnesses and deaths avoided as a result of finalizing the proposed rule. Current regulatory requirements may cause applicants to unnecessarily submit RFDs, or to make misguided judgments regarding the need to confirm product classification or assignment. The reduction in uncertainty about the RFD process will, thereby, potentially allow sponsors to make more informed decisions regarding product development and seeking marketing authorization, and potentially allow sponsors and FDA personnel to divert resources used under current regulations to other areas, such as to product development and marketing applications. We are not able to

quantify or to identify specific ways by which the proposed rule would lead to avoided illnesses or deaths and therefore do not include public health benefits in our net estimates.

FDA is able to quantify the resource savings to both the Agency and industry from the proposed rule associated with streamlining and clarifying the appeals process for product classification and assignments. Our primary estimate of total cost savings to industry and FDA is approximately $28,000 annually. The present value of these savings over ten years is $241,000 at a 3 percent discount rate, and $198,000 at a 7 percent discount rate. Potential resource savings to FDA and industry from the optional electronic submission of RFDs are not included in this estimate because of the uncertainty in the number of sponsors who would choose to submit electronically.

Our best estimate of the quantifiable net social effect of the proposed rule is a cost of approximately $103,000 in the first year and a cost savings of approximately $28,000 each year starting in year 2. The net present discounted value of the quantifiable cost savings over 10 years is approximately $114,000 at a 3 percent discount rate and approximately $76,000 at a 7 percent discount rate. The total annualized net effect of the proposed rule is estimated to produce an average net cost savings ranging from $13,000 at a 3 percent discount rate and $11,000 at a 7 percent discount rate.

Executive Order 13771 requires that the costs associated with significant new regulations "shall, to the extent permitted by law, be offset by the elimination of existing costs associated with at least two prior regulations." We believe that the proposed rule, if finalized, is not significant under Executive Order 12666 and is deregulatory under Executive Order 13771.

The present value of our primary net cost estimate of the proposed rule, using an infinite time horizon, is approximately -$281,000, discounted at 7 percent, with a lower bound of approximately -$165,000 and an upper bound of approximately -$1.2 million. The annualized net cost of the proposed rule is approximately -$20,000, discounted at 7 percent on an infinite time horizon, with a lower bound of approximately -$12,000 and an upper bound of approximately -$83,000. Discounted at 3 percent, the present value of our primary net cost estimate of the proposed rule is approximately -$814,000, with a lower bound of approximately -$634,000 and an upper bound of approximately -$2.9 million. The annualized net cost of the proposed rule is approximately -$24,000, discounted at 3 percent on an infinite time horizon, with a lower bound of approximately -$19,000 and an upper bound of approximately -$86,000. The estimated net costs under Executive Order 13771 are summarized in Table 3.

The Regulatory Flexibility Act requires Agencies to prepare an initial regulatory flexibility analysis if a proposed rule would have a significant economic impact on a substantial number of small entities (including small businesses, small non-profit organizations, and small governmental jurisdictions). FDA has examined the economic implications of the proposed rule as required by the Regulatory Flexibility Act. This rule, if finalized, will not impose any new burdens on small entities, and thus will not have a significant economic impact on a substantial number of small entities.

Table 3: Summary of Executive Order 13771 Net Costs of the Proposed Rule[a,b]

	Primary (7%)	**Lower Bound (7%)**	**Upper Bound (7%)**	Primary (3%)	Lower Bound (3%)	Upper Bound (3%)
Present Value of Costs	**$122,000**	**$81,000**	**$192,000**	$127,000	$84,000	$200,000
Present Value of Benefits	**$403,000**	**$357,000**	**$1,266,000**	$941,000	$834,000	$2,953,000
Present Value of Net Costs[c]	**-$281,000**	**-$165,000**	**-$1,184,000**	-$814,000	-$634,000	-$2,869,000
Annualized Costs	**$9,000**	**$6,000**	**$13,000**	$4,000	$3,000	$6,000
Annualized Benefits	**$28,000**	**$25,000**	**$89,000**	$28,000	$25,000	$89,000
Annualized Net Costs[c]	**-$20,000**	**-$12,000**	**-$83,000**	-$24,000	-$19,000	-$86,000

[a] We use an infinite time horizon for this rule with payments occurring at the end of each period.
[b] All dollar values are rounded to the nearest $1,000.
[c] A negative net cost implies a net cost savings.

II. Preliminary Regulatory Impact Analysis

A. Background and Description of the Proposed Rule

FDA proposes to amend its 21 CFR part 3 regulations by clarifying the scope of the regulations, updating the language to reflect statutory provisions, simplifying the process for appealing classification and assignment determinations, removing advisory content that is incomplete or out of date, and otherwise clarifying the regulations, including revising the language to reflect Agency practices and policies. Current regulations may lead to confusion and duplicative efforts by sponsors.

1. Background

Under 21 CFR 3.2, a combination product may be a drug-device, biologic-device, drug-biologic, or drug-device-biologic. There are three categories of combination products. When a single product physically, chemically, or otherwise combines or mixes two or more regulated components, it forms a "single-entity" combination product. A "co-packaged" combination product consists of two or more separate products combined in the same package or packaged together as a unit. Finally, a "cross-labeled" combination product consists of a separately packaged drug and device, biologic and device, drug and biologic, or drug, device and biologic, that are intended for use with one another (investigational or approved) where both are required to achieve the intended use, indication, or effect of the combination product, among other criteria.

Section 503(g) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353(g)), which was added by the Safe Medical Devices Act of 1990 (Pub. L. No. 101-629),

requires that FDA assign a component of the Agency to have primary jurisdiction for the regulation of a combination product. That assignment must be based upon a determination of the primary mode of action of the combination product. For example, if the primary mode of action of a combination product is that of a biological product, the product is to be assigned to the FDA component responsible for the premarket review of that biological product. In situations where it is not possible to determine the primary mode of action with reasonable certainty, assignment is based on the decision-making process specified in 21 CFR 3.4. Section 563 of the FD&C Act (21 U.S.C. 360bbb-2) directs FDA to determine the classification of a product as a drug, biological product, device, or combination product, or the component of the Agency that will regulate the product, in response to a request submitted under this section of the FD&C Act.

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA) (Pub. L. No. 107-250) further modified section 503(g) of the act to require the establishment of an Office (Office of Combination Products (OCP)) within the Office of the Commissioner (OC). The purpose of OCP is to ensure the prompt assignment of combination products to Agency components, the timely and effective premarket review of such products, and consistent and appropriate postmarket regulation of combination products. MDUFMA also requires the Agency to review each agreement, guidance, or practice specific to the assignment of combination products to Agency components, consult with stakeholders and the directors of the Agency Centers, and determine whether to continue in effect, modify, revise, or eliminate such agreements, guidances, or practices.

OCP is responsible for FDA action on all RFDs submitted by industry in accordance with 21 CFR part 3, "Product Jurisdiction." This responsibility includes responding to requests for classification of a particular product as a biological product, device, drug, or combination product, as well as requests for product assignment. FDA issued 21 CFR part 3 in 1991 establishing the RFD process.

2. Objectives of the Proposed Rule

The objective of this proposed rule is to amend the regulations concerning the classification of products as biological products, devices, drugs, or combination products and their assignment to Agency components for premarket review and regulation. The proposed rule attempts to clarify the scope of the regulations, update the regulations to reflect changes in statutory law, simplify the process for appealing classification and assignment determinations, remove advisory content that is incomplete or out of date, and otherwise to clarify 21 CFR Part 3, including adjusting the rule to reflect Agency practices and policies. Intended effects of proposed changes to the rule include (a) streamlining the process for appealing an FDA decision classifying a product as a drug, biological product, device, or combination product, or assigning a product to an Agency component for premarket review and regulation; and (b) clarifying that sponsors may submit separate applications for combination products unless FDA determines that a single application is necessary. Several other changes to the regulations are proposed in addition to the two addressed in this section, but are not discussed in more detail in this analysis. See the proposed rule for a more complete discussion of all provisions and the corresponding sections of 21 CFR Part 3 directly affected by the proposed rule [see Docket No. FDA-2004-N-0191 at www.https://www.regualtions.gov].

a. Streamlining and Clarifying the Appeals Process for Product Classifications and Assignments

Under 21 CFR 3.8(c), sponsors may request that the product jurisdiction officer reconsider product classification and assignment if the sponsor does not agree with OCP's initial determination. Sponsors may also make a supervisory appeal in accordance with 21 CFR 10.75 if they do not agree with OCP's initial determination or with OCP's response to such a "request for reconsideration".

OCP's determinations are made after a thorough review of information provided by the sponsor and otherwise available to the Agency in consultation with regulatory, legal, and scientific staff from other interested Agency components, as appropriate. Additionally, the current appeals process does not allow for sponsors to submit new information in the request for reconsideration. Because determinations under Part 3 are made through a robust process, further evaluation of the same data and information by OCP through the request for reconsideration process generally has not resulted in changes to OCP's determination.

The request for reconsideration process can be confusing to sponsors who do not realize they do not have to make a request for reconsideration before they may submit a 21 CFR 10.75 appeal, and is inefficient for sponsors and Agency staff. Thus, FDA proposes to remove the request for reconsideration process codified at 21 CFR 3.8(c).

b. Clarifying When Sponsors May Submit Separate Applications for Constituent Parts

Current regulations (21 CFR 3.4(c)) state that the Agency can require, in appropriate cases, separate applications for constituent parts of a combination product. However, section 3038 of the 21st Century Cures Act (Pub. L. No. 114-255) amended section 503(g) of the FD&C Act to state that combination products shall be reviewed under a single application whenever appropriate, and that sponsors may submit separate applications for the constituent parts of a combination product unless FDA determines that a single application is necessary. Sponsors may find the language of § 3.4(c) confusing in relation to the new statutory provisions, and this may lead to inefficient planning for product development and obtaining market access. Thus, FDA proposes to remove § 3.4(c) to avoid confusion that might arise from maintaining this different articulation of Agency authority on this topic, and intends to issue guidance regarding implementation of the new statutory provisions as needed in light of Agency experience with implementing them.

B. Market Failure Requiring Federal Regulatory Action

The need for this regulation stems from the institutional failure related to inefficiencies in the process for determining the classification and product assignment for medical products due to confusing or outdated language. For instance, the current process to appeal product classification and assignment determinations can lead to unnecessary effort by sponsors and FDA personnel. In addition, as explained more fully in the proposed rule, several changes to relevant statutory law and FDA policies have not been updated in 21 CFR part 3 that may lead to inefficient planning for product development.

Lack of clarity may create uncertainty about how and where to submit applications for medical products. FDA believes that clarifying the language in 21 CFR part 3 regulations to be more consistent with recent changes to statutory law, FDA policies, and FDA practices and removing the duplicative appeals process will result in a more efficient, transparent premarket review process for these products.

C. Parties Affected by the Proposed Rule

The proposed rule would update 21 CFR part 3 to clarify the scope of the regulations, reflect changes in statutory provisions, simplify the process for appealing classification and assignment determinations, remove advisory content that is incomplete or out of date, and otherwise clarify 21 CFR part 3, including adjusting it to reflect Agency practices and policies.

1. Number of Entities Affected

The proposed rule will minimally affect drug, device, biologic product, and combination product manufacturers.

There are approximately 22,000 device manufacturers, 1,000 drug manufacturers, 125 biological product manufacturers, and 475 combination product manufacturers. We use the distribution of the approximately 1,100 combination products on the market by application type to determine the primary industry of each applicant. Seventy-four percent of combination products have Premarket Notifications (510(k)s) or Premarket Approval Applications (PMAs), 19 percent have Abbreviated New Drug Applications or New Drug Applications, and 7 percent have Biologics License Applications. We estimate there are approximately 352 firms with Center for Devices and Radiological Health (CDRH) applications, 90 firms with Center for Drug Evaluation and Research (CDER) applications, and 33 firms with Center for Biologics Evaluation and Research (CBER) applications.

We do not expect that all medical product manufacturers will be affected by the rule because the classification and assignment of most products are unambiguous.

2. Value of Time

We expect the firms affected by this regulation to be representatives of ten industries. The industries are separated into North American Industry Classification System (NAICS) codes that allow us to attach wage and employment data for the analysis. The ten industries are NAICS 325412 (Pharmaceutical Preparation Manufacturing), NAICS 325413 (In-Vitro Diagnostic Substances Manufacturing), NAICS 325414 (Biological Product (Except Diagnostic) Manufacturing), NAICS 334510 (Electro-medical and Electrotherapeutic Apparatus Manufacturing), NAICS 334517 (Irradiation Apparatus Manufacturing), NAICS 339112 (Surgical and Medical Instrument Manufacturing), NAICS 339113 (Surgical Appliances and Supplies Manufacturing), NAICS 339114 (Dental Equipment and Supplies Manufacturing), NAICS 339115 (Ophthalmic Goods Manufacturing), and NAICS 621991 (Blood and Organ Banks).

Our estimates of the value of time are based on mean hourly wages. We use national industry-specific occupational employment and wage estimate data from the Bureau of Labor Statistics (BLS) to define wages for personnel within the affected industries who will likely be responsible for complying with the proposed rule if finalized (Ref. 1). BLS does not provide wage data at the more granular 6-digit NAICS level. We use the wage data for the Pharmaceutical and Medicine Manufacturing (NAICS 325400), Navigational, Measuring, Electromedical, and Control Instruments Manufacturing (NAICS 334500), Medical Equipment and Supplies Manufacturing (NAICS 339100), and All Other Ambulatory Health Care Services (NAICS 621990) as proxies. Table 4 lists the 2016 hourly rates for the average workers in the occupations possibly affected by the regulation for each NAICS code. We double these mean wages in the analysis to account for benefits and overhead.

We place all firms and products into categories based on the FDA Center responsible for approving or clearing the application. As a result, the wage rates used for CBER and CDRH applicants will be averages of Standard Occupational Classification (SOC) codes across industries. CBER applicants will be assigned wage rates that are the average of NAICS 325400 and NAICS 621990. CDRH applicants will be assigned wage rates that are the average of NAICS 334500 and NAICS 339100.

Table 4: Occupations within Firms Possibly Affected by the Proposed Rule with Mean Hourly Wage

Occupation (SOC Code[a])		Mean Hourly Wage
NAICS 325400	Management Occupations (110000)	$69.81
	Compliance Officers (131041)	$39.20
	Lawyers (231011)	$86.63
	Office and Administrative Support Occupations (430000)	$21.38
NAICS 334500	Management Occupations (110000)	$71.33
	Compliance Officers (131041)	$40.88
	Lawyers (231011)	$88.09
	Office and Administrative Support Occupations (430000)	$22.52
NAICS 339100	Management Occupations (110000)	$66.79
	Compliance Officers (131041)	$37.99
	Lawyers (231011)	$78.69
	Office and Administrative Support Occupations (430000)	$19.32
NAICS 621990	Management Occupations (110000)	$50.40
	Compliance Officers (131041)	$29.17
	Lawyers (231011)	$93.57
	Office and Administrative Support Occupations (430000)	$17.87

[a] See http://www.bls.gov/soc/home.htm for more information.

We account for the value of time for FDA employees based on the hourly cost per full-time equivalent (FTE) employee for the Agency. The current annual value of a CBER FTE is approximately $270,375. The current annual value of a CDER FTE is approximately $273,737. The current annual value of a CDRH FTE is approximately $260,286. The current annual value of an OC FTE is approximately $292,699. We estimate the hourly rate for an FTE using 2,080 annual hours. This translates into hourly wage rates of approximately $130 (= $270,375 / 2,080

hours) for CBER, $132 (=$273,737 / 2,080 hours) for CDER, $125 (=$260,286 / 2,080 hours) for CDRH, and $141 (=$292,699 / 2,080 hours) for OC. This rate includes benefits and overhead.

D. Assumptions and Baseline Conditions

Due to uncertainty regarding current and expected firm behavior and incomplete data, we must make certain assumptions, including our baseline, to estimate the potential effects of the proposed rule. In this section, we list out the assumptions and identify the baseline used to estimate the impact of the proposed regulation. We present averages or primary estimates in the quantified sections of costs and cost savings, Section E and Section G, respectively. Upper and lower bounds around these estimates and results from relaxing our assumptions are presented at the end of the cost and cost savings sections.

1. Assumptions

What follows is a list of assumptions we make in order to estimate the potential costs and potential cost savings of the proposed rule. We relax many of these assumptions in the uncertainty sections of our cost and cost savings analyses. We request comment on these assumptions.

Assumptions:

(a) All application holders of medical products likely to use the RFD process will spend resources reading and understanding the regulation.
(b) The proposed regulation will not alter the current or future number or Center distribution of
    a. combination products applications submitted,
    b. combination products applications accepted, or
    c. firms submitting combination product applications.
(c) The proposed regulation will not alter the number of RFDs submitted to OCP.

2. Baseline Conditions

The impact of the proposed rule will depend on the number of entities affected and their current practices. To estimate the effects of the proposed rule we must first identify the pre-regulation baseline or the state of the affected parties prior to implementation of the regulation. Our estimates of the effect of the proposed regulation will be compared to the approximated baseline. We use the most recent and complete years of reporting and firm data as our baseline.[1] We request comment on our estimation of the baseline.

OCP receives an average of approximately 60 RFDs annually from approximately 45 sponsors. Approximately 20 of these RFDs result in decisions with 10 determined to be combination products and 10 determined to be non-combination products. Sponsors have 15

[1] MDUFMA mandated that FDA submit an Annual Report to Congress on the activities and impact of the Office of Combination Products. These reports have been submitted since 2003 and are publicly available at https://www.fda.gov/aboutfda/reportsmanualsforms/reports/performancereports/combinationproducts/default.htm.

days of OCP's original determination to submit a request for reconsideration that may not be longer than 5 pages. OCP receives an average of 1.5 Part 3 requests for reconsideration per year. In addition, OCP receives approximately 320 informal queries from stakeholders regarding classification annually.

E. Costs of the Proposed Rule

We do not currently expect the proposed rule to add any costs to FDA or consumers. The proposed rule should not affect the price or availability of medical products.

We organize the presentation of cost estimates under subheadings of the actual cost to industry. Primary estimates presented under each subheading are our best point estimates and should be thought of as the approximated mean estimate. Due to uncertainty in the means and sensitivity to the assumptions we make, we present a 90 percent confidence interval around simulated mean estimates at the end of this section.

1. Reading and Understanding the Proposed Regulation

All affected entities may incur costs relating to learning about the rule from reading the preamble, changes to the codified, and any new guidance documents related to publication of the regulation. This activity requires facility representatives and lawyers to read the rule and associated documents, interpret its provisions, and determine which provisions they would have to implement.

FDA has no precise estimate of one-time costs for reading and understanding a proposed regulation, but we expect this administrative burden to be incurred by regulatory affairs-equivalent personnel spending an average of 30 minutes for each entity affected by this rule. We use the average hourly wage rate of the "Lawyer" occupation code (SOC 23-1011) as a proxy for regulatory affairs personnel. We use $180 as the value of regulatory affairs personnel in a firm producing a CBER-regulated combination product, $172 as the value of regulatory affairs personnel in a firm producing a CDER-regulated combination product, and $167 value of regulatory affairs personnel in a firm producing a CDRH-regulated combination product.[2]

FDA is also unsure of how many manufacturers will spend resources to read and understand the regulation. We base our estimate of the expected number of firms affected by the regulation using the ratio of informal queries FDA receives each year to the total number of medical product applications received each year, and multiplying this ratio by the total number of medical product manufacturers.

OCP receives approximately 320 informal queries and sponsors of medical products submit approximately 5,000 applications per year. The resulting ratio is 320:5,000. We get a total of approximately 1,550 firms that may spend resources to read and understand the regulation.

[2] The CBER value is equal to the average of $86.63 (NAICS 325400) and $93.57 (NAICS 621990) doubled to include overhead. The CDER value is equal to $86.63 (NAICS 325400) doubled to include overhead. The CDRH value is equal to the average of $88.09 (NAICS 334500) and $78.69 (NAICS 339100) doubled to include overhead. Values are presented in Table 4.

We distribute the firms over product Centers and get 110 CBER-regulated firms (= 1,550 * 7%), 295 CDER-regulated firms (= 1,550 * 19%), and 1,145 CDRH-regulated firms (= 1,550 * 74%).

The best estimate of the total up-front cost to the approximately 110 firms producing CBER-regulated products for reading and understanding the proposed regulation is approximately $10,000 (= 110 firms * 1 regulatory affairs manager * $180 wage rate doubled to include overhead * 0.5 hour). The best estimate of the total up-front cost to the approximately 295 firms producing CDER-regulated products for reading and understanding the proposed regulation is approximately $26,000 (= 295 firms * 1 regulatory affairs manager * $172 wage rate doubled to include overhead * 0.5 hour). The best estimate of the total up-front cost to the approximately 1,145 firms producing CDRH-regulated products for reading and understanding the proposed regulation is approximately $95,000 (= 1,145 firms * 1 regulatory affairs manager * $167 wage rate doubled to include overhead * 0.5 hour).

Our best, average estimate of the one-time costs to industry for reading and understanding the proposed rule equals approximately $131,000 (= $10,000 + $26,000 + $95,000). We expect these costs to only be incurred during the first year the rule goes into effect. The estimated average up-front costs associated with reading and understanding the regulation annualized over 10 years are approximately $15,000 at the 3 percent discount rate and approximately $17,000 at the 7 percent discount rate.

We request comment on our estimate of the number of firms affected by the proposed regulation and the estimated time burden placed on the affected firms.

2. Uncertainties Relating to Cost Estimates

The cost estimates presented in Section II.E.1 are calculated using best average estimates; however, we are uncertain of the precise time firms will spend reading and understanding the regulation. We relax the assumption that it will take 30 minutes to read and understand the proposed rule and provide plausible lower and upper bounds around a simulated mean in order to present the uncertainties in our analysis. We then run a Monte Carlo simulation[3] using @Risk[4] to estimate the distribution of the proposed rule's estimated costs to society.

We base our primary estimates presented in the cost section on previous regulatory analyses of FDA regulations. We create a lower bound by halving the expected time and an upper bound by doubling the expected time to account for some of the variability in these best estimates. We then apply a pert distribution[5] using the primary estimates and bounds. The lower bound and upper bound estimates of a 90 percent confidence interval are presented in columns 2 and 4 of Table 5, respectively.

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[3] A simulation technique that involves taking multiple random draws from the distribution for each critical parameter, calculating the model output for each draw, and using the results to represent the distribution of the outcome measure.

[4] A Microsoft Excel add-in from Palisade Corporation used to simulate values from a probability distribution (@Risk™ version 7.5, Palisade Corporation http://www.palisade.com).

[5] A probability distribution defined by minimum, most likely, and maximum values. The mean is the weighted average of the three parameters, with the most likely value receiving four times the weight of the other two values.

3. Summary of the Costs of the Proposed Rule

Table 5 summarizes the best estimate primary up-front cost of the proposed rule along with the minimum and maximum values from the uncertainty analysis. The up-front primary costs translate to net present values (NPV) of $127,000 at a 3 percent discount rate and $122,000 at a 7 percent discount rate. We estimate total annualized costs over a 10-year time period to be approximately $15,000 at a 3 percent discount rate and $17,000 at a 7 percent discount rate.

Table 5: Summary of Estimated Costs and Uncertainty[a]

	Minimum	Primary	Maximum
Total Up-front Costs	$87,000	$131,000	$206,000
Net Present Value 3%	$84,000	$127,000	$200,000
Net Present Value 7%	$81,000	$122,000	$192,000
Annualized 10 years 3%	$10,000	$15,000	$23,000
Annualized 10 years 7%	$12,000	$17,000	$27,000

[a] Dollar values are rounded to the nearest $1,000.

F. Discussion of the Non-quantified Benefits of the Proposed Rule

Public health benefits from adoption of the proposed rule would be the value of the illnesses and deaths avoided as a result of finalizing the proposed rule. The proposed rule is intended to promote public health by improving the scope and clarity of 21 CFR part 3 regulations. Lack of clear instructions may lead to uncertainty for sponsors of when to use the part 3 process for determining a medical product's classification and/or assignment. The costs for development and seeking marketing authorization for a medical product can vary depending on the product's classification and assignment (for example, fiscal year 2018 user fees for new drug applications vary from $1.2 million to $2.4 million,[6] while those for device applications range from $10,566 for a 510(k) to $310,764 for a PMA[7]). Failure to engage with the Agency regarding the classification or assignment of a medical product because the manufacturer does not realize the classification or assignment is unclear or uncertain, may lead a manufacturer to invest tens or hundreds of thousands of dollars or more in developing a product only to learn subsequently that the costs of seeking marketing authorization are higher than expected and the return on investment if approved would not be acceptable from that manufacturer's perspective. The reduced uncertainty also should decrease the time required to comply with existing requirements and the number of exchanges with FDA personnel, freeing up FDA and sponsor personnel and resources to perform other tasks that may improve public health. These improvements to the regulation may increase the efficiency in the process of determining the classification and assignment for medical products, including the appeal of such determinations, and in submitting appropriate premarket submissions for medical products for which the classification or assignment is unclear or uncertain. We are unable to quantify these expected benefits; nonetheless, we do not expect that these annual public health benefits will be large due to the small number of such annual applications and appeals.

[6] "Prescription Drug User Fee Rates for Fiscal Year 2018" available at http://www.gpo.gov/fdsys/pkg/FR-2017-09-14/pdf/2017-19494.pdf.

[7] "Medical Device User Fee Rates for Fiscal Year 2018" available at http://www.gpo.gov/fdsys/pkg/FR-2017-08-29/pdf/2017-18378.pdf.

G. Quantifiable Cost Savings of the Proposed Rule

Sponsors of medical products and FDA may realize resource-savings with finalization of the proposed rule. First, streamlining and clarifying the appeals process for product classification and assignments will eliminate an unnecessary step in the appeals process. Second, clarifying the scope of the 21 CFR part 3 regulations and increasing the consistency between the regulation, recent legislative changes, and FDA policies and practices will result in more efficient product developmental and premarket review processes.

These cost savings will recur annually. Primary estimates presented under each subheading should be thought of as the approximated primary estimate. Due to uncertainty in the primary estimates and sensitivity to the assumptions we make, we present lower and upper bounds around these estimates at the end of this section.

1. Streamlining the Appeals Process for Product Classification and Assignments

FDA proposes to remove the duplicative appeals process for appealing an FDA decision classifying a product as a drug, biological product, device, or combination product, and/or assigning such product to an FDA Center with primary jurisdiction for premarket review and regulation. Current regulations codified at 21 CFR 3.8(c) allows for sponsors to request that OCP reconsider classification and assignment determinations made under 21 CFR part 3. Sponsors also may make a supervisory appeal in accordance with 21 CFR 10.75 if they do not agree with OCP's initial determination or response to such a request for reconsideration.

Current regulation may lead to confusion and unnecessary effort by sponsors because some sponsors do not realize that appealing under 21 CFR 3.8(c) is not a prerequisite for submitting a supervisory appeal, and this may also lead to unnecessary effort by Agency staff. In addition, OCP's process of determining a product's classification and assignment is robust and sponsors are not permitted to submit new information to OCP in a request for reconsideration under § 3.8(c). As a result, appeals under § 3.8(c) can be a wasted step. Removing the § 3.8(c) appeals process will streamline the process for appealing product classification and assignment determinations for sponsors and FDA staff, making the process more efficient.

a. Cost Savings to Industry from Streamlining the Appeals Process

The Agency expects that the § 3.8(c) and § 10.75 appeals processes are similar, thus requiring essentially the same effort to submit only a § 10.75 supervisory appeal. As a result, removal of the § 3.8(c) appeal to OCP would only result in a marginal resource-savings to industry. The savings to industry will include the reduced effort by industry personnel in preparing the request for reconsideration and the savings in paper, labor, and postage from submitting it to OCP.

We include labor savings for the request for reconsideration submissions because submitting the § 3.8(c) request will no longer be allowed. We calculate labor costs of submitting a § 3.8(c) request by multiplying the time spent performing the activity by person's wage rate doubled to include overhead.

One category of labor-savings will be realized since industry personnel will no longer have to prepare the request for reconsideration. We estimate preparing the § 3.8(c) request and the § 10.75 appeal are similar, however, not equal. Therefore, we do not expect industry will gain 100 percent of the resources saved from eliminating the § 3.8(c) request. We estimate that approximately 20 hours will be saved per request. We estimate the value of the time saved by equally distributing the 20 hours over management (SOC 11-0000), compliance officer (SOC 13-1041), and lawyer occupations (SOC 23-1011). We average the fully-loaded wage rates of all sponsors affected using the distribution of application types. We estimate this fully-loaded wage rate would be $137 per hour[8] for management occupations, $78 per hour[9] for compliance officer occupations, and $169 per hour[10] for lawyer occupations. This equals $2,600 per appeal submission (= (6.67 hours * $137 per hour) + (6.67 hours * $78 per hour) + (6.67 hours * $169 per hour)) for writing the 3.8(c) request.

Regulations limit the length of the § 3.8(c) appeal to 5 pages. We estimate the average page length of an appeal to be 2 pages and the average cost to print a page to be $0.03 per page. FDA thus estimates an average § 3.8(c) appeal to cost $0.06 (= 2 pages * $0.03 per page). In addition, cost savings will accrue equal to a person in the office and administrative support occupation to print and place the document in an envelope. We estimate this will take approximately 3 minutes, or 0.05 hours. We use the average hourly wage rate of the "Office and Administrative Support" occupation code (SOC 43-0000) as a proxy. We average the fully-loaded wage rates of all sponsors affected using the distribution of application types. We estimate this fully-loaded wage rate would be $42 per hour.[11] This equals $2.10 per appeal submission (= 0.05 hours * $42 per hour) for printing and placing the document in an envelope. Total labor-savings equal $2,602 (= $2,600 writing labor + $2.10 printing labor).

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[8] The CBER value is equal to the average of $69.81 (NAICS 325400) and $50.40 (NAICS 621990) doubled to include overhead, or $120.21 (= (($69.81 + $50.40) / 2) * 2). The CDER value is equal to $69.81 (NAICS 325400) doubled to include overhead, or $139.62 (= $69.81 * 2). The CDRH value is equal to the average of $71.33 (NAICS 334500) and $66.79 (NAICS 339100) doubled to include overhead, or $138.12 (= (($71.33 + $66.79) / 2) * 2). We come to the $137 hourly wage used in the analysis by summing these values by their distribution (= ($120.21 * 7%) + ($139.62 * 19%) + ($138.12 * 74%)). Values are presented in Table 4.

[9] The CBER value is equal to the average of $39.20 (NAICS 325400) and $29.17 (NAICS 621990) doubled to include overhead, or $68.37 (= (($39.20 + $29.17) / 2) * 2). The CDER value is equal to $39.20 (NAICS 325400) doubled to include overhead, or $78.40 (= $39.20 * 2). The CDRH value is equal to the average of $40.88 (NAICS 334500) and $37.99 (NAICS 339100) doubled to include overhead, or $78.87 (= (($40.88 + $37.99) / 2) * 2). We come to the $78 hourly wage used in the analysis by summing these values by their distribution (= ($68.37 * 7%) + ($78.40 * 19%) + ($78.87 * 74%)). Values are presented in Table 4.

[10] The CBER value is equal to the average of $86.63 (NAICS 325400) and $93.57 (NAICS 621990) doubled to include overhead, or $180.20 (= (($86.63 + $93.57) / 2) * 2). The CDER value is equal to $86.63 (NAICS 325400) doubled to include overhead, or $173.26 (= $86.63* 2). The CDRH value is equal to the average of $88.09 (NAICS 334500) and $78.69 (NAICS 339100) doubled to include overhead, or $166.78 (= (($88.09 + $78.69) / 2) * 2). We come to the $169 hourly wage used in the analysis by summing these values by their distribution (= ($180.20 * 7%) + ($173.26 * 19%) + ($166.78 * 74%)). Values are presented in Table 4.

[11] The CBER value is equal to the average of $21.38 (NAICS 325400) and $17.87 (NAICS 621990) doubled to include overhead, or $39.25 (= (($21.38 + $17.87) / 2) * 2). The CDER value is equal to $21.38 (NAICS 325400) doubled to include overhead, or $42.76 (= $21.38 * 2). The CDRH value is equal to the average of $22.52 (NAICS 334500) and $19.32 (NAICS 339100) doubled to include overhead, or $41.84 (= (($22.52 + $19.32) / 2) * 2). We come to the $42 hourly wage used in the analysis by summing these values by their distribution (= ($39.25 * 7%) + ($42.76 * 19%) + ($41.84 * 74%)). Values are presented in Table 4.

Postage costs are determined by speed of delivery and distance to destination. The § 3.8(c) appeal to OCP must be submitted in paper within 15 days of OCP's original determination, so we assume firms will submit paper documents using a first-class mail courier at their overnight rate. We use current parcels rates from two first class mail couriers to estimate the average cost of shipping these documents (Ref. 2; Ref. 3). The average rate for shipping an envelope overnight is $62 from domestic origins and $93 from foreign origins. We expect that approximately 20 percent of appeals will be mailed from a foreign address, giving us an average shipping cost estimate of $68 (= ($62 * 80% domestic) + ($93 * 20% foreign)) per appeal.

FDA receives an average of 1.5 part 3 appeals each year. The primary total cost savings to industry for not submitting a § 3.8(c) appeal in paper form is equal to approximately $3,900 (= ($2,602 labor cost + $0.06 printing cost + $68 postage cost) * 1.5 appeals per year).

b. Cost Savings to FDA from Streamlining the Appeals Process

FDA has 15 days to respond to § 3.8(c) appeals. The Agency estimates 6 to 20 FDA employees will review each appeal, spending a total of 120 hours on the review. A majority of the time spent on review will be by OCP and the Office of the Chief Counsel (OCC), but the Centers also routinely review the request to provide recommendations to OCP for how to respond.

We estimate OCP will spend 60 hours and OCC will spend 10 hours on the review. The remaining 50 hours will be split among the appropriate Centers based on the distribution of application types. We apply a time burden of 3.5 hours (= 50 hours * 7%) for CBER review, 9.5 hours (= 50 hours * 19%) for CDER review, and 37 hours (= 50 hours * 74%) for CDRH review. The FTE hourly rate is $141 for OCP and OCC, $130 for CBER, $132 for CDER, and $125 for CDRH. We estimate the average burden to FDA for reviewing a Part 3 appeal to be $16,200 (= (60 hours * $141 per OCP FTE hour) + (10 hours * $141 per OCC FTE hour) + (3.5 hours * $130 per CBER FTE hour) + (9.5 hours * $132 per CDER FTE hour) + (37 hours * $125 per CDRH FTE hour)).

FDA receives an average of 1.5 part 3 appeals each year. The primary total cost savings to FDA for not receiving and reviewing a § 3.8(c) appeal is equal to approximately $24,300 (= $16,200 cost to FDA per appeal * 1.5 appeals per year).

c. Total Cost Savings from Streamlining the Appeals Process

Our best, average estimate of the total annual cost savings from streamlining the appeals process for product classification and assignments is approximately $28,200 (= $3,900 to industry + $24,300 to FDA) per year.

2. Clarifying 21 CFR part 3 Language

We expect implementation of the proposed rule will result in an improvement in the process for preparing and submitting an application for a medical product. Sponsors may find the

request for designation process confusing due to inconsistencies between current regulations, recent legislative changes, and FDA policies and practices. This lack of clarity may lead to a lack of sufficient information and multiple correspondences between FDA and sponsors trying to determine their product's classification and where their application should be submitted. Most queries to the Agency about product jurisdiction may be handled quickly with limited burden on a few personnel in the same office; however, some may require consultation from multiple offices or submission of an RFD. Therefore, we expect that clarification may lead to an improvement in planning for product development and obtaining market access, and reduce the amount of correspondence between sponsors and FDA to get the correct information.

In addition to formal activities such as responding to RFD submissions, OCP performs an average of approximately 700 premarket review and postmarket regulation documented activities per year. Most of these activities are premarket review issues and may be reduced with the finalization of the proposed rule. For instance, OCP estimates it receives approximately 320 informal stakeholder inquiries related to product classification and jurisdiction assignment annually. This number includes requests for informal assessments for which FDA provided feedback, requests about the classification or assignment of a particular product that did not provide sufficient information for the Agency to provide feedback, and more general or procedural questions relating to product classification and assignment.

It is possible that the proposed regulation once finalized will reduce the number of queries and activities, or may at least reduce the burden placed on sponsors and FDA for some queries and activities. These additional potential cost savings are not quantified due to the large amount of uncertainty about baseline activities and the extent to which changes to current regulations will alter industry behavior.

3. Potential Cost Savings not Estimated

Industry and FDA could potentially realize an additional cost saving as a result of the proposed rule in addition to the ones estimated in Sections II.G.1-2. The proposed rule would allow sponsors to submit RFDs to FDA electronically instead of requiring a hard copy to be submitted. Electronic submissions of RFDs would reduce printing and postage costs to industry, and processing costs to FDA. While we assume some sponsors will choose to submit RFDs electronically, we do not have expectations of by how many will choose to submit RFDs electronically, and therefore, these additional potential cost savings are, at the moment, not quantified. Since all RFDs are currently submitted in paper form, we do expect that submitting RFDs electronically would increase the cost savings of the proposed rule. FDA requests comments on baseline activities and how the proposed regulation may affect the potential cost savings mentioned in this section and any additional cost savings inadvertently left out of this analysis.

4. Uncertainties Relating to Cost Savings Estimates

The cost savings estimates presented in the preceding section are calculated using best average estimates. In order to present a number of possibilities, we relax several of our assumptions and provide plausible upper and lower bounds around a simulated mean, using our

best estimates, in this section. We begin by discussing the uncertainties we have. We then run a Monte Carlo simulation using @Risk to estimate the distribution of the proposed rule's estimated cost savings to society.

Our main uncertainty around our cost savings estimates concern the number of § 3.8(c) requests for reconsideration we may receive annually. OCP estimates they receive between 1 and 2 requests each year, with a maximum possible of 5. We estimate our primary cost savings using an average of 1.5 appeals avoided annually. We use a lower bound of 1 appeal per year avoided and an upper bound of 5 appeals per year avoided in our uncertainty analysis. We then apply a triangular distribution using the primary estimates and bounds.

Regulations limit the length of an appeal to 5 pages. We use an average of 2 pages as our primary estimate. We use a lower bound of 1 printed page per year avoided and an upper bound of 5 printed pages per year avoided in our uncertainty analysis. We then apply a triangular distribution using the primary estimates and bounds.

We also have uncertainties about the estimates we use for the time it will take industry and FDA to perform tasks required in the proposed rule. We base our primary estimates presented in the cost savings section on previous regulatory analyses of FDA regulations. To account for some of the variability in these best estimates we create a lower bound by halving the expected time and an upper bound by doubling the expected time. We then apply a pert distribution using the primary estimates and bounds.

Another uncertain variable is the cost of postage per appeal. We estimate our primary cost savings estimates using the average of all overnight rates from two first-class mail couriers, or $62 for domestic postage and $93 for foreign postage. We use the minimum and maximum values for both domestic and foreign postage to establish lower and upper bounds, respectively. We then apply a pert distribution using the primary estimates and bounds.

Our final uncertainty revolves around the distribution of domestic and foreign firms that may choose to appeal a determination. We use 20 percent as our best estimate of foreign entities appealing a determination based on the number of foreign submissions of post-approval reports from previous regulations. We create a lower bound by halving the expected percentage of foreign appeals and an upper bound by doubling the expected percentage of foreign appeals to account for some of the variability in our primary estimates. We then apply a pert distribution using the primary estimates and bounds.

Table 6 presents the values of primary, lower bound, and upper bound for the variables for which there is uncertainty. The first column identifies the cost savings variable. The second, third, and fourth columns present the minimum, primary, and maximum values used in the uncertainty analysis, respectively.

Table 6: Summary of Uncertainties around Primary Cost Savings Estimates

Uncertain Variable	Minimum	Primary	Maximum
Annual 3.8(c) Appeals	1	1.5	5
Pages per Appeal	1	2	5
Sponsor Time to Write 3.8(c) Appeal	10 hours	20 hours	40 hours
Sponsor Time to Submit 3.8(c) Appeal	1.5 minutes	3 minutes	6 minutes
FDA Time to Review Appeal	60 hours	120 hours	240 hours
Domestic First-Class Overnight Postage	$40	$62	$77
Foreign First-Class Overnight Postage	$48	$93	$138
Distribution of Appeals from Foreign Firms	10 percent	20 percent	40 percent

5. Summary of the Quantifiable Cost Savings of the Proposed Rule

Table 7 summarizes the proposed rule's total primary, lower bound, and upper bound cost savings estimates by year, with the minimum and maximum results being the lower and upper bounds of a 90 percent confidence interval. Our primary estimate of annual cost savings is approximately $28,000. We estimate total annualized primary cost savings over a 10-year period to approximately equal $28,200 at a 3 percent discount rate and $28,000 at a 7 percent discount rate. These values translate to present discounted values of $241,000 at a 3 percent discount rate and $198,000 at a 7 percent discount rate.

Table 7: Summary of Estimated Cost Savings and Uncertainty[a]

	Minimum	Primary	Maximum
Total Recurring Cost Savings	$25,000	$28,000	$89,000
Net Present Value 3%	$213,000	$241,000	$759,000
Net Present Value 7%	$175,000	$198,000	$625,000
Annualized 10 years 3%	$25,000	$28,000	$89,000
Annualized 10 years 7%	$25,000	$28,000	$89,000

[a] Dollar values are rounded to the nearest $1,000.

H. Summary of Quantified Costs and Cost Savings of the Proposed Rule

Table 8 summarizes our best estimates of the proposed rule's total net costs by year. We identify net cost savings with a minus (-) sign. The total year 1 net effect of the proposed rule is estimated to be a net social cost of approximately $103,000. Subsequent annual recurring net effects are estimated to be net social cost savings of approximately $28,000. We estimate total annualized net cost savings over a 10-year time period to equal approximately $13,000 at a 3 percent discount rate and approximately $11,000 at a 7 percent discount rate. These values translate to net present values of approximately $114,000 at a 3 percent discount rate and approximately $76,000 at a 7 percent discount rate.

Table 8: Summary of Quantified Costs and Cost Savings[a]

Year	Costs	Cost Savings	Net Costs[b]
Year 1	$131,000	$28,000	$103,000
Year 2	$0	$28,000	-$28,000
Year 3	$0	$28,000	-$28,000
Year 4	$0	$28,000	-$28,000
Year 5	$0	$28,000	-$28,000
Year 6	$0	$28,000	-$28,000
Year 7	$0	$28,000	-$28,000
Year 8	$0	$28,000	-$28,000
Year 9	$0	$28,000	-$28,000
Year 10	$0	$28,000	-$28,000
NPV 3%	$127,000	$241,000	-$114,000
NPV 7%	$122,000	$198,000	-$76,000
Annualized 3%	$15,000	$28,000	-$13,000
Annualized 7%	$17,000	$28,000	-$11,000

[a] Dollar values are rounded to the nearest $1,000.
[b] The values are equal to cost savings minus costs.

Table 9 presents the results of our uncertainty analysis of the net effect of the proposed rule. The second, third, and fourth columns present the minimum, most likely, and maximum value results, respectively, with the minimum and maximum results being the lower and upper bounds of a 90 percent confidence interval. We identify net cost savings with a minus (-) sign. The present value of these net cost savings over ten years is $114,000 at a 3 percent discount rate, and $76,000 at a 7 percent discount rate. Annualizing these net cost savings over a ten year period, we estimate total annualized net costs to be $13,000 at a 3 percent discount rate, and $11,000 at a 7 percent discount rate.

Table 9: Uncertainty Analysis of Net Costs[a,b]

Uncertain Variable	Minimum	Primary	Maximum
Net Present Value 3%	-$658,000	-$114,000	-$29,000
Net Present Value 7%	-$526,000	-$76,000	$1,000
Annualized 10 years 3%	-$77,000	-$13,000	-$3,000
Annualized 10 years 7%	-$75,000	-$11,000	$1,000

[a] Dollar values are rounded to the nearest $1,000.
[b] The values are equal to costs minus cost savings.

I. International Effects

The pharmaceutical and medical device industries are global, with manufacturing and consumption of a product often taking place in different parts of the world. Among other changes to clarify and update part 3, the proposed rule would eliminate a potential step in the process for appealing an FDA decision that a product will be regulated as a drug, biological product, device or combination product or regarding the Center to which the product will be assigned. Foreign applicants holding or developing medical products would incur the same costs associated with reading and understanding the regulation as those anticipated for domestic firms.

We believe the proposed rule would be unlikely to alter the current mix of foreign and domestic firms producing medical products due to the small number of firms affected and the relatively small burden the rule will place on firms. FDA requests comments and data on the proposed rule's effects on foreign firms and its perceived effect on the current mix of foreign and domestic production of medical products.

III. Initial Small Entity Analysis

The Regulatory Flexibility Act requires Agencies to prepare an initial regulatory flexibility analysis if a proposed rule would have a significant economic impact on a substantial number of small entities (including small businesses, small non-profit organizations, and small governmental jurisdictions). FDA has examined the economic implications of the proposed rule as required by the Regulatory Flexibility Act. If a rule will have a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires agencies to analyze regulatory options that would lessen the economic effect of the rule on small entities.

This rule will not impose any new burdens on small entities, and thus will not have a significant economic impact on a substantial number of small entities. As a result, we do not provide additional options to the proposed regulation. We propose to certify that the proposed rule will not have a significant economic impact on a substantial number of small entities. We request comment on our determination and possible alternatives to consider.

IV. References

The following references are cited in the analysis. The references not displaying a Uniform Resource Locator (URL) have been placed on display in the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. FDA has verified the Web site addresses for the references displaying a URL, but FDA is not responsible for any subsequent changes to the Web sites after this document publishes in the Federal Register.

1. U.S. Bureau of Labor Statistics, Occupational Employment Statistics, May 2016, National Industry-Specific Occupational Employment and Wage Estimates, http://data.bls.gov/oes/, accessed October 31, 2017.

2. FedEx, "2016 Service Guide," available at http://images.fedex.com/us/services/pdf/Service_Guide_2017.pdf, accessed March 13, 2017.

3. UPS, "2017 UPS Rate and Service Guide," available at http://www.ups.com/media/en/daily_rates.pdf, accessed March 13, 2017.