DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Microbiology Devices; Classification of In Vitro Diagnostic Device for Bacillus Species Detection

Docket No. FDA-2011-N-0103

Final Regulatory Impact Analysis
Final Regulatory Flexibility Analysis
Unfunded Mandates Reform Act Analysis

Economics Staff
Office of Planning
Office of Policy, Planning, and Legislation
Office of the Commissioner

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I. Introduction and Summary

A. Introduction

We have examined the impacts of the final 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 final 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 of the small impact expected from this rule, we certify that the final 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 $150 million, using the most current (2017) Implicit Price Deflator for the Gross Domestic Product. This final rule would not result in an expenditure in any year that meets or exceeds this amount.

FDA refers to devices that were commercially distributed prior to May 28, 1976, the date of enactment of the Medical Device Amendments of 1976, as "preamendments devices." An unclassified device is a preamendments device for which a classification regulation has not been promulgated. FDA classifies preamendments devices after FDA: (1) receives a recommendation from a device classification panel (an FDA advisory committee); (2) publishes the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) publishes a final regulation classifying the device. FDA followed these procedures to classify in vitro diagnostic devices for *Bacillus* spp. detection.

The purpose of this rule is to classify in vitro diagnostic devices for *Bacillus* spp. detection into class II (special controls), establish special controls in a special controls guideline [1], and restrict the use and distribution of these devices. These devices are prescription devices used to detect and differentiate among *Bacillus* spp. and presumptively identify *B. anthracis* and other *Bacillus* spp. from cultured isolates or clinical specimens as an aid in the diagnosis of anthrax and other diseases caused by *Bacillus* spp.

B. Summary of Costs and Benefits

Quantifiable benefits of this rule are cost savings resulting from a reduction in the time burden of inquiries manufacturers submit to the Food and Drug Administration (FDA). The cost savings involve manufacturers, who no longer need to submit as many inquiries related to submissions for these devices, because much of the necessary information is provided by this rule and guideline, and the FDA who no longer needs to use resources to respond to these inquiries. A 20-year time horizon was chosen for this analysis because this industry has been stable and there is no reason to expect disruptions for the foreseeable future. The primary present value of the benefits, over a 20-year time horizon from 2018 to 2038 are estimated to be $258,054, at a 7% discount rate and $353,393, at a 3% discount rate. The primary estimate of the annual benefits, over a 20-year time horizon from 2018 to 2038, are estimated to be $22,258 a year.

Table 1. Summary of Benefits, Costs, and Distributional Effects of the Final Rule in 2017 Dollars over a 20-Year Time Horizon

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Benefits	Annualized Monetized $/year	$22,258	$7,419	$37,096	2017	7%	20	
		$22,258	$7,419	$37,096	2017	3%	20	
	Annualized Quantified					7%		
						3%		
	Qualitative							
Costs	Annualized Monetized $/year	$1,092	$733	$1,455	2017	7%	20	
		$887	$595	$1,183	2017	3%	20	
	Annualized Quantified					7%		
						3%		
	Qualitative							
Transfers	Federal Annualized Monetized $/year					7%		
						3%		
	From/ To	From:			To:			
	Other Annualized Monetized $/year					7%		
						3%		
	From/To	From:			To:			
Effects	State, Local or Tribal Government: Small Business: Wages: Growth:							

This rule has a onetime upfront cost for current manufacturers of these devices as they may need to develop new labeling. There are 7 total products on the market and each labeling redesign is estimated to cost $1,096. We estimate the total labeling cost to be $7,674. The 6 existing

manufacturers (one firm has two products) also face a onetime upfront cost of having to read the rule and guideline which we estimate to be $1,138 for the manufacturers. Finally, there is an annual cost of reading the rule to firms who may submit inquiries in the future. We estimate this annual cost to be $332. The primary present value of the costs, over a 20-year time horizon from 2018 to 2038, are estimated to be $12,659 at a 7% discount rate and $14,081 at a 3% discount rate. The primary annualized costs, over a 20-year time horizon from 2018 to 2038, are estimated to be $1,092 at a 7% discount rate and $887 at a 3% discount rate. The total net benefit of the rule is estimated to be $245,395 at a 7% discount rate and $339,312 at a 3% discount rate. The annualized net benefits of this rule are estimated to be $21,166 at a 7% discount rate and $21,371 at a 3% discount rate.

In line with Executive Order 13771, in Table 2 we estimate present and annualized values of costs and cost savings over an infinite time horizon. Based on these cost savings this final rule would be considered a deregulatory action under EO 13771. Our primary estimate for the present value of the net costs is -$319,974 (or a cost savings of $319,974) at a 7% discount rate and -$729,462 at a 3% discount rate in 2016 dollars.

Table 2. EO 13771 Summary Table (in 2016 Dollars, Over an Infinite Time Horizon)

	Primary (7%)	Lower Bound (7%)	Upper Bound (7%)	Primary (3%)	Lower Bound (3%)	Upper Bound (3%)
Present Value of Costs	$13,614	$9,133	$18,094	$19,812	$13,265	$26,358
Present Value of Cost Savings	$333,588	$77,548	$555,938	$749,273	$174,181	$1,248,789
Present Value of Net Costs	($319,974)	($68,415)	($537,843)	($729,462)	($160,916)	($1,222,430)
Annualized Costs	$891	$597	$1,184	$577	$386	$768
Annualized Cost Savings	$21,823	$5,073	$36,370	$21,823	$5,073	$36,372
Annualized Net Costs	($20,933)	($4,476)	($35,186)	($21,246)	($4,687)	($35,605)

C. Comments on the Preliminary RIA and Our Responses

In 2015, the FDA published the proposed rule “Microbiology Devices; Classification of In Vitro Diagnostic Device for Bacillus Species Detection” [2]. We prepared a comprehensive preliminary regulatory impact analysis for the 2015 proposed rule [3]. We received no comments on our analysis.

D. Summary of Changes

There have been several changes to the Proposed Regulatory Impact Analysis (PRIA). The cost savings calculations have been updated. The PRIA calculated cost savings based on clarifications that would help potential new manufacturers develop their 510(k) submissions. Given there have been no new 510(k) submissions in several years this is unlikely to be a significant source of cost savings. However, the FDA receives formal written inquiries (Q-submissions or Q-subs) on a regular basis. This rule will provide cost savings by providing clarification that will diminish the burden of these inquiries for both the industry and the FDA. In

the cost section, the labeling cost model has been updated and we have included the time cost of firms reading the rule.

II. Final Regulatory Impact Analysis

A. Background

The purpose of this rule is to classify in vitro diagnostic devices for *Bacillus* spp. detection into class II (special controls), establish special controls in a special control guideline, and restrict the use and distribution of these devices. This regulation applies to devices with the following product codes: NVQ, NPO, NRL, NHT, NWZ. These devices are used to test for *Bacillus anthracis*, commonly called anthrax, as well as other diseases caused by *Bacillus* spp. in human samples. There are products that test for anthrax in environmental samples, but they are not covered by this regulation. Anthrax has a history as a naturally occurring disease that is more commonly thought of today as a biological weapon.

1. The History of Anthrax

The written history of anthrax goes back to the Ancient Greeks and Romans [4]. Since its first written record anthrax has be documented regularly as a naturally occurring disease in both humans and livestock. Humans contract naturally occurring anthrax through contact with infected animals, wool, meat, or hides; however, anthrax is not passed person to person. The first anthrax vaccine for livestock was invented in 1881. By the late 1930s, livestock vaccination was common and subsequently there was a significant decline in human cases of anthrax. The first anthrax vaccination and anthrax detection devices for humans were developed in the 1950s. Vaccines in humans are recommended for at risk populations such as people handling potentially infected animals, certain laboratory workers, and some military personnel [5].

In 2006, for the first time in 30 years, there was a case of naturally occurring anthrax in a human in the US. Since 2006 there have been two additional cases. In two of these cases, in 2006 and 2009, anthrax was contracted from animal hides used to make drums. In the third case, in 2011, it was contracted by a Florida resident on a cross country road trip. The source of his infection is unknown. All three patients eventually recovered from their infections [4].

2. Anthrax as Biological Weapon

While anthrax has been naturally inflicting humans for millennia it has also been used as a biological weapon in recent years. Anthrax was first used by the German army as a biological weapon during World War I to infect Argentinian livestock that they intended to trade to the Allied Nations. Since then many nations have experimented with anthrax as a biological weapon. The 1972 Convention on the Prohibition of the Development, Production, and Stockpiling of Biological and Toxic Weapons and on Their Destruction was signed by over 100 nations and

limited, among other things, the amount of anthrax a country could hold to the amount needed to develop vaccines and medical devices [4].

In September 2001, the largest anthrax as a biological weapon attack on the US was perpetrated. Letters containing anthrax laced powder were mailed to politicians and media outlets. Twenty-two people were sickened and five people died in this attack.

3. Anthrax Detection Devices

While anthrax is uncommon in the US, the threat of anthrax as a biological weapon means it is important to have well-functioning anthrax detection devices in the event of an outbreak. If in vitro diagnostic devices for *Bacillus* spp. detection are not properly regulated, there can be significant negative consequences. Negative outcomes include a false negative, which can cause someone to not receive important treatment and potentially delay addressing the source of the outbreak, a false positive, which may lead to unnecessary treatment for the patient and fear of an outbreak, and the potential exposure of the person preforming the test to anthrax.

In vitro diagnostic devices for *Bacillus* spp. detection are "preamendments devices," meaning they were in commercial distribution prior to May 28, 1976, the date of enactment of the Medical Device Amendments of 1976. These devices are currently unclassified. This rule classifies in vitro diagnostic devices for *Bacillus* spp. detection into class II (special controls), establishes special controls in a special controls guideline, and restricts the use and distribution of these devices to decrease the risk and to clarify important information about this type of device.

B. Market Failure Requiring Federal Regulatory Action

This rulemaking addresses informational asymmetry in the market for these devices. First, the final rule restricts distribution of these devices to laboratories that follow public health guidelines, and the special controls guideline requires clear labeling of directions for safe use of these devices. In the absence of this information there is an increased risk that there will be an adverse event such as false negatives, false positives, or inadvertent exposure to anthrax.

Second, without this rulemaking, medical device manufacturers would not have access to the necessary information about in vitro diagnostic devices for Bacillus spp. unless they submitted an inquiry to the FDA. This informational asymmetry would lead to device manufacturers being unclear about the requirements these devices. Manufacturers may subsequently spend more than the optimal allocation of time submitting inquiries. FDA employees would likewise spend more than the optimal allocation of time responding to these uninformed inquiries.

C. Purpose of the Proposed Rule

The purpose of this rule is to classify in vitro diagnostic devices for *Bacillus* spp. detection into class II (special controls), establish special controls in a special control guideline [1], restrict the device to prescription use, and restrict distribution of these devices to laboratories that follow

public health guidelines that address appropriate biosafety conditions, interpretation of test results, and coordination of findings with public health authorities.

D. Baseline Conditions

As of July 2018, there are seven in vitro diagnostic devices for *Bacillus* spp. detection that are cleared to be marketed in the US. Two of these devices are made by the same company so there are only six manufacturers. Two of the device manufacturers are federal agencies, the Centers for Disease Control and the Department of Defense. The 510(k)s for currently marketed devices were submitted between 2003 and 2014. This regulation is designed to ensure that these devices are used safely because they have significant potential risks if improperly used. All the devices cleared by the FDA are already following most of the special controls because the device manufacturers recognized the potential risks of their devices. The only change current manufacturers may need to make are minor updates to the device labeling. Therefore, this regulation will have little impact on current manufacturers, but it ensures that all future 510(k) submissions will comply with these requirements.

Without this rule, industry may be uncertain about requirements for 510(k) submissions and subsequently submit information requests to the FDA. This rule provides important clarification on the five product codes (NVQ, NHT, NRL, NPO, NWZ) covered by this rule making it easier to understand the various types of devices and therefore reducing the number of inquiries, or Q-subs, submitted to the FDA.

E. Benefits of the Rule

1. Non-quantifiable Benefits

We are unable to quantify the public health benefits of the final rule because the rule would require the adoption of practices which manufacturers of currently marketed devices already follow and would not change the expected use of the diagnostic device. There are also no reported adverse events associated with these devices. Therefore, there is no way to quantify an impact on public health. We acknowledge that it is possible that mishandling could occur in the future and it is possible that clear, consistent instructions may avoid some potential future mishandling, but we cannot quantify any benefit based on this eventuality.

While there may be no quantifiable public health benefits, this regulation provides reasonable assurance of safety and effectiveness of this important diagnostic tool and ensures all new 510(k) submissions meet the same standards as the currently marketed devices. In vitro diagnostic devices for *Bacillus* spp. detection provide important public health benefits through rapid diagnosis, resulting in the rapid treatment of a potentially fatal disease, or rapid identification that treatment is not necessary. The finalized regulation will provide additional assurance that the current level of public health protection is maintained.

2. Quantifiable Benefits

While there are no quantifiable public health benefits, this regulation and the special controls guideline provide benefits to potential manufacturers of new devices by clarifying important information about the devices. These clarifications generate cost savings by cutting down on the time and effort it takes to inquire about developing a new device. Likewise, it will decrease the time needed by the FDA to respond to new inquiries as the inquiries will either be no longer necessary or easier to address given the industries improved understanding of the devices.

Formal inquiries are called Q-subs or Q-submissions and they require the manufacturer to file a detailed information request. Inquiries are costly to both the manufacturer and the FDA as the manufacturer must develop their inquiry and the FDA must respond appropriately. Between 2012 and 2018, the FDA has received 11 Q-subs and 5 Q-sub supplements for anthrax related devices. Of the 11 Q-subs one was submitted by a federal agency and the others were submitted by private domestic firms. There is a chance that a future Q-sub may come from a federal agency but we assume all future Q-subs are submitted by private domestic firms. We assume that for both industry and the FDA a Q-sub supplement takes about one quarter of the time to develop or respond to as a Q-sub. Therefore, in the past 7 years, we estimate that there have been 1.75 [=(11+(0.25*5))/7] Q-subs equivalent submissions per year.

Inquiries may ask about multiple types of anthrax related devices, including devices not covered by this regulation. This could include devices that detect anthrax in environmental rather than human samples. Therefore, this final rule is likely to diminish the volume and intensity of inquiries, but not stop them entirely. We estimate that this rule will decrease the frequency of inquiries by 10 to 50% with our primary estimate of 30%. We estimate that the time to write an inquiry and to respond are approximately the same. Therefore, we assume that the avoided time burden for industry and the FDA are the same.

We estimate it will take about 200 hours of work to develop a Q-sub. We estimate it will take 185 hours for the scientific staff, 10 hours for lawyers, and 5 hours of managerial time. The mean wage for a biological scientist (occupation code 19-1020) in the Medical Equipment and Supplies Manufacturing (NCAIS code 339100) makes $37.90 per hour [6]. We double this to get a fully loaded wage rate of $75.80. The mean manager (occupation code 11-0000) in the Medical Equipment and Supplies Manufacturing (NCAIS code 339100) makes $68.96 an hour with a fully-loaded wage rate of $137.92. The mean lawyer (occupation code 23-1011) in the Medical Equipment and Supplies Manufacturing (NCAIS code 339100) makes $84.59 or a fully loaded wage rate of $169.18. Therefore, the total cost to a manufacturer to develop a Q-sub is $16,404 [=(185*75.80)+(5*137.92)+(10*169.18)]. Assuming that this rule will decrease the Q-sub burden by 10 to 50% and there are, on average, 1.75 Q-subs a year then the cost savings to industry will be $2,871 [=0.1*1.75*16,404] to $14,354 [=0.5*1.75*16,404].

We assume that the FDA has the same time burden, 200 hours, as industry to respond to the Q-subs; however, we value their resources using the average fully loaded cost of a full time equivalent employee of the Center for Devices and Radiological Health (CDRH) which is $129.95 per hour. The cost to the FDA to review one Q-sub is estimated to be $25,990 [=200*129.95]. If CDRH responds to 1.75 Q-subs a year and this rule will reduce that burden by 10 to 50% then the annual cost savings to the FDA is between $4,548 and $22,742 with a primary estimate of $13,645.

Table 3. Cost Savings Estimates

	Low	Primary	High
Q-Subs per Year	1.75	1.75	1.75
% of Q-Sub Addressed	10%	30%	50%
Industry Time			
Scientific Staff Hours	185	185	185
Scientific Staff Fully Loaded Wage	$76	$76	$76
Lawyer Hours	10	10	10
Lawyer Fully Loaded Wage	$169	$169	$169
Manager Hours	5	5	5
Manager Fully Loaded Wage	$138	$138	$138
Cost Savings to Industry	**$2,871**	**$8,612**	**$14,354**
FDA Time			
Staff Hours	200	200	200
Staff Fully Loaded Wage	$130	$130	$130
Cost Savings to FDA	**$4,548**	**$13,645**	**$22,742**
Total Cost Savings	**$7,419**	**$22,258**	**$37,096**

We estimate the final regulation, will result in quantifiable cost saving benefits of avoiding unnecessary inquiries of $22,258 a year. This equates to a present value of $258,054 at a 7% discount rate and $353,393 at a 3% discount rate over a 20-year time horizon.

F. Costs of the Rule

Since the products that are already on the market meet most of the requirements of this rule there are not likely to be many incremental compliance costs. The guideline requires specific wording on the labeling of devices that clarifies that only experienced and appropriate personnel may interpret the test results. Further, the guideline includes detailed information on what must be included in labeling, which may require minor revision to the labeling. It is not expected that the labeling changes would be substantial enough to require an updated 510(k) submission [7]. The only other cost to manufacturers with cleared 510(k)s is reading and comprehending the rule and guideline to make sure they are in compliance. Likewise, any firm submitting a Q-sub would need to read and comprehend this rule to inform their inquiry submission. Two of the existing manufacturers are federal agencies rather than private businesses so their costs will be calculated separately, though we believe all manufacturers will face the same costs.

1. Costs of Relabeling

The required labeling is similar to the cleared indications for use labeling of currently cleared devices, so little change from current labeling is expected. Nevertheless, we have estimated that manufacturers may incur the cost of minor revisions to their labeling after regulatory staff review the rule and guideline. We have estimated the cost of a labeling changes to be between $654 and $1,308 per labeling change per device. This estimate is based on a labeling cost estimate by ERG for sunlamps, another class II medical device [8]. The ERG report was used to estimate the number of labor hour and non-labor costs of a labeling change. The wages used in the estimation are based off current wages in the Medical Equipment and Supplies Manufacturing (NCAIS code 339100) sector. This cost includes labor hours for graphic designers to make the changes, labor hours of management to review the changes and the cost of making plate changes for the printer. For our low end estimate we assume that the labeling redesign will take 2 hours for the graphic designer and 4 hours for the manager. For the upper bound estimate, we assume it will take 4 hours for the graphic designer and 8 hours for a manager. The mean Graphic Designer (occupation code 27-1024) in the Medical Equipment and Supplies Manufacturing (NCAIS code 339100) makes $25.62 an hour with a fully loaded wage rate of $51.24 an hour. Plates and other costs of the labeling change are estimated to be between $85 and $145. The cost to redesign labeling for all 7 devices is estimated to be between $5,174 and $10,173 with a primary estimate of $7,674. These costs can be broken out into public and private costs. For the two federal agencies, the primary labeling cost estimate is $2,192 and for the five private firm's devices, the primary labeling cost estimate is $5,481.

Table 4. Labeling Cost Estimate

	Low	**Primary**	**High**
Graphic Design Labor Hours	2	3	4
Fully Loaded Wage per Hour	$51	$51	$51
Labor Cost	$102	$154	$205
Manager Labor Hours	4	6	8
Loaded Wage per Hour	$138	$138	$138
Labor Cost	$552	$828	$1,103
Labor Costs per Device	$654	$981	$1,308
Plate Charge	$60	$65	$70
Other Charges	$25	$50	$75
Total Cost per Device	**$739**	**$1,096**	**$1,453**
Cost for Two Federal Agencies Devices	$1,478	$2,192	$2,907
Cost for Five Private Firms Devices	$3,696	$5,481	$7,267
Total Costs	**$5,174**	**$7,674**	**$10,173**

2. Costs of Reading and Understanding the Rule

The cost of reading the rule is calculated using the time cost of a manager at each firm. We expect all 6 firms to read the rule when it is published. Additionally each firm that would have submitted a Q-sub prior to this rule is also expected to read the rule. In the benefits section we estimated that there are currently about 1.75 Q-subs each year. Combined the guideline and the rule have 11,000 words. The average reader can read 200 words per minute, so on the low end these documents should take about 55 minutes (0.92 hours) to read. However, it may take longer to fully understand this regulation so for our upper estimate we double the reading time to allow for comprehension time. This yields 110 minutes (1.83 hours). The cost of reading is between $126 and $253 per inquiry, with a primary estimate of $190. For the 6 existing manufacturers this will have a onetime cost of between $759 and $1,517 with a primary estimate of $1,138. This cost can be broken out into public and private costs. For the two federal agencies, the primary reading cost estimate is $379 and for the four private firms, the primary reading cost estimate is $759. There are estimated to be 1.75 Q-subs per year, so we expect an annual reading cost of between $221 and $442 for private firms submitting inquiries, with a primary estimate of $332.

Table 5. Reading Time Estimate

	Low	**Primary**	**High**
Reading time (Hours)	0.92	1.38	1.83
Fully loaded Wage ($ per hour)	$138	$138	$138
Cost per firm	$126	$190	$253
Cost to Two Federal Agencies	$253	$379	$506
Cost to Four Private Firms	$506	$759	$1,011
Total Onetime Cost	**$759**	**$1,138**	**$1,517**
Ongoing Cost to Private Firms:			
Firms per year	1.75	1.75	1.75
Total Ongoing Cost	**$221**	**$332**	**$442**

We have estimated that the rule, would result in annualized costs of $887 at a 3% discount rate and $1,092 at a 7% discount rate. This equates to a present value of $14,081 at a 3% discount rate and $12,659 at a 7% discount rate over a 20-year time horizon.

G. Summary of Costs and Benefits

The summary of the primary undiscounted stream of cost and benefits for this rule are presented in Table 6. The labeling costs and reading cost to current manufacturers are onetime

upfront costs while the cost savings and reading costs to firms submitting inquiries are reoccurring costs starting in years zero and continuing though year 20.

Table 6. Summary of Costs and Benefits – Primary Undiscounted Stream in2017 Dollars

	Benefits	Labeling costs		Reading costs			
Year	Cost Savings	for Federal Agencies	for Private Firms	for Federal Agencies	for Private Firms	for Firms Submitting Q-subs	Net Benefits
0	$22,258	$2,192.48	$5,481.20	$379	$759	$332	$13,114
1	$22,258					$332	$21,926
2	$22,258					$332	$21,926
3	$22,258					$332	$21,926
4	$22,258					$332	$21,926
5	$22,258					$332	$21,926
6	$22,258					$332	$21,926
7	$22,258					$332	$21,926
8	$22,258					$332	$21,926
9	$22,258					$332	$21,926
10	$22,258					$332	$21,926
11	$22,258					$332	$21,926
12	$22,258					$332	$21,926
13	$22,258					$332	$21,926
14	$22,258					$332	$21,926
15	$22,258					$332	$21,926
16	$22,258					$332	$21,926
17	$22,258					$332	$21,926
18	$22,258					$332	$21,926
19	$22,258					$332	$21,926
20	$22,258					$332	$21,926

H. Distributional Effects

We do not expect there to be any distributional effects of this rule. If this rule changes the number of 510(k) submissions for the devices, it would cause an increase or decrease in user fees paid to the FDA by the sponsor of the 510(k) submission. However, we do not expect this rule to have a significant impact on the number of future 510(k) submissions.

I. International Effects

We do not expect there to be any significant international effects of this rule. None of the current manufacturers of in vitro diagnostic devices for *Bacillus* spp. are international firms. Of the 11 Q-subs in the last 7 years none were submitted by an international firm. If international firms submitted any inquiries regarding anthrax detection devices we would expect them to achieve the same cost savings as any domestic firm submitting an inquiry.

J. Regulatory Alternatives

We identified three alternatives to the rule.

1. Continue to regulate as an unclassified device. This alternative would not provide an assurance of safety and effectiveness and would continue the current level of inconsistent information for potential new marketers. There would be no costs and benefits associated with this alternative as it would be the same as the baseline.

2. Regulate this diagnostic test as a class I device. General controls alone are not sufficient for the potential risks and would not provide reasonable assurance of the safety and effectiveness of the device. Further, sufficient information was available to develop special controls for this device. If this device was classified as class I we would expect the lower quantifiable benefits as the device would not be subject to special controls, such as those established in the special controls guideline. This may decrease the clarification value of the rule and therefore diminish the cost savings. This alternative would also eliminate the need for labeling changes and decrease the time burden of reading the rule. Therefore, this alternative would reduce both the cost savings and the costs, and is expected to have a lower net benefit than the final rule.

3. Regulate this diagnostic test as a class III device. Premarket approval and clinical data collection are not appropriate for the potential risks of this device. Sufficient information exists to determine that special controls would provide reasonable assurance of safety and effectiveness. The alternative would provide the same cost savings by providing important clarification information to the industry. However, it would also increase the cost to existing manufacturers by requiring them to meet a higher regulatory standard without an increase in assurances of safety and effectiveness. Further, this alternative my cause some firms to leave the market, or keep new firms from entering the market due to the greater costs. Overall, we expect this alternative to have a lower net benefit than the final rule.

III. Final 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 cost savings of this rule outweigh the costs, we certify that the final rule will not 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 Final Regulatory Flexibility Analysis, as required under the Regulatory Flexibility Act. 33911.

A. Description and Number of Affected Small Entities

In the Surgical and Medical Instrument Manufacturing (NAICS code 339112) a business is considered small if it has fewer than 1,000 employees [9]. Of the 6 firms approved to manufacture these devices, 3 are small businesses, 2 are federal agencies, and 1 is a large business according to Dun & Bradstreet data. Given that 75 percent of the private firms are small businesses, we expect about 75 percent of the firms submitting inquiries are also small businesses.

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

For current manufacturers of in vitro diagnostic devices for *Bacillus* spp., they will each have an upfront cost of about $1,286 [=190+1,096] to read the rule and update their labeling. This is a small cost that will not have a significant impact on a significant number of small businesses. For small businesses that may submit inquiries about anthrax devices this rule will have a cost savings effect. Overall, we expect about 75 percent of the net benefits of this rule to go to small businesses.

C. Alternatives to Minimize the Burden on Small Entities

We expect this rule to have net cost savings for small businesses. Since small businesses make up about 75% of the market the discussion of regulatory alternatives in Section III.I applies to small businesses. Regulating these devices as class I would slightly decrease the cost while not providing reasonable assurance of the safety and effectiveness of these devices. Regulating these devices as class III would have no improvement in risk reduction but would increase the cost to small businesses.

IV. References

[1] Center for Devices and Radiological Health, "Class II Special Controls Guideline: In Vitro Diagnostic Devices for Bacillus spp. Detection," Food and Drug Administration, Silver Spring, 2018.

[2] Center for Devices and Radiological Health , "Microbiology Devices; Classification of In Vitro Diagnostic Devices for Bacillus Species Detection," Food and Drug Administration, Silver Spring, 2015.

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