DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Safety and Effectiveness of Consumer Antiseptic Rub Products; Topical Antimicrobial Drug Products for Over-the-Counter Human Use

Docket No. FDA-2016-N-0124

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

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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." This final rule is a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Although the additional costs this rule imposes on small entities are small, the consumer antiseptic rub product industry is mainly composed of establishments with 500 or fewer employees. Therefore, we find that the final rule will have a significant economic impact on a substantial number of small entities. We have analyzed various regulatory options to minimize the impact on 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 issuing "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.

B. Summary of Costs and Benefits

As discussed in the preamble to the final rule, this rule applies to active ingredients used in over-the-counter (OTC) consumer antiseptic rub products, including hand "sanitizers" and consumer antiseptic wipes. Here, we refer to consumer antiseptic rubs or consumer rubs as those products that are intended to be used when soap and water are not available and are not intended to be rinsed off with water. An OTC drug is covered by the OTC Drug Review if its conditions of use existed in the OTC drug marketplace on or before May 11, 1972 (37 FR 9464). The only active ingredients used in OTC consumer antiseptic rub products that are eligible for consideration under the OTC Drug Review are ethyl alcohol (referred to subsequently as alcohol), isopropyl alcohol, and benzalkonium chloride. In response to requests submitted to the Agency following the publication of the proposed rule in the Federal Register (FR) of June 30, 2016 (81 FR 42912) (2016 Consumer Antiseptic Rub PR), FDA has deferred regulatory action on these active ingredients. Accordingly, FDA does not make a generally recognized as safe and effective determination regarding these three active ingredients in this final rule. The monograph or non-monograph status of these three active ingredients will be addressed, either after completion and analysis of studies to address the safety and effectiveness data gaps of these active ingredients or at a later date, if these studies are not completed.

This final rule establishes that all other consumer antiseptic rub active ingredients are not eligible for consideration under the OTC Drug Review for use in consumer antiseptic rub products. Drug products containing the 28 ineligible active ingredients identified in the 2016 Consumer Antiseptic Rub PR will require approval under a new drug application (NDA) or abbreviated new drug application (ANDA) prior to marketing. However, we expect that manufacturers of consumer antiseptic rub products with ineligible active ingredients will either reformulate and relabel their products to include the active ingredients which are eligible for consideration under the OTC Drug Review, discontinue production of their consumer antiseptic rub products, or reformulate their products as antiseptic-free topical cleansers or wipes. In Table 1, we provide a summary of the estimated costs of the final rule, which involve product reformulation and relabeling of consumer rub products that contain active ingredients that are ineligible for consideration under the OTC Drug Review for use in consumer rubs. Manufacturers of consumer antiseptic rub products that contain the deferred active ingredients may also incur additional costs associated with the necessary safety and effectiveness testing

required to demonstrate that the deferred active ingredient is generally recognized as safe/generally recognized as effective (GRAS/GRAE). However, these testing costs are not included in the regulatory impact analysis for this final rule because this rule does not require any testing. Although the testing costs are not attributable to this final rule, we estimate and present these costs separately in this analysis.

We estimate that the present value of the one-time costs associated with compliance with this final rule range from $1.07 million to $2.50 million with a primary estimate of $1.87 million. Annualizing upfront costs over a 10-year period at a discount rate of 3%, the costs of this final rule are estimated to be between $0.13 million and $0.29 million per year; the corresponding estimated cost at a discount rate of 7% is between $0.15 million and $0.36 million per year.

A potential benefit of this final rule is that the removal of potentially harmful antiseptic active ingredients in consumer antiseptic rub products may prevent health consequences associated with exposure to such active ingredients. FDA lacks the necessary information to estimate the impact of exposure to antiseptic active ingredients in consumer antiseptic rub products on human health outcomes. We are, however, able to estimate the reduction in the aggregate exposure to antiseptic active ingredients found in currently marketed consumer antiseptic rub products. The final rule will lead to an estimated reduction in aggregate exposure to benzethonium chloride that ranges from 110 pounds to 254 pounds per year. This final rule may also result in reduced exposure to other ineligible active ingredients in currently marketed consumer antiseptic rub products (see Table 3). However, FDA can only estimate the reduced exposure to benzethonium chloride at this time. Furthermore, we are unable to translate the aggregate exposure to benzethonium chloride into monetized benefits at this time because we lack information on the change in the short- and long-term health risks associated with a one-pound increase in exposure to each antiseptic active ingredient in consumer antiseptic rub products.

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

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Benefits						7%	10 years	

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
	Annualized Monetized $millions/year					3%	10 years	
	Annualized Quantified	182	110	254		7%	10 years	Values represent pounds of reduced annual exposure to ineligible active ingredients
		182	110	254		3%	10 years	Values represent pounds of reduced annual exposure to ineligible active ingredients
	Qualitative							
Costs	Annualized Monetized $millions/year	$0.27	$0.15	$0.36	2017	7%	10 years	
		$0.22	$0.13	$0.29	2017	3%	10 years	
	Annualized Quantified					7%		
						3%		
	Qualitative							
Transfers	Federal Annualized Monetized $millions/year					7%		
						3%		
	From/ To	From:			To:			
	Other Annualized Monetized $millions/year					7%	10 years	
						3%	10 years	
	From/To	From:			To:			

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Effects	State, Local or Tribal Government: none Small Business: Wages: Growth:							

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 costs this final rule would be considered a regulatory action under EO 13771.

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

Item	Primary Estimate (7%)	Lower Estimate (7%)	Upper Estimate (7%)	Primary Estimate (3%)	Lower Estimate (3%)	Upper Estimate (3%)
Present Value of Costs	$1.77	$1.02	$2.37	$1.77	$1.02	$2.37
Present Value of Cost Savings	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Present Value of Net Costs	$1.77	$1.02	$2.37	$1.77	$1.02	$2.37
Annualized Costs	$0.12	$0.07	$0.17	$0.05	$0.03	$0.07
Annualized Cost Savings	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Annualized Net Costs	$0.12	$0.07	$0.17	$0.05	$0.03	$0.07

C. Comments on the Preliminary Regulatory Impact Analysis and Our Responses

The FDA received comments pertaining to the Proposed Regulatory Impact Analysis which we summarize and address below.

Comment #1:

One commenter suggested that the FDA overestimated benefits and failed to account for some costs associated with the rule, including the costs of increased negative health outcomes related to a reduction in antiseptic use. The commenter included a reference to support the claim that reduced use of antiseptics could lead to increased negative health outcomes (Ref. 1).

Response #1:

FDA does not agree that the benefits are overestimated because neither the preliminary nor the final RIA monetized the health benefits of reduced exposure to active ingredients in consumer rub antiseptic products.

The study provided by the commenter estimated the impacts of reduced antiseptic use (exclusively) in a hospital setting on health care costs. The costs and benefits of use of health care antiseptic drug products used in a hospital setting do not generalize well to consumer use in the home. In the absence of empirical evidence on the impact of consumer rub products on health care costs, we are unable to estimate this potential cost. Furthermore, this final rule is estimated to affect less than 3 percent of the consumer antiseptic rub market.

Comment #2:

The commenter noted that we did not monetize benefits of the proposed rule, and suggested that if the active ingredients are safe, that no benefit is realized by avoiding exposure to them.

Response to Comment #2:

As we explained above, although FDA can estimate the reduced exposure to benzethonium chloride as a result of the rule, we are unable to translate the reduction in aggregate exposure into monetized benefits because we lack information on the change in the short- and long-term health risks associated with a reduction in exposure to benzethonium chloride in consumer antiseptic rub products.

D. Summary of Changes

The economic analysis has changed to reflect the changes between the proposed and final rule. Specifically, the final RIA only considers the impact of removing products containing ineligible active ingredients from the market. We do not consider the impact of removing OTC

consumer antiseptic drug products from the market that contain the three eligible active ingredients because no GRAS/GRAE determination for these three active ingredients is made in this final rule.

II. Final Regulatory Impact Analysis

A. Background

Antiseptics are marketed to consumers and various industries, such as research institutions, food handlers, textile manufacturers, and health care providers. This final rule, however, only covers consumer antiseptic rub products that are sometimes referred to as rubs, leave-on products or hand "sanitizers." Consumer antiseptic rubs are designed as a personal care product to be used if soap and water are unavailable. These products are marketed in various formulations, including liquids, foams, gels, sprays, as well as single-use towelettes and wipes. As opposed to antiseptic washes, antiseptic rubs are products that are not intended to be rinsed off after use. Antiseptic rubs contain active ingredients that are intended to reduce the number of bacteria on the skin.

The concern over the safety and effectiveness of antiseptic rubs has grown over time, with the increased use of such products in consumer settings. There are many more products containing antiseptic active ingredients in households today relative to the past. For example, a recent study found that while there were just a few dozen products in the mid-1990s containing antibacterial agents, the number today is over 700 (Ref. 2). Total hand sanitizer sales amounted to $173.5 million in 2012, and existing evidence indicates that the market is saturated with consumer antiseptic products containing alcohol as an active ingredient (Ref. 3).

Antiseptic rubs may be used on a daily basis by consumers. Given the growth in the presence and use of consumer antiseptic rubs, additional evidence is required to ensure that extended exposure to antiseptic active ingredients in these products does not cause damage to human health. Several important scientific developments that affect the evaluation of the safety and effectiveness of active ingredients used in consumer antiseptic rubs have occurred since FDA's 1994 evaluation of the safety and efficacy of antiseptic active ingredients under the OTC Drug Review. Improved analytical methods now exist that can detect and more accurately measure these active ingredients at lower levels in the bloodstream and tissue. Consequently, we now know that, at least for certain consumer antiseptic active ingredients, systemic exposure is

higher than previously thought, and new information about the potential risks from systemic absorption and long-term exposure has become available (Ref. 4-8). Currently, the significance of this new information is unknown. The benefits of any eligible active ingredient will need to be weighed against its risks once both the effectiveness and safety have been better characterized in order to determine GRAS/GRAE status.

B. Market Failure Requiring Federal Regulatory Action

This regulation addresses the market failure arising from inadequate information about the potential health risks associated with consumers' daily use of antiseptic rubs and the effectiveness of these products. This final rule is also a part of our ongoing evaluation of the safety and effectiveness of drug products containing these antiseptic active ingredients. Consumer antiseptic rub products that contain ineligible active ingredients cannot be lawfully marketed unless they obtain approval under an NDA or ANDA.

Firms that market consumer antiseptic rub products containing antiseptic active ingredients differentiate these products from other products that are intended for cleansing or moisturizing the skin by making antibacterial claims on their labels. The purpose behind the distinctive labeling as an antiseptic drug is to convey information about a health benefit resulting from the use of antiseptic rubs. In consumer settings, there currently is insufficient evidence to support the efficacy claim that consumer antiseptic rub products reduce bacteria on the skin, and there are unresolved safety considerations regarding long-term daily use of these products.

Despite the lack of evidence demonstrating safety and effectiveness, product demand and revenue growth of the hand sanitizer industry are strong (Ref. 9). Consumer demand for consumer rub antiseptic products may not adequately account for the lack of safety and efficacy evidence. Furthermore, information to which consumers have access may not reflect the current state of knowledge regarding the safety and effectiveness of consumer antiseptic rubs. Given the demand for antibacterial products, firms have an incentive to make antibacterial claims on their product labels (irrespective of actual effectiveness).

Consumers are not generally equipped with the necessary tools to evaluate the efficacy of a consumer antiseptic rub product directly, through their experience with the product, because the benefits conferred by such products are not visible to the human eye. Consumers are also not

equipped to evaluate the safety of consumer antiseptic rub products directly, particularly with respect to long-term health outcomes. Firms are in a better position to know about the health advantages, or lack thereof, from using consumer antiseptic rub products. This is a case of asymmetric information where producers potentially know more about their product's characteristics than do consumers. If the private marginal cost of obtaining safety and effectiveness information exceeds the private marginal benefit, however, there will be insufficient incentive for producers to obtain and act on this information in the absence of regulatory actions. Because it is time-consuming and resource-intensive to generate the evidence needed for consumers to make fully informed choices, private market incentives are insufficient to provide adequate assurances of product safety and effectiveness. Regulation is justified in a case such as this because there is a market failure resulting from inadequate information.

If consumers are boundedly rational, complex decision-making may exacerbate the market failure resulting from inadequate information regarding the safety and effectiveness of antiseptic rubs. Consumers are boundedly rational if their rationality is limited by the information they have, their cognitive capacity, or the time available when making purchase decisions. Constraints such as these may cause consumers to less than fully understand or be aware of adverse health effects associated with using consumer antiseptic rub products, which could result in suboptimal choices in the marketplace. For example, long periods of time may be required before potentially health-damaging effects of consumer antiseptic rub consumption are realized. To the extent that benefit-cost calculations associated with using antiseptic rub products are complicated, bounded rationality among consumers may result in overconsumption of these products relative to a benchmark in which consumers are fully informed and rational.

C. Purpose of the Rule

In this rule, FDA determines that certain active ingredients used in OTC consumer antiseptic rub products are not eligible for consideration under the OTC Drug Review for inclusion in the OTC consumer antiseptic rub monograph. Any OTC consumer antiseptic rub drug products containing an active ingredient found in the final rule to be ineligible for consideration under the OTC Drug Review for the OTC consumer antiseptic rub monograph

cannot be introduced or delivered for introduction into interstate commerce unless they are the subject of an approved NDA or ANDA.

The final rule explains that the Agency does not have sufficient evidence to demonstrate that certain active ingredients are eligible for evaluation under the OTC Drug Review for use in consumer antiseptic rub products. This final rule would require manufacturers of OTC consumer antiseptic rub drug products containing these ineligible active ingredients to obtain approval under an NDA or ANDA in order to lawfully market their products as consumer antiseptic rubs. Manufacturers producing consumer antiseptic rub products containing ineligible active ingredients could also reformulate their products to contain eligible active ingredients (i.e., one of the deferred active ingredients – alcohol, isopropyl alcohol, or benzalkonium chloride). Individuals who were using products containing ineligible antiseptic active ingredients would then be able to substitute those products with products containing one of the deferred active ingredients.

Manufacturers of consumer rubs containing ineligible antiseptic active ingredients could also choose to exit the market if the costs to comply with the rule exceed the benefits of continued production. Available market data provided by AC Nielsen (Ref. 10), as discussed below, indicate that a small fraction of consumer antiseptic rubs contain ineligible active ingredients.

D. Baseline Conditions

Data from AC Nielsen, which provides nationally representative product sales information, is used to estimate the baseline or the state of the world in the absence of the regulatory action. Baseline conditions are characterized by describing the marketplace in terms of sales and aggregate exposure to antiseptic active ingredients associated with the use of such products. The most recent data available are for the 52 weeks ending in September 5, 2009. The baseline analysis is restricted to products with positive sales over this period. FDA acknowledges that while this is the most recent data available, it is more than nine years old. Since the publication of the proposed rule, we have not received more recent data. While it would be ideal to observe trends in the consumer antiseptic rub market since 2009, the use of this data ensures that all changes in the market that occurred due to the publication of other antiseptic rules, including the proposed rule, in anticipation of this final rule, are captured as costs. However, we

acknowledge that there are numerous important factors that may have acted on the consumer antiseptic rub market outside of this rule between this time and when the final rule is published. While estimating how these confounding factors have affected the antiseptic market would be ideal, disentangling the effects of the rule with those outside of the rule is not feasible.

1. Active Ingredients in Currently Marketed OTC Consumer Antiseptic Rub Products

As a first step in characterizing the consumer rub product market, for each antiseptic active ingredient, we estimated the fraction of universal product codes (UPCs) and total equivalent (16 oz.) units currently on the market. In Table 3, we show the distribution of active ingredients in consumer antiseptic rub products by dosage form as represented in the AC Nielsen data. At this time, alcohol and benzalkonium chloride are the two most widely used active ingredients in consumer antiseptic rub products. Alcohol, in particular, accounts for a substantial share of active ingredients in currently marketed UPCs in both dosage form categories. For example, it accounts for 92 percent of rubs that are consumed as liquids, gels, or foams (hereafter referred to as "liquids"), and 100 percent of rubs that are consumed as single-use wipes or towelettes (hereafter referred to as "non-liquids"). Among liquid consumer rub products, other used antiseptic active ingredients include benzalkonium chloride, benzethonium chloride, polyhexamethylene biguanide and triclosan. Over this period, no consumer rub product contained isopropyl alcohol as an antiseptic active ingredient. Using total equivalent units sold, alcohol is the most commonly used antiseptic active ingredient in the consumer rub product market.

The AC Nielsen data indicate that 97 percent of consumer antiseptic rub products contain alcohol or benzalkonium chloride. The remaining 3 percent of products contain other antiseptic active ingredients that are ineligible for evaluation under the OTC Drug Review for use in consumer antiseptic rub products. These other antiseptic active ingredients include benzethonium chloride, polyhexamethylene biguanide, and triclosan. The remaining active ingredients affected by this final rule had no sales data, suggesting that manufacturers may have stopped marketing consumer antiseptic rubs with these active ingredients. A.C. Nielsen data indicate that manufacturers stopped selling consumer antiseptic rub products containing polyhexamethylene biguanide as their active antiseptic ingredient. An extensive internet search also indicates that

retailers and pharmacies continue to market consumer rubs containing benzethonium chloride, but that they stopped marketing consumer rubs containing triclosan.[1]

Table 3. Estimated Distribution of Active Ingredients in Consumer Rub Products for 52 Weeks Ending in September 5, 2009, by Dosage Form

Antiseptic Active Ingredient	Liquid, Gel, and Foam		Wipes and Towelettes	
	Percent of UPCs	Percent of Total Equivalent (16 oz.) Units Sold	Percent of UPCs	Percent of Total Equivalent (16 oz.) Units Sold
Benzalkonium Chloride	5.2	0.3	0.0	0.00
Alcohol	91.8	99.1	100.0	100.0
Isopropyl Alcohol	0.0	0.0	0.0	0.00
Total Deferred	**97.05**	**99.44**	**100.00**	**100.00**
Benzethonium Chloride	1.8	0.3	0.0	0.00
Polyhexamethylene Biguanide	0.5	0.0	0.0	0.00
Triclosan	0.7	0.3	0.0	0.00
Total Ineligible	**2.95**	**0.56**	**0.00**	**0.00**
Total (Deferred + Ineligible)	100.0	100.0	100.0	100.0

2. Number of Affected Products and Product Sales in the Current Market for OTC Consumer Antiseptic Rubs

In a recent internet search of consumer antiseptic rub products, we could not find any currently marketed products containing isopropyl alcohol, polyhexamethylene biguanide or

[1] Most recent search conducted November 2018 and included a variety of retail websites as well as direct searches for consumer hand rub products with specific active ingredients using multiple search engines.

triclosan as an antiseptic active ingredient.[2] Thus, the analysis below focuses on the other ingredients (alcohol, benzalkonium chloride, and benzethonium chloride). As a complement to the characterization of the consumer antiseptic rub product market using total equivalent unit sales, Table 4 shows the dollar sales of products by active ingredient and dosage form. The total number of UPCs and sales over the 52-week period ending in September 5, 2009 amounted to 460 and $121.72 million (in 2017 dollars), respectively. Nielsen data include product and sales information derived from purchases made in supermarkets, drug stores, and mass merchandisers (excluding Walmart). In July 2015, IBIS World estimated revenue in the hand sanitizer manufacturing industry to be $248 million (in 2017 dollars), of which 81% derived from purchases outside the health care setting (Ref. 9). To account for underrepresentation of product and sales information, we apply an adjustment factor of 1.65 (0.81*248/121.72) to UPC counts, formulas, annual unit sales, and annual dollar sales to obtain estimates representing the entire market of affected products. Table 4 provides our estimated product counts and dollar sales by active ingredient and dosage form. In the aggregate, we estimate that the consumer rub market includes a total of 760 products with sales of these products amounting to $197 million. Similar to the values seen in Table 3, consumer antiseptic rub products that contain alcohol account for the vast majority of sales.

Table 4. Number of Products and Dollar Sales (in millions) for 52 Weeks Ending in September 5, 2009, by Active Ingredient and Dosage Form

Antiseptic Active Ingredient	Liquid, Gel, and Foam		Wipes and Towelettes	
	Number of Products	Dollar Sales (in Millions)	Number of Products	Dollar Sales (in Millions)
Benzalkonium Chloride	38	$1.23	0	$0.00
Alcohol	668	$186.72	41	$7.55
Isopropyl Alcohol	0	$0.00	0	$0.00
Total Deferred	**706**	**188**	**41**	**8**
Benzethonium Chloride	13	$1.49	0	$0.00

[2] Most recent search conducted November 2018 and included a variety of retail websites as well as direct searches for consumer hand rub products with specific active ingredients using multiple search engines.

Total Ineligible	**13**	**1**	**0**	**0**
Total (Deferred + Ineligible)	719	$189.45	41	$7.55

3. Antiseptic Active Ingredient Usage in Consumer Antiseptic Rub Products

Because in this final rule certain active ingredients are found ineligible for evaluation under the OTC Drug Review for use in consumer antiseptic rubs, FDA does not make a determination of whether these ineligible active ingredients are generally recognized as safe and effective for use in OTC consumer antiseptic rub products. FDA lacks the necessary data to estimate the short- and long-term health risks associated with using consumer rub products containing ineligible antiseptic active ingredients. Without information on the change in health risks associated with a one-unit increase in exposure to each antiseptic active ingredient in consumer rub products, we are unable to translate the aggregate exposure figures into monetized benefits. As an intermediate measure of the baseline risk resulting from the use of consumer antiseptic rub products, we estimate the annual consumption of antiseptic active ingredients found in consumer topical antiseptic products and then use estimated concentration levels for each active ingredient to calculate annual exposure. We begin by standardizing sales units to estimate the consumption of consumer rub products by antiseptic active ingredient and dosage form. Table 5 shows that, in the 52 weeks leading up to September 5, 2009, about 30.1 million and 62.6 million equivalent units of liquid and non-liquid rub products were sold. Also, as before, consumer antiseptic rub products containing alcohol, one of the deferred active ingredients, account for most of unit sales.

Table 5. Total Equivalent Unit (16 oz.) Sales for 52 Weeks Ending in September 5, 2009, by Active Ingredient and Dosage Form

Antiseptic Active Ingredient	**Liquid, Gel, and Foam**	**Wipes and Towelettes**
Benzalkonium Chloride	96,454	0
Alcohol	29,791,212	62,356,553
Isopropyl Alcohol	0	0
Total Deferred	**29,887,666**	**62,356,553**
Benzethonium Chloride	81,013	0
Total Ineligible	**81,013**	**0**

Total (Deferred + Ineligible)	30,068,301	62,580,387

In Table 6, we express the estimated consumption of liquid (non-liquid) consumer antiseptic rub products in volume (weight). For example, we estimate that about 14.1 million liters (or 29.8 million 16 oz. units x 0.473 liters per 16 oz.) of liquid consumer antiseptic rub products containing alcohol are consumed per year.

Table 6. Estimated Annual Consumption of Consumer Antiseptic Rub Products, by Active Ingredient and Dosage Form

Antiseptic Active Ingredient	**Liquid (includingGel and Foam) (In Liters)**	**Wipes and Towelettes (In Pounds)**
Benzalkonium Chloride	45,640	0
Alcohol	14,096,487	62,356,553
Isopropyl Alcohol	0	0
Total Deferred	**14,142,126**	**62,356,553**
Benzethonium Chloride	38,334	0
Total Ineligible	**38,334**	**0**
Total (Deferred + Ineligible)	14,180,460	62,356,553

Next, we translate the annual consumption of consumer antiseptic rub products into annual usage of antiseptic active ingredients. The FDA National Drug Code Directory is used to obtain ranges of concentration levels of each antiseptic active ingredient. In some cases, we are unable to provide a range because we do not have sufficiently reliable information. Concentration level is expressed as weight per unit of volume (w/v) for liquids and weight per unit of weight (w/w) for non-liquids. We find a wide range for alcohol (between 14 percent and 72 percent), and much narrower ranges for the other antiseptic active ingredients.

Table 7. Estimated Concentration Level (in w/v or w/w), by Active Ingredient

Antiseptic Active Ingredient	**Low**	**Midpoint**	**High**
Benzalkonium Chloride	0.10%	0.13%	0.15%
Alcohol	14.0%	43.0%	72.0%
Isopropyl Alcohol	No Information to estimate		
Benzethonium Chloride	0.13%	0.22%	0.30%

Finally, we use the estimated concentration level ranges in Table 7 to estimate annual exposure to antiseptic active ingredients in consumer antiseptic rub products. The values for each antiseptic active ingredient are expressed in weight for ease of interpretation. In the aggregate, as shown in Table 8, we estimate that consumers are exposed to between 13.1 million and 67.3 million pounds of antiseptic active ingredients every year. Alcohol accounts for the vast majority of the exposure to antiseptic active ingredients through the use of consumer antiseptic rub products.

Table 8. Estimated Exposure to Consumer Antiseptic Active Ingredients (in Pounds per Year), by Active Ingredient

Antiseptic Active Ingredient	**Low**	**Midpoint**	**High**
Benzalkonium Chloride	101	126	151
Alcohol	13,080,753	40,176,598	67,272,443
Isopropyl Alcohol	No Information to estimate		
Total Deferred	**13,080,853**	**40,176,724**	**67,272,594**
Benzethonium Chloride	110	182	254
Total Ineligible	**110**	**182**	**254**
Total (Deferred + Ineligible)	13,080,963	40,176,905	67,272,847

E. Benefits of the Rule

This final rule establishes that certain active ingredients are not eligible for consideration under the OTC Drug Review for inclusion in the OTC consumer antiseptic rub monograph. Consumer antiseptic rubs containing these ineligible ingredients require approval under an NDA or ANDA prior to marketing. Because these consumer antiseptic rub active ingredients are ineligible for evaluation under the OTC Drug Review, we do not make a GRAS/GRAE determination for use of these ingredients in consumer antiseptic rub products. The benefits of this final rule include consumers' reduced exposure to potentially unsafe consumer antiseptic rub products, as well as avoiding the deadweight loss associated with consumption of ineffective products.

Data linking consumer exposure to these ineligible antiseptic active ingredients and the resulting short- and long-run health impacts are unavailable. Thus, we are unable to monetize the reductions in aggregate exposure to antiseptic active ingredients associated with the rule.

However, any health risks associated with the use of these products containing ineligible active ingredients are expected to decline along with the decreased exposure to antiseptic ingredients once these products are removed from the marketplace. Using the midpoint estimate of ineligible antiseptic active ingredient usage in consumer rubs as a proxy for exposure, we estimate that antiseptic active ingredient exposure to benzethonium chloride could be reduced by 182 pounds per year. Table 9 includes the ineligible active ingredients affected by the rule.

Table 9. Ineligible active ingredients to be removed from market

Active Ingredient	Products (by UPC count)	Reduced Exposure (pounds per year)		
		Low	Midpoint	High
Benzethonium Chloride	13	110	182	254
Polyhexamethylene Biguanide	3	No information to estimate		
Triclosan	5	No information to estimate		
Total	21	110	182	254

This final rule also remedies information asymmetry associated with the consumption of potentially ineffective products that the consumer does not have the ability to evaluate directly prior-to or following use. The efficacy of a consumer antiseptic rub product cannot be evaluated by the average consumer because the average consumer is not equipped to measure the bacteria on their hands prior-to and following the use of a consumer antiseptic rub. When consumers purchase ineffective products labelled as a consumer antiseptic rub, a deadweight loss is generated because individuals will purchase too much of the good at too high a price. The reduction in resources allocated to ineffective products labeled as consumer antiseptic rubs creates a social benefit. Although these benefits are not monetized here, it is expected that these benefits will increase as the consumption of potentially ineffective consumer rub products decreases.

F. Costs of the Rule

The final rule generates two primary costs associated with compliance: relabeling and product reformulation costs. If a manufacturer's product is affected by the rule, then a likely

response is that it will choose to reformulate the affected product to contain a deferred antiseptic active ingredient or reformulate the affected product as a non-antimicrobial consumer rub by removing the antiseptic active ingredient and relabeling the product to reflect the change in the product's ingredient list. Although the analysis below assumes that all manufacturers will reformulate their product to some extent, it is possible that some manufacturers will choose not to reformulate and instead choose to market the existing formulation as a cosmetic product, or exit the market entirely. If a manufacturer chooses to market their product as a cosmetic, they would still be required to relabel the product, removing any antimicrobial claims from the packaging.

1. Relabeling Costs

Relabeling costs are a function of the type of printing method, number of color changes, whether the products are nationally branded or private label, and the compliance period for implementing such label changes.

To estimate relabeling costs, we use a model developed by one of our contractors, Research Triangle International (RTI). The model includes the costs associated with labor inputs, material inputs, and discarded inventory. We consider that any label changes required by the final rule will be "major" (in the context of the labeling cost model), as they will likely involve multiple color changes that require redesigning of labels. In Table 10, we show estimates of the affected UPCs by brand and coordination type. Because some manufacturers will be able to coordinate regulatory label changes with routine voluntary label changes, compliance costs in such cases will be lower than uncoordinated changes. For a compliance period of 12 months, the RTI relabeling model assumes that 96% and 97% of branded and private-label products, cannot be coordinated with planned label changes, which explains the smaller estimated number of coordinated label changes.

Table 10. Number of UPCs, by Brand and Coordination Type

Brand Type	Uncoordinated	Coordinated	Total
Branded	11.9	0.5	12.4
Private	3.5	0.1	3.6
Total	15.4	0.6	16.0

In Table 11, we show estimates of the relabeling costs per UPC, by brand and coordination type. For uncoordinated changes, we estimate that the relabeling costs for nationally branded products will be between $8,490 and $25,237 per UPC; the corresponding range for private-label products is $12,145 and $31,329 per UPC. The difference in costs for branded and private-label products stems from the fact that private labelers incur higher costs associated with discarded inventories. For both branded and private-label products, the estimated relabeling costs range between $368 and $2,964 per coordinated UPC change.

Table 11. Estimated Labeling Change Costs per UPC, by Brand and Coordination Type

	Costs per Uncoordinated UPC		
Brand Type	**Low**	**Medium**	**High**
Branded	$8,490	$15,037	$25,237
Private	$12,145	$19,910	$31,329
	Costs per Coordinated UPC		
Brand Type	**Low**	**Medium**	**High**
Branded	$368	$1,283	$2,964
Private	$368	$1,283	$2,964

2. Reformulation Costs

A manufacturer's decision to reformulate will depend on the difference between the expected return to reformulating its product to meet the conditions set forth by the final rule and the expected return to not reformulating. The expected return to product reformulation, or the difference between the expected revenue and cost streams generated by reformulating a product, will be a function of consumer market demand. It is difficult to know how consumers will react to changes in market offerings or the composition of products in the market for consumer antiseptic rubs. We account for this uncertainty by presenting ranges for reformulation costs.

We assume that within a brand, products containing the same antiseptic ingredient and possessing the same concentration and dosage form share the same formulation. Of the affected UPCs, we estimate that there are 201 unique formulations. Previously published estimates of the reformulation cost of OTC cough-cold combination drug products (67 FR 78158) ranged from

$100,000 to $500,000. We inflate these values by approximately 132% to reflect the increase in the Producer Price Index for pharmaceutical preparation manufacturing between 2002 and 2017 to arrive at an estimated range of between $231,742 and $1,158,708. We use the lower end of this range as the estimated per-UPC cost to reformulate the average consumer antiseptic rub product will cost less to reformulate than the average OTC cough-cold combination drug product. The removal of the ineligible active ingredients to reformulate products will likely not result in a net increase in ingredient costs as likely substitute ingredients are in general not costlier. That is, the cost of substitute active ingredients would be no more than the cost of the ineligible active ingredient being removed. Furthermore, the higher levels of the reformulation estimates are for more complex products, such as OTC cough-cold products, where manufacturing may be difficult. For example, with a more complex product, a manufacturer may need to redo production processes, change suppliers, and conduct stability testing. The manufacture of a consumer antiseptic rub is not as complex and therefore costs to reformulate are likely at the lower end of the estimate.

3. Costs

The fraction of manufacturers that will choose to reformulate and relabel their products is unknown, and thus estimating the fraction of products that will be affected by the resulting regulation-induced changes is difficult. We show ranges to capture this uncertainty. The total estimated cost of labeling changes is obtained by summing the cost of uncoordinated changes (number of uncoordinated UPC changes) and the cost of coordinated changes (number of coordinated UPC changes multiplied by the per-UPC cost for coordinated UPC changes). Table 12 and Table 13 contain the range of estimated costs of labeling changes and reformulation, respectively. In this scenario, relabeling costs are estimated to range between $143,619 and $411,401; the corresponding range for reformulation costs is between $926,967 and $2,085,675.

Table 12. Estimated Costs of Labeling Changes (Assuming All Eligible Ingredients are Determined to be GRAS/E), by Brand Type

Brand Type	Low	Medium	High
Branded	$101,260	$179,653	$301,922
Private	$42,358	$69,513	$109,480
Total	$143,619	$249,166	$411,401

Table 13. Estimated Reformulation Costs (Assuming All Eligible Ingredients Are Determined to be GRAS/E)

Estimate	**Percent of Products Reformulated**		
	25	50	75
Estimated Cost of Reformulation per Product	$231,742	$231,742	$231,742
Estimated Number of Reformulations	4	7	9
Estimated Total Reformulation Costs	$926,967	$1,622,192	$2,085,675

4. Summary of Total Costs

A summary of the total one-time costs and annualized costs over a 10-year period is shown in Table 14. The total one-time costs of relabeling and reformulation range from $1.02 to $2.37 million.

The annualized cost over 10 years is estimated to range from $0.13 million and $0.29 million per year at a 3 percent discount rate and from $0.15 million and $0.36 million per year at a 7 percent discount rate. This value does not include testing costs, which we estimated to approximately equal an additional $16.42 million. However, these testing costs are not included in the primary analysis for this final rule because this rule does not require any testing.

Table 14. Estimated Total Costs (in millions)

Cost Category	**One-Time Costs**			**Annualized Costs Over 10-Year Period**					
				3% Discount Rate			7% Discount Rate		
	Low	Med.	High	Low	Med.	High	Low	Med.	High
Relabeling Costs	$0.14	$0.25	$0.41	$0.02	$0.03	$0.05	$0.02	$0.04	$0.06
Reformulation Costs	$0.93	$1.62	$2.09	$0.11	$0.19	$0.24	$0.13	$0.23	$0.30
Total Costs	$1.07	$1.87	$2.50	$0.13	$0.22	$0.29	$0.15	$0.27	$0.36

G. Testing Costs

To demonstrate that an eligible antiseptic active ingredient is GRAS/GRAE, manufacturers of the three deferred active ingredients would incur additional costs associated with safety and effectiveness testing. We do not know how many manufacturers will ultimately conduct these tests and whether any of these tests would be conducted to support an NDA. However, we do not attribute these testing costs to this final rule because the deferred active ingredients are outside the scope of this final rule. If a final rule is issued addressing any of these deferred active ingredients, a regulatory impact analysis describing the costs and benefits associated with any testing, formulation, or labeling requirements would accompany that rule. If any costs were incurred in anticipation of such final rule, they would also be included in the analysis. We only estimate testing costs for alcohol and benzalkonium chloride because these are the only two of the three eligible ingredients that are currently marketed.

The safety and effectiveness data required for a GRAS/GRAE determination are similar to those required for an approved NDA. In FY 2018, if manufacturers decide to submit an NDA, they would be required to pay approximately $2.42 million in user fee costs for each application requiring clinical data. Manufacturers of an approved NDA would, however, benefit from a period of marketing exclusivity, which increases the potential for recovery of NDA-related costs. In addition to the cost to manufacturers of preparing and submitting an NDA, the submission of an NDA would also generate incremental review costs to FDA. The most recent available data on standard costs associated with review of human drug applications (including rent, overhead, and centrally funded costs) published by FDA indicate that in FY 2016 the average cost to FDA for reviewing an NDA with clinical data for a non-new molecular entity is approximately $1.82 million (Ref. 11).

1. Efficacy Testing

To demonstrate effectiveness for the deferred active ingredients under the rule, a manufacturer must conduct an in vivo test twice and three types of in vitro tests (i.e. minimum inhibitory concentration tests, time-kill tests, and antimicrobial spectrum tests). These studies must also meet stricter standards than those under the 1994 TFM. The FDA lacks precise data on the cost of clinical simulation studies. However, we can approximate the cost of these studies using the estimated cost of efficacy studies conducted for new drug development. Estimates of

efficacy studies range from $2.1 million to $16 million per clinical trial (Ref. 12). The costs will be at the low end of this estimate given the likely limited clinical trial size for efficacy studies; moreover, we did not receive any public comment or data on this conclusion. Therefore, we use a value of $2.1 million for the cost of efficacy testing.

2. Safety Testing

To demonstrate safety for the deferred active ingredients under the rule, manufacturers must provide adequate data on the following nonclinical studies: absorption, distribution, metabolism, and excretion (ADME) in animals, human pharmacokinetic (maximal usage trials (MUsT)), oral and dermal carcinogenicity in animals, hormonal effects, developmental and reproductive toxicity (DART) in animals, and resistance potential. As laid out in the proposed rule and deferral letters, because some data already exist, not all studies will be required for each active ingredient. Each study requires several tests, which are discussed in a previous regulatory impact analysis (Safety and Effectiveness of Consumer Antiseptics; Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Proposed Amendment of the Tentative Final Monograph; Reopening of Administrative Record, 78 FR 76443-76478 (Dec. 27, 2013)) for the consumer washes antiseptic rule. That analysis also calculates the average costs associated with each safety study. These results are summarized and reported in Table 15.

Table 15. Estimated Cost Per Study Associated With Nonclinical Safety Data Requirements (2017 dollars)

Safety Study	Human Pharmacokinetic (MUsT)	Animal Pharmacokinetic (ADME)	Oral Carcinogenicity	Dermal Carcinogenicity	Developmental and Reproductive Toxicity	Potential Hormonal Effects	Bacterial Resistance	Sum Total Costs (Millions, $2017 dollars)
Total Costs (in millions, 2017 dollars)	$2.80	$0.60	$3.22	$3.22	$0.23	$1.24	No Data	$11.32

The proposed impact analysis that accompanied the consumer antiseptic washes proposed rule (78 FR 76443-76478) did not include estimates of the costs associated with carrying out resistance studies. We conducted a literature review to check whether other researchers estimated this particular cost. However, we were unable to identify any papers studying this topic. Hence, our cost estimates may understate the actual safety testing costs.

Some manufacturers have already submitted adequate data for certain tests. The results indicate that the following antiseptic active ingredients have adequate data for:

- Benzalkonium chloride: oral carcinogenicity, DART, and potential hormonal effects;
- Alcohol: ADME, oral and dermal carcinogenicity, DART, potential hormonal effects, and bacterial resistance;

Given the above values, we estimate the total one-time costs to conduct the various safety tests associated with each antiseptic active ingredient that is currently marketed as follows:

- Benzalkonium chloride: $6.62 million (=$2.80 million per human pharmacokinetic study + $0.60 million per animal pharmacokinetic study + $3.22 million per dermal carcinogenicity study). Benzalkonium chloride would also require resistance studies. However, no data are available to estimate this cost, and thus these total safety testing costs do not include the expenditures associated with conducting resistance studies.
- Alcohol: alcohol only requires one human pharmacokinetic study. We estimate these costs to approximately equal $2.80 million.

To summarize, total efficacy and safety testing costs for both benzalkonium chloride and alcohol (not including potential bacterial resistance testing) are expected to equal $16.42 million (= $4.2 million to evaluate efficacy and $12.22 million to evaluate safety). We emphasize that we attribute these costs to a subsequent rule in which a GRAS/GRAE determination is made for these deferred ingredients.

H. Analysis of Regulatory Alternatives to the Rule

We have estimated the costs of the final rule by assuming a 12-month compliance period. We now examine how the costs of the final rule would change if the compliance period were shortened or lengthened by 6 months. These otherwise identical rules would have different relabeling costs because a shorter (or longer) compliance period would allow for fewer (or more) coordinated labeling changes. While the RTI Relabeling Cost Model assumes that 3-4% of changes can be coordinated with planned changes if the compliance period is 12 months, the assumed percentage falls to 0% if the compliance period is 6 months and increases to 9-12% if it is 18 months. In Table 16, we show the estimated costs for each of these regulatory alternatives.

Reducing (or increasing) the compliance period would cause total costs to increase (or decrease). For example, requiring a 6-month compliance period would increase one-time total costs by approximately $60,000 and $380,000 relative to the costs of a 12-month compliance period; if, instead, an 18-month compliance period were required, one-time total costs would decrease by between $50,000 and $140,000.

Table 16. Estimated Total Costs of Regulatory Alternatives (in millions), by Scenario

Cost Category	**One-Time Costs**			**Annualized Costs Over a 10-Year Period**					
				3% Discount Rate			7% Discount Rate		
	Low	Med.	High	Low	Med.	High	Low	Med.	High
Alternative 1: 6 Month Compliance									
Relabeling Costs (6 Months)	$0.20	$0.39	$0.80	$0.02	$0.05	$0.09	$0.03	$0.06	$0.11
Reformulation Costs	$0.93	$1.62	$2.09	$0.11	$0.19	$0.24	$0.13	$0.23	$0.30
Total Costs	$1.13	$2.02	$2.88	$0.13	$0.24	$0.34	$0.16	$0.29	$0.41
Change from 12 Months	$0.06	$0.14	$0.38	$0.01	$0.02	$0.05	$0.01	$0.02	$0.05
Alternative 2: 18 Month Compliance									
Relabeling Costs (18 Months)	$0.09	$0.16	$0.27	$0.01	$0.02	$0.03	$0.01	$0.02	$0.04
Reformulation Costs	$0.93	$1.62	$2.09	$0.11	$0.19	$0.24	$0.13	$0.23	$0.30
Total Costs	$1.02	$1.79	$2.36	$0.12	$0.21	$0.28	$0.15	$0.25	$0.34
Change from 12 Months	-$0.05	-$0.08	-$0.14	-$0.01	-$0.01	-$0.02	-$0.01	-$0.01	-$0.02

I. Cost-Effectiveness

We assess the cost-effectiveness of the final rule and regulatory alternatives by examining the annualized costs over a 10-year period per pound of reduced exposure to potentially harmful ineligible active ingredients at 3 percent and 7 percent discount rates. Table 17 displays the reduced exposure to active ingredients by compliance period.

It is important to note that the cost-effectiveness of the final rule and regulatory alternatives ultimately depends on the currently unknown underlying health risks associated with exposure to ineligible active ingredients. For example, suppose tests indicate that exposure to ingredient X in consumer antiseptic rub products is hazardous to health. In such a case, this final rule would lead to decreased exposure to ingredient X through the use of consumer antiseptic

rubs and the corresponding health benefits would be realized. While the dollars per pound of reduced exposure figures vary substantially by scenario, the cost-effectiveness of the rule and regulatory alternatives are a function of the safety and effectiveness of the ineligible active ingredients.

Table 17. Cost-Effectiveness, by Compliance Period (in Dollars per Pound of Reduced Exposure)

Compliance Period	3% Discount Rate			7% Discount Rate		
	Low	Medium	High	Low	Medium	Hight
6 Months	$726	$1,298	$1,856	$882	$1,577	$2,254
12 Months	$690	$1,205	$1,608	$838	$1,464	$1,953
18 Months	$658	$1,151	$1,520	$799	$1,398	$1,846

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. Although this rule only affects 3 percent of the consumer antiseptic rub market, we believe that the affected firms include many small entities. Thus, we find that the final rule will have a significant economic impact on a substantial number of small entities. This analysis, as well as other sections in this document, serves as the Final Regulatory Flexibility Analysis, as required under the Regulatory Flexibility Act.

A. Description and Number of Affected Small Entities

The final rule would affect firms in the toilet preparation manufacturing industry (NAICS code 325620). According to the 2007 Economic Census of Manufacturers, there are 854 manufacturers in this industry. The Economic Census does not provide entity counts for relabelers, repackers, and distributors. However, manufacturers of consumer antiseptic rub products are expected to incur the vast majority of product reformulation and relabeling costs. Table 18 shows the number of establishments and the average value of their shipments by total number of employees. According to the Small Business Administration, a business entity is

considered small if it employs 500 or fewer individuals. Based on this size standard, about 97 percent of toilet preparation manufacturers are small entities, and the average value of their shipments range from $1,488,815 to $217,831,979. For small entities, the average value of shipments is $24,823,395 per small entity.

Table 18. Toilet Preparation Manufacturers by Total Number of Employees

Total Number of Employees	Number of Establishments	Average Value of Shipments (in millions)
0 to 4	315	$1.49
5 to 9	122	$6.50
10 to 19	90	$9.54
20 to 49	115	$10.75
50 to 99	82	$32.87
100 to 249	63	$88.43
250 to 499	41	$217.83
500 to 999	22	$952.40
1,000 to 2,499	4	$1,890.28
2,500 or more	0	—

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

Using the FDA Drug Product Registration Database, we estimate that about 69 percent of consumer antiseptic rub products are manufactured by small entities. We assume that the costs associated with the final rule that are incurred by small entities are proportional to the size of the small-entity product market. Table 19 shows the estimated total costs for small businesses by scenario. One-time total costs for small businesses are estimated to range from $0.74 million and $1.72 million. This amounts to between $892 and $2,081 per small entity, which is 0.004-0.008 percent of the average value of shipments for a small business.

Table 19. Estimated Total Costs for Small Businesses (in millions)

Cost Category	One-Time Costs			Annualized Costs Over a 10-Year Period					
				3% Discount Rate			7% Discount Rate		
	Low	Med.	High	Low	Med.	High	Low	Med.	High
Relabeling Costs	$0.10	$0.17	$0.28	$0.01	$0.02	$0.03	$0.01	$0.02	$0.04
Reformulation Costs	$0.64	$1.12	$1.44	$0.07	$0.13	$0.17	$0.09	$0.16	$0.20
Total Costs	$0.74	$1.29	$1.72	$0.09	$0.15	$0.20	$0.11	$0.18	$0.25

C. Alternatives to Minimize the Burden on Small Entities

1. Exemption for Small Businesses

If small businesses receive an exemption from the final rule, then 97 percent of the consumer antiseptic rub product industry will receive regulatory relief. The burden on the industry would fall by between $865 and $2,018 per small business. Since small businesses make up a substantial share of the consumer antiseptic rub product market, this alternative was not chosen because an exemption for small business would forgo most of the potential benefits generated by the final rule.

2. Longer Compliance Period for Small Businesses

Extending the compliance period for small businesses is another alternative for regulatory relief. We examined the change in costs associated with lengthening the compliance period for small businesses to 18 months. It is important to note that approximately 69 percent of consumer antiseptic rub products are manufactured by small businesses, so extending the compliance period for small businesses would leave over two-thirds of the products affected by the rule unchanged for 6 additional months after the effective date. This alternative was not chosen because extending the effective date for products containing antiseptic active ingredients not found to be eligible would lead to continued exposure and delay the potential benefits of this rule.

As shown in Table 20, this would lead to a reduction in the costs borne by small businesses relative to the compliance period of 12 months currently specified in the final rule. The estimated one-time cost per small business ranges between $851 and $1,966.

Table 20. Estimated Total Costs for Small Businesses Under 18-Month Compliance Period (in millions)

Cost Category	One-Time Costs			Annualized Costs Over 10-Year Period					
				3 % Discount Rate			7% Discount Rate		
	Low	Med.	High	Low	Med.	High	Low	Med.	High
Relabeling Costs (18 Months)	$0.07	$0.11	$0.19	$0.01	$0.01	$0.02	$0.01	$0.02	$0.03
Reformulation Costs	$0.64	$1.12	$1.44	$0.07	$0.13	$0.17	$0.09	$0.16	$0.20
Total Costs	$0.70	$1.23	$1.63	$0.08	$0.14	$0.19	$0.10	$0.18	$0.23

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