DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Substances Generally Recognized as Safe

Docket No. FDA-_____

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

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

Table of Contents

Executive Summary

This proposed rule, if finalized, would revise the procedures by which a person introducing a human or animal food substance into interstate commerce notifies FDA of a conclusion that the use of such substance is generally recognized as safe (GRAS) under the conditions of its intended use in accordance with section 201(s) of the Federal Food, Drug, & Cosmetic Act (FD&C Act. Specifically, the proposed rule would require the submission of GRAS notices to FDA unless an exemption applies. Under the GRAS provision of the FD&C Act, a substance that is GRAS under its conditions of intended use does not require pre-market review as a food additive by FDA. Under our current regulations, a person who concludes that the use of a substance is GRAS under the conditions of its intended use is not required to notify FDA of this conclusion, and GRAS notices are voluntary. If the proposed rule is finalized, such uses of substances in food will be presumed not to be GRAS if the notification requirements are not met.

We identify qualitative benefits in the form of increased information to FDA and consumers regarding human and animal foods. We quantify costs to the manufacturers of substances previously introduced into interstate commerce without notice to FDA and future GRAS submissions for new substances and uses, as well as to FDA reviewers. We estimate that the annualized costs of the proposed rule are approximately $6.8 million, with a lower bound of $1.9 million and an upper bound of $18.0 million, discounted at 3 percent over 10 years in 2024 dollars. At a 7 percent discount rate, annualized costs are approximately $7.5 million, with a lower bound of $2.1 million and an upper bound of $20.3 million.

I. **Introduction and Summary**

A. Introduction

We have examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, Executive Order 14192, 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 benefits and costs of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits. Rules are "economically significant" under Executive Order 12866 if they "have an annual effect on the economy of $100 million or more; or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities." The Office of Information and Regulatory Affairs (OIRA) has determined that this proposed rule [is or is not] a significant regulatory action under Executive Order 12866.

Executive Order 14192 requires that any new incremental 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 ten prior regulations." This proposed rule, if finalized as proposed, is expected to be an Executive Order 14192 regulatory action.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because we estimate that the economic impact of this proposed rule is more than 3 percent of annual revenue, we find that the proposed rule will have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (Section 202(a)) requires us to prepare a written statement, which includes estimates of anticipated impacts, 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 $187 million, using the most current (2024) Implicit Price Deflator for the Gross Domestic Product. This proposed rule would not result in an expenditure in any year that meets or exceeds this amount.

B. Overview of Benefits, Costs, and Transfers

This proposed rule would revise the procedures by which a person introducing a human or animal food substance into interstate commerce notifies FDA of a conclusion that the use of such substance is GRAS under the conditions of its intended use. Specifically, the proposed rule would require the submission of GRAS notices to FDA. Under the GRAS provision of the FD&C Act, a substance that is GRAS under the conditions of its intended use does not require pre-market review as a food additive by FDA. Under FDA's current regulations, a person who concludes that the use of a substance is GRAS under the conditions of its intended use is not required to notify FDA of this conclusion, and GRAS notices are voluntary. If the proposed rule is finalized, such uses of substances in food will be presumed not to be GRAS if the notification requirements are not met.

The primary benefits of the proposed rule, if finalized, come from increased information to FDA and consumers regarding substances used in human and animal foods. One-time costs of the proposed rule to persons who introduce a substance into interstate commerce under the GRAS provision of the FD&C Act include reading the rule and revising standard operating

procedures regarding GRAS notices. Other one-time costs of the proposed rule are preparing and submitting certain information for substances that were already used in food before the effective date of a final rule, for companies that choose to submit this information during the limited-time option for such submissions instead of a GRAS notice. Costs associated with these activities may include translation costs for manufacturers in non-English speaking countries. Recurring costs to affected manufacturers include preparing and submitting GRAS notices for new substances or new uses of substances introduced into interstate commerce under the GRAS provision of the FD&C Act after the effective date of a final rule. Costs to FDA include one-time costs of reviewing submissions related to substances introduced into interstate commerce before the effective date of a final rule and annual costs of reviewing GRAS notices.

We estimate that the present value of the costs of the proposed rule are approximately $57.9 million, with a lower bound of $16.6 million and an upper bound of $153.2 million, discounted at 3 percent at 10 years in 2024 dollars. At a 7 percent discount rate, the present value of costs is approximately $52.8 million, with a lower bound of $14.7 million and an upper bound of $142.6 million. We estimate that the annualized costs of the proposed rule are approximately $6.8 million, with a lower bound of $1.9 million and an upper bound of $18.0 million, discounted at 3 percent over 10 years. At a 7 percent discount rate, annualized costs are approximately $7.5 million, with a lower bound of $2.1 million and an upper bound of $20.3 million. The estimated benefits and costs of the proposed rule are summarized in Table 1.

Table 1. Summary of Benefits, Costs, and Distributional Effects of the Proposed Rule (millions of 2024 dollars)

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Benefits	Annualized Monetized					7%		
						3%		

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
	($millions/year)							
	Annualized Quantified					7%		
						3%		
	Qualitative	Increased information regarding substances used in human and animal foods						
Costs	Annualized Monetized ($millions/year)	$7.5	$2.1	$20.3	2024	7%	10 years	
		$6.8	$1.9	$18.0	2024	3%	10 years	
	Annualized Quantified					7%		
						3%		
	Qualitative							
Transfers	Federal Annualized Monetized ($millions/year)					7%		
						3%		
		From:			To:			
	Other Annualized Monetized ($millions/year)					7%		
						3%		
		From:			To:			
Effects	State, Local or Tribal Government: None Small Business: Costs of approximately $3,700 to $39,000 per affected small entity Wages: None Growth: None							

Note: Benefits encompass positive and negative benefits. Costs encompass costs and cost savings.

In line with Executive Order 14192, we estimate present and annualized values of costs, cost savings, and net costs over an infinite time horizon in Table 2. The net present value of the costs of the proposed rule are approximately $60.2 million, with a lower bound of $23.0 million and an upper bound of $143.1 million, discounted at 7 percent over an infinite time horizon in 2024 dollars. The annualized costs of the proposed rule are approximately $4.2 million, with a lower bound of $1.6 million with an upper bound of $10.0 million.

Table 2. EO 14192 Summary Table (millions of 2024 dollars, discounted over an infinite time horizon at a 7 percent discount rate)

	Primary Estimate	Low Estimate	High Estimate
Present Value of Costs	$60.2	$23.0	$143.1
Present Value of Cost Savings	$0	$0	$0
Present Value of Net Costs	$60.2	$23.0	$143.1
Annualized Costs	$4.2	$1.6	$10.0
Annualized Cost Savings	$0	$0	$0
Annualized Net Costs	$4.2	$1.6	$10.0

II. **Preliminary Economic Analysis of Impacts**

A. Background

In 1958, Congress enacted the Food Additives Amendment (the 1958 amendment) to the FD&C Act. Under the 1958 amendment, any substance intentionally added to or used in connection with food is a food additive and is subject to pre-market approval by FDA unless the use of the substance is GRAS under the conditions of its intended use (or otherwise excepted from the definition of food additive - e.g., color additives).

Since the 1958 amendment, we have revised our regulations several times to adapt our approach to the GRAS provision of the FD&C Act to the nation's changing food supply. Currently, FDA maintains a voluntary GRAS notification program to help ensure that these ingredients are safe for the ways in which they will be used and to help industry meet its responsibility for ensuring the GRAS status of ingredients they intend to use in human and animal food. Under the voluntary GRAS notification program, any person may (but is not required to) notify FDA of a view that a substance is not subject to the pre-market approval requirements of section 409 of the FD&C Act based on that person’s conclusion that the substance is GRAS under the conditions of its intended use.

When FDA evaluates a GRAS notice, we consider whether the notice demonstrates that the ingredient is safe under the conditions of its intended use and whether the criteria for general recognition of safety are satisfied. For the use of an ingredient to be considered GRAS, all data

necessary to establish safety must be publicly available and its safe use must be generally recognized by qualified experts. In addition, GRAS uses must meet the same safety standard as for food additives, a reasonable certainty of no harm under the conditions of its intended use and have the same quantity and quality of information that would support the safety of a food additive.

B. Need for Federal Regulatory Action

The voluntary nature of the existing GRAS notification program creates the potential for informational asymmetries which may lead to institutional and market failures.[1] Consumers rely on food producers to provide them with accurate information about the substances in their food. Although consumers may not be familiar with all the substances in their food, they often assume that the substances are safe based on information from food producers. When foods are marketed with substances that are purported to be GRAS, but are not GRAS, it creates an informational asymmetry as the consumer's assumption about the safety of the food may be incorrect. When consumers unknowingly purchase foods which contain substances that are not GRAS, this leads to market failure. The establishment of a mandatory GRAS notification program would help to correct this market failure.

The potential for institutional failures results from the FDA not having a complete picture of all the substances in food introduced into interstate commerce: another form of informational asymmetry. Under the voluntary GRAS notification program, firms can introduce substances into interstate commerce based on an independent conclusion of GRAS status without notifying FDA. FDA may have little or no knowledge about such conclusions and may only become aware

[1] Informational asymmetries occur when there is an imbalance of information between parties in a transaction. This imbalance can lead to inefficient market outcomes, particularly when a less-informed party must make decisions based on incomplete or uncertain information.

of an independent conclusion of GRAS status after a public health concern emerges. There have been adverse events which have resulted in FDA making post-market determinations that the use of a substance is not GRAS under the conditions of its intended use (Ref. 1). Under a mandatory GRAS notification program, FDA may have been able to mitigate the occurrence of these adverse events. The establishment of a mandatory GRAS notification program would help to correct this institutional failure and help us to carry out Congress's mandate in the FD&C Act: prohibit the use of unsafe additives in food.

C. Purpose of the Proposed Rule

The proposed rule, if finalized, would amend our GRAS regulations in parts 170 and 570 to replace the voluntary GRAS notification program with a mandatory GRAS notification program.

D. Baseline Conditions

1. GRAS Notices

Since 1998, there have been 1,309 GRAS notices submitted to FDA. FDA's Center for Food Safety and Applied Nutrition (currently FDA's Human Foods Program) filed its first GRAS notice in 1998 under the interim pilot program, and as of March 2025, HFP has filed 1,234 GRAS notices for human food substances (Ref. 2). FDA's Center for Veterinary Medicine established its interim pilot program and filed its first GRAS notice more recently (both in 2010) and, since then, has filed 75 GRAS notices for animal food substances (Ref. 3). The distribution of GRAS notices by type (animal or human food) is presented in Table 3.

Table 3. GRAS Notices Submitted for Human and Animal Food Substances

	GRAS Notice Submissions	Notifiers
Animal Food Substances	75 (5.73%)	36 (5.35%)
Human Food Substances	1,234 (94.27%)	637 (94.65%)

Total Substances	1,309	673

FDA's response to a GRAS notice may be a (1) "no questions" letter (FDA has no questions at this time regarding the notifier's conclusion that the notified substance is GRAS under the conditions of its intended use); (2) "insufficient basis" letter (FDA concludes that the notice does not provide a sufficient basis for the conclusion that the notified substance is GRAS under the conditions of its intended use); or (3) "cease to evaluate" letter (a letter from FDA granting a request from a notifier that FDA cease to evaluate their GRAS notice). FDA also reports the number of GRAS notices that are pending evaluation. The distribution of outcomes for submitted GRAS notices ("no questions" letter, pending, "cease to evaluate" letter, or "insufficient basis" letter) is presented in Table 4. As of March 2025, 94 of the submitted notices are pending. Of the 1,215 notices submitted that are not pending, 961 notices received a "no questions" letter. For 231 of the submitted GRAS notices, FDA has granted requests from notifiers that we cease to evaluate their GRAS notice. For 23 of the submitted GRAS notices, FDA has determined that the notice does not provide a sufficient basis for a conclusion that the notified substance is GRAS under the conditions of its intended use.

Table 4. Distribution of Outcomes for Submitted GRAS Notices

	Animal Food	Human Food	Total
GRAS Notices Submitted	75	1,234	1,309
"No Questions" Letter Issued[1]	37 (49.33%)	924 (74.88%)	961 (73.41%)
Pending[2]	4 (5.33%)	90 (7.29%)	94 (7.18%)
Cease to Evaluate Letter Issued[3]	28 (37.33%)	203 (16.45%)	231 (17.65%)
Insufficient Basis Letter Issued[4]	6 (8%)	17 (1.38%)	23 (1.76%)

Notes: [1] FDA has no questions at this time regarding the notifier's conclusion that the notified substance is GRAS under the conditions of its intended use; [2] Currently under FDA evaluation;
[3] FDA has granted a request from a notifier that we cease to evaluate their GRAS notice; [4] FDA concludes that the notice does not provide a sufficient basis for the conclusion that the notified substance is GRAS under the conditions of its intended use.

Overall, 617 GRAS notices (47.1 percent) have been submitted by foreign firms. 503 GRAS notices (38.4 percent) have been submitted by foreign firms located in countries where English is not the primary language. The distribution of GRAS notices submitted by foreign firms and foreign firms located in countries where English is not the primary language is presented in Table 5.

Table 5. Distribution of GRAS Notices Submitted by Firms Located in Foreign and Non-English-Speaking Countries

	Animal Food	Human Food	Total
Domestic Notifier	49	643	692 (52.9%)
Foreign Notifier	26	591	617 (47.1%)
English speaking	55	751	806 (61.6%)
Non-English speaking	20	483	503 (38.4%)

2. Independent Conclusions of GRAS Status

Although the current number of substances purported to be GRAS in human and animal foods is unknown, a 2011 study estimated that at that time there were 1,000 substances in human food purported to be GRAS based on an independent conclusion of GRAS status (Ref. 4). For this analysis, we take the 2011 study as a lower bound and assume that there are between 1,000 and 3,000 human and animal food substances purported to be GRAS based on an independent conclusion of GRAS status. We take the midpoint of that range as our primary estimate. We assume the same distribution for substances on the market purported to be GRAS based on an independent conclusion of GRAS status as for GRAS notices submitted for human and animal food substances (see Table 3).[2] We request comment on whether the assumed number of substances introduced into interstate commerce based on an independent conclusion of GRAS status currently is accurate. We assume that the characteristics of substances purported to be

[2] There may be fewer independent conclusions of GRAS status for substances used in animal food, as some state feed regulatory agencies do not recognize independent conclusions of GRAS status.

GRAS based on an independent conclusion of GRAS status are similar to the substances in the GRAS notice inventories, including both the GRAS Notice Inventory and the Animal Food GRAS Notice Inventory. Likewise, we assume the characteristics of firms manufacturing substances purported to be GRAS based on an independent conclusion of GRAS status are similar to the firms which have submitted GRAS notices to FDA. These distributions are summarized in Table 6. We request comment on these assumptions.

Table 6. Assumed Distribution of Substances Purported to be GRAS Based on an Independent Conclusion of GRAS Status Currently Introduced into Interstate Commerce

	Primary	Low	High
	2,000	1,000	3,000
Food Type			
Animal	114.6	57.3	171.9
Human	1,885.4	942.7	2,828.1
Firm Location			
Domestic	1,057.3	528.6	1,585.9
Foreign	942.7	471.4	1,414.1
Language			
English	1,231.5	615.7	1,847.2
Non-English	768.5	384.3	1,152.8

3. Affected Entities

Entities affected by the proposed rule include firms that currently submit voluntary GRAS notices to FDA as well as firms who make independent conclusions of GRAS status. As we do not know how many firms are currently making independent conclusions of GRAS status, we estimate this by assuming that the number of firms that are making such conclusions is proportionate to the percentage of substances that are GRAS based on an independent conclusion of GRAS status. We estimate that there are approximately 1,028 firms with independent conclusions of GRAS status, with a lower bound of 514 firms and an upper bound of 1,542

firms.[3] In addition to firms producing substances purported to be GRAS based on an independent conclusion of GRAS status, there are food manufacturers that are using these substances in food products currently introduced into interstate commerce. We estimate the number of food manufacturers affected by this proposed rule using U.S. Census Bureau Economic Survey data (Ref. 5).[4] The total number of affected firms includes the number of firms that have submitted GRAS notices to FDA, the estimated number of firms which have made independent conclusions that a substance is GRAS under the conditions of its intended use, and the number of total firms in the U.S. in NAICS 311 organized as a C corps. These numbers are summarized in Table 7. We request comment on the methods, assumptions, and data sources utilized to estimate the affected entities.

Table 7. Number of Affected Entities

	Primary	Low	High
Unique Firms in GRAS Notice Database	673	673	673
GRAS Notice Submissions	1,309	1,309	1,309
Estimated Independent Conclusions of GRAS Status	2,000	1,000	3,000
Estimated Unique Firms with Independent Conclusions of GRAS Status	1,028	514	1,542
Estimated Total Affected GRAS Substance Producers	1,701.3	1,187	2,215
Estimated Affected Food Manufacturers	10,665.4	7,110	14,221
Total Estimated Affected Firms	**12,366.7**	**8,297**	**16,436**

[3] We estimate the number of firms manufacturing substances based on an independent conclusion of GRAS status which have not submitted a GRAS notice to FDA by assuming that the distribution of all firms (firms that submit GRAS notices plus firms that do not submit) is proportional to the distribution of all GRAS notices. For the primary estimate, we assume that there are 2,000 substances already introduced into interstate commerce based on an independent conclusion of GRAS status that have not been submitted to FDA's voluntary GRAS notification program. As discussed in section II.D.1 of this document, there have been 1,309 GRAS notices. Under the assumption that 2,000 substances have already been introduced into interstate commerce based on an independent conclusion of GRAS status that have not been submitted to FDA's voluntary GRAS notification program, around 40 percent of total substances purported to be GRAS have submitted a GRAS notice (1,309/(2,000+1,309)=.395). As discussed above, 673 notifiers have submitted GRAS notices. Therefore, the estimated number of firms that have already introduced substances into interstate commerce based on an independent conclusion of GRAS status and have not submitted a GRAS notice is approximately 1,028 (=673 / (1,309 / (1,309 + 2,000)) - 673). We request comment on this assumption.

[4] The total number of firms organized as C-corporations in Food Manufacturing (NAICS 311) and Soft Drink and Ice Manufacturing (NAICS 31211), less Animal Slaughtering and Processing (NAICS 3116).

E. Benefits of the Proposed Rule

Although we lack sufficient data to quantify the benefits of the proposed rule, we include a qualitative discussion of expected benefits. Mandating the submission of GRAS notices will provide FDA with information on the uses of substances that are currently in interstate commerce based on an independent conclusion of GRAS status. This would increase the level of knowledge and transparency about substances in the U.S. food supply that are purported to be GRAS under their conditions of intended use, giving FDA, consumers, and industry more information about the substances that are being added to human and animal food. This would allow FDA to ensure that GRAS conclusions have a scientific basis and that appropriate documentation supporting those conclusions is maintained, which could lead to the submission of higher quality GRAS notices. This would also help strengthen public confidence in FDA's ability to oversee the safety of the U.S. food supply.

A mandatory GRAS notification program would also help to ensure that human food safety, as well as target animal safety in the case of animal food GRAS notices, is fully assessed as part of a notifier's GRAS conclusion. This information would help us to determine whether a substance is GRAS under the conditions of its intended use, or whether it constitutes an unapproved food additive that requires a food additive regulation to be lawfully marketed. The extent to which food introduced into interstate commerce contains substances purported to be GRAS that are not GRAS determines the scope of the proposed rule's potential generation of benefits.

The proposed rule would help provide FDA and U.S. consumers with a more complete picture of all the substances that are being used in food. For certain nutrients, dietary exposure estimates are approaching the tolerable upper intake level (UL) established by the Institute of

Medicine (IOM). A nutrient's UL is the highest level of daily intake that is likely to pose no risk of adverse health effects (Ref. 6). Knowledge of actual levels of added nutrients in foods would enable FDA to obtain more accurate dietary exposures for the U.S. population. The extent to which substances purported to be GRAS based on an independent conclusion may cause consumption of nutrients to exceed the UL determines the scope for the proposed rule's potential generation of benefits.

F. Costs of the Proposed Rule

The proposed rule, if finalized, amends certain criteria in the regulations related to the GRAS provision of the FD&C Act and replaces the voluntary GRAS notification program with a mandatory GRAS notification program. The level of effort required by a firm to reach the conclusion that a substance is GRAS under the conditions of its intended use remains unchanged by the proposed rule. Once firms reach the conclusion that a substance is GRAS under the conditions of its intended use, however, they would be required to notify FDA. Additionally, firms would be required to follow the GRAS notice requirements specified in the proposed rule. Because the proposed rule would require submission of GRAS notices, we estimate incremental annual costs for firms to notify FDA of the conclusion that a substance is GRAS under the conditions of its intended use. In addition to annual costs for new GRAS notices, for substances that were already used in food before the effective date of a final rule, firms may choose to submit certain information about these substances during the limited- time option for such submissions instead of a GRAS notice. Notifiers and submitters would also incur one-time costs to read and understand the rule and to revise their standard operating procedures (SOPs).

1. One-time Costs

a. Cost of Reading and Understanding the Rule

We expect that all affected firms will spend time reading and understanding the requirements of a final rule and revising SOPs for preparing and submitting GRAS notices. Based on the length of the proposed rule (approximately 34,000 words) and using the average reading speed ranging from 200 to 250 words per minute as recommended by the Department of Health and Human Services (Ref. 7), it will take approximately 2.52 hours for 1 person to read and understand the rule, with a lower bound of 2.27 hours and an upper bound of 2.83 hours. Due to the number of provisions in the proposed rule, we anticipate that 2 managers will perform this task. Drawing on a composite hourly wage rate from the 2016 GRAS Final Regulatory Impact Analysis (Ref. 8) and Bureau of Labor Statistics (BLS) data for food manufacturing (Ref. 9) and basic chemical manufacturing (Ref. 10), and doubling for benefits and overhead, we estimate that the fully-loaded hourly wage rate for food and chemical product manufacturers is approximately $83.38 in 2024 dollars.[5] Each affected notifier will incur a one-time cost to read and understand the rule of approximately $419.99 (= $83.38 x 2 x 2.52 hours), with a lower bound of $377.99 (= $83.38 x 2 x 2.27 hours) and an upper bound of $472.49 (= $83.38 x 2 x 2.83 hours).[6] We estimate that the total costs of reading and understanding the rule are approximately $5.2 million (= 12,367 x $83.38 x 2 x 2.52 hours) in 2024 dollars, with a lower bound of $3.1 million (= 8,297 x $83.38 x 2 x 2.27 hours) and an upper bound of $7.8 million (= 16,436 x $83.38 x 2 x 2.83 hours). These costs are summarized in Table 8.

Table 8. Total Costs of Reading and Understanding the Rule (2024 dollars)

	Primary	Low	High
Number of affected firms[1]	12,367	8,297	16,436
Composite hourly wage of managers[2]	$83.38	$83.38	$83.38

[5] The 2016 GRAS FRIA estimates an average hourly wage for food and chemical product manufacturing by averaging the BLS hourly mean wages for compliance officers and business and financial operations employees in Food Manufacturing (NAICS 311000), Basic Chemical Manufacturing (NAICS 325100), and Other Chemical Product and Preparation Manufacturing.

[6] Throughout our analysis, discrepancies between calculations in the text and corresponding values in tables may arise due to rounding.

Number of managers	2	2	2
Approximate number of words in rule	34,000	34,000	34,000
Number of words read per minute	225	250	200
Reading time burden (hours)	2.519	2.27	2.83
Reading cost per firm	$419.99	$377.99	$472.49
Total cost of reading and understanding the rule	**$5,193,869**	**$3,136,338**	**$7,765,782**

Notes: [1] Number of firms that have submitted GRAS notices to FDA, the estimated number of firms which have made independent conclusions that a substance is GRAS under the conditions of its intended use, and the number of total firms in the U.S. in NAICS 311 organized as a C corps. [2] Composite wage rate is drawn from the 2016 GRAS FRIA (Ref. 8) and is the mean fully-loaded wage rate of compliance officers and business and financial operations employees in Food Manufacturing (NAICS 311000), Basic Chemical Manufacturing (NAICS 325100), and Other Chemical Manufacturing and Preparation (NAICS 329500).

b. Cost of Revising Standard Operating Procedures

We anticipate that firms will revise their SOPs to conform to the requirements of a final rule. Drawing on estimates from the 2016 GRAS Final Regulatory Impact Analysis (Ref. 8), we estimate that notifiers will spend approximately 35 hours performing this task, with a lower bound of 10 hours and an upper bound of 60 hours. Because revising and writing SOPs require effort from both clerical workers and managers, we use a weighted average hourly wage of approximately $74.49 (25 percent of the hourly wage for 1 clerical worker and 75 percent of the hourly wage for 1 manager).[7] Each notifier will incur a one-time cost to revise and write SOPs of approximately $2,606.98 (= $74.49 x 35 hours), with a lower bound of $744.85 (= $74.49 x 10 hours) and an upper bound of $4,469.10 (= $74.49 x 60 hours). The total cost associated with revising SOPs also depends on the number of firms that currently conclude that their use of substances is GRAS and have not voluntarily submitted a notice to FDA. We estimate that between 638 and 1,914 firms are currently reaching such independent conclusions of GRAS status. We estimate the total costs to revise standard operating procedures are approximately $2.7

[7] The composite wage is drawn from BLS wage data and estimates in the 2016 GRAS FRIA, including the wage rate for food and chemical product manufacturers ($83.38) and the average hourly wage for office clerk employees in Food Manufacturing (NAICS 311000), Basic Chemical Manufacturing (NAICS 325100), and Other Chemical Product and Preparation (NAICE 325900).

million (= 1,028.266 x $74.485 x 35 hours) in 2024 dollars, with a lower bound of $383.0 thousand (= 514.133 x $74.485 x 10) and an upper bound of $6.9 million (= 1,542.399 x $74.485 x 60 hours). These costs are summarized in Table 9.

Table 9. Cost of Revising Standard Operating Procedures (2024 dollars)

	Primary	Low	High
Number of affected firms (currently reaching independent conclusions of GRAS status but not voluntarily submitting a GRAS notice to FDA)	1,028	514	1,542
Composite hourly wage of food industry clerical and management workers	$74.49	$74.49	$74.49
Hours to revise standard operating procedures	35	10	60
Cost per firm to revise standard operating procedures	$2,606.98	$744.85	$4,469.10
Cost to Revise Standard Operating Procedures	**$2,680,663**	**$382,952**	**$6,893,134**

Notes: Number of affected firms is drawn from Table 7 (Number of Affected Entities). Composite wage rate and time burden to revise standard operating procedures is drawn from the 2016 GRAS FRIA (Ref. 8) and is the weighted sum of the manager composite wage ($83.38, 75% weight) and clerical worker composite wage ($47.80, 25% weight).

c. Cost of Preparing and Submitting Certain Information Regarding Substances Already Introduced into Interstate Commerce Before the Effective Date of a Final Rule

Manufacturers currently using substances that are already introduced into interstate commerce before the effective date of a final rule based on an independent conclusion of GRAS status would have the opportunity to submit certain information about the substance and its use to FDA instead of submitting a mandatory GRAS notice. Although these submissions are not expected to require expenditures equivalent to that of a GRAS notice, firms would incur costs associated with this activity. We assume that the submission of certain information would require between 10 percent and 25 percent of the time expenditure of a GRAS notice, with a central estimate of 17.5 percent. We request comment on our assumption of the time burden associated with submitting certain information.

Because food manufacturers are ultimately accountable for the substances in the food they produce, we assume that, in addition to the firms that manufacture substances purported to be GRAS based on an independent conclusion, firms that manufacture human and animal foods that utilize substances purported to be GRAS based on an independent conclusion will submit this information to FDA. If a substance purported to be GRAS based on an independent conclusion is sourced from a supplier that sells to multiple food manufacturers, this could lead to multiple submissions for some substances. We assume that on average, each substance purported to be GRAS based on an independent conclusion will be submitted 1 to 4 times, with a central estimate of 2.5 submissions. We request comment on this assumption. As mentioned in section II.D.2 of this document, we assume that there are currently between 1,000 and 3,000 substances purported to be GRAS based on an independent conclusion currently in use, with a central estimate of 2,000 substances.

The proposed rule requires that any material submitted in or referenced by a GRAS notice that is in a foreign language must be accompanied by an accurate and complete English translation. We therefore anticipate that some foreign manufacturers of GRAS substances will need to translate their submissions to English. We estimate that approximately 38.4 percent of submissions are not initially in English, and that the average number of words in a GRAS submission is approximately 30,000 words. We assume that the time burden of translation is approximately 15 times that of the time burden of reading and understanding the rule, with a lower bound of 10 times and an upper bound of 20 times the time burden of reading. We request comment on this assumption. We use the fully loaded BLS wage rate for technical writers ($88.14) to estimate the hourly cost of English translation (Ref. 11).

To estimate the cost to food manufacturers of preparing and submitting certain information for substances that were already used in food before the effective date of a final rule, we multiply the number of substances introduced into interstate commerce based on an independent conclusion of GRAS status but have not been submitted to FDA's voluntary GRAS notification program (2,000, with a lower bound of 1,000 and an upper bound of 3,000) by the number of firms submitting notices for each affected GRAS substance (2.5, with a lower bound of 1 and an upper bound of 4), the time burden of submitting the GRAS notice (31.5 hours, with a lower bound of 17 hours and an upper bound of 47.5 hours), and the fully-loaded composite hourly wage for food industry clerical/management workers ($65.59). We estimate that the one-time costs of preparing and submitting certain information for substances that were already used in food before the effective date of a final rule is approximately $10.3 million (= 2,000 x 2.5 x 31.5 hours x $65.59), with a lower bound of approximately $1.1 million (= 1,000 x 1 x 17 hours x $65.59) and an upper bound of approximately $37.4 million (= 3,000 x 4 x 47.5 hours x $65.59). To estimate the additional cost of translation for some foreign manufacturers, we multiply the number of substances introduced into interstate commerce based on an independent conclusion of GRAS status by the percent of GRAS notices submitted by firms operating in non-English speaking countries (38.4 percent), the time burden of translation (33.3 hours, with a lower bound of 20 hours and an upper bound of 50 hours), and the hourly wage of technical writers ($88.14). We estimate that the one-time costs of translation for preparing and submitting certain information for substances that were already used in food before the effective date of a final rule is approximately $2.3 million (= 2,000 x 38.43% x 33.33 hours x $88.78), with a lower bound of $682.4 thousand (= 1,000 x 38.43% x 20 hours x $88.78) and an upper bound of $5.1 million (= 3,000 x 38.43% x 50 hours x $88.78).

In total, the estimated costs of preparing and submitting certain information for substances that were already used in food before the effective date of a final rule are approximately $13.4 million (= $11.1 million + $2.3 million) in 2024 dollars, with a lower bound of $1.9 million (= $1.2 million + $682.4 thousand) and an upper bound of $46.2 million (= $41.1 million + $5.1 million). These costs are summarized in Table 10.

Table 10. Total Costs of Preparing and Submitting Certain Information for Substances That Were Already Introduced into Interstate Commerce Based on an Independent Conclusion of GRAS Status Before the Effective Date of a Final Rule (2024 dollars)

	Primary	Low	High
Number affected firms	2,000	1,000	3,000
Number of firms preparing and submitting certain information for substances that were already introduced into interstate commerce before the effective date of a final rule per existing substance purported to be GRAS based on an independent conclusion	2.5	1	4
Time burden of submitting certain information relative to a full GRAS notice	17.5%	10%	25%
Time burden of full GRAS notice submission (hours)	180	170	190
Time burden of preparing and submitting certain information for substances that were already introduced into interstate commerce before the effective date of a final rule	31.5	17	47.5
Composite hourly wage of food industry clerical and management workers	$65.59	$65.59	$65.59
Cost of preparing and submitting certain information for substances that were already introduced into interstate commerce before the effective date of a final rule	$10,330,425.00	$1,115,030.00	$37,386,300.00
Percent that will require resubmission	7.5%	5%	10%
Number of resubmissions	375	50	1,200
Cost of FDA re-review	$774,781.88	$55,751.50	$3,738,630.00
Percent of submissions not in English	38.43%	38.43%	38.43%
Approximate number of words in typical GRAS notice submission	30,000	30,000	30,000
Time burden of reading (hours)	2.22	2.00	2.50
Reading/translation multiplier	15	10	20
Time burden of translating submission of certain information for substances that were already introduced into interstate commerce before the effective date of a final rule	33.33	20	50
Hourly wage of technical writer	$88.78	$88.78	$88.78
Cost of translation per submission of certain information for substances that were already introduced into interstate commerce before the effective date of a final rule	$2,959.33	$1,775.60	$4,4393.00

Total cost of translation	$2,274,543.60	$682,363.08	$5,117.723.10
Total cost of preparing and submitting certain information for substances that were already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule	**$13,379,750**	**$1,853,145**	**$46,242,653**

Notes: Time burden of full GRAS notice submission is drawn from the 2016 GRAS FRIA (Ref. 8).

d. FDA Costs of Reviewing Submissions of Certain Information for Substances That Were Already Introduced into Interstate Commerce Based on an Independent Conclusion of GRAS Status Before the Effective Date of a Final Rule

The proposed rule, if finalized, would require FDA to post in a publicly available list the information we receive about substances that were already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule. The posting of this information does not mean that we have reviewed the GRAS status of substances' conditions of intended use. We estimate that FDA will receive approximately 5,000 submissions (= 2,000 substances already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule x 2.5 firms submitting certain information per substance), with a lower bound of 1,000 submissions (= 1,000 substances x 1 submitting firm) and an upper bound of 12,000 submissions (= 3,000 substances x 4 submitting firms). We assume that a submission will be reviewed for posting by the appropriate FDA staff and estimate a composite hourly wage rate using U.S. Office of Personnel Management (OPM) General Schedule (GS) data for 1 GS13-5 level employee of $124.77 (= $129,759 / 40 / 52 * 2) and 1 GS14-5 level employee of $151.91 (= $157,982 / 40 / 52 * 2) in the Washington-Baltimore-Arlington metropolitan area, doubled for benefits and overhead (Ref. 12). We estimate that the time burden of reviewing a submission for posting is approximately 35 percent of the time burden of preparing and submitting certain information for substances that were already introduced into interstate commerce based on an independent conclusion of GRAS status,

yielding a per submission FDA time burden of approximately 11.03 hours (= 31.5 hours * 35%), with a lower bound of 5.95 hours (= 17 hours * 35%) and an upper bound of 16.63 hours (= 47.5 hours * 35%). We multiply the number of submissions by the composite hourly wage of FDA reviewers and the time burden of review to yield a cost of initial review of certain information for substances that were already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule of approximately $15.3 million (= 5,000 x $276.674 x 11.03 hours), with a lower bound of $1.6 million (= 1,000 x $276.674 x 5.95 hours) and an upper bound of $55.2 million (= 12,000 x $276.674 x 16.63 hours).

We expect that some submissions may not be complete or may otherwise be inadequate. We estimate that approximately 7.5 percent, or 375 submissions (= 5,000 x 7.5%) would be resubmitted, with a lower bound of 50 submissions (= 1,000 x 5%) and an upper bound of 1,200 submissions (= 12,000 x 10%). We estimate that the costs of reviewing resubmissions for posting are approximately $1.1 million (= 375 x $276.67 x 11.03 hours), with a lower bound of $82.3 thousand (= 50 x $276.67 x 5.95 hours) and an upper bound of $5.5 million (= 1,200 x $276.67 x 16.63 hours).

The total costs of reviewing for posting submissions of certain information for substances that were already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule are approximately $16.4 million (= $15.3 million + $1.1 million), with a lower bound of $1.7 million (= $1.6 million + $82.3 thousand) and an upper bound of $60.7 million (= $55.2 million + $5.5 million). These costs are summarized in Table 11.

Table 11. Total Cost of Reviewing for Posting Submissions of Certain Information for Substances That Were Already Introduced into Interstate Commerce Based on an Independent Conclusion of GRAS Status Before the Effective Date of a Final Rule (2024 dollars)

	Primary	Low	High
Potential number of submissions	5,000	1,000	12,000
Composite hourly wage of FDA reviewers	$276.67	$276.67	$276.67
Time burden of review (hours)	11.03	5.95	16.63
Cost of initial review	$15,251,656	$1,646,211	$55,196,471
Percent that will resubmit	7.5%	5%	10%
Number of resubmissions	375	50	1,200
Cost of FDA re-review	$1,143,874.23	$82,310.53	$5,519,647.07
Total costs of FDA review	**$16,395,531**	**$1,728,521**	**$60,716,118**

The total one-time costs of preparing, submitting, and reviewing for posting submissions of certain information for substances that were already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule are approximately $29.8 million (= $13.4 million + $16.4 million) in 2024 dollars, with a lower bound of approximately $3.6 million (= $1.85 million + $1.73 million) and an upper bound of approximately $107.0 million (= $46.24 million + $60.7 million). Table 12 summarizes these costs.

Table 12. Total Costs of Preparing, Submitting, and Reviewing for Posting Submissions of Certain Information for Substances That Were Already Introduced into Interstate Commerce Based on an Independent Conclusion of GRAS Status Before the Effective Date of a Final Rule (2024 dollars)

	Primary	Low	High
Cost of preparing/submitting submissions of certain information (industry)	$13,379,750	$1,853,145	$46,242,653
Cost of reviewing submissions of certain information (FDA)	$16,395,531	$1,728,521	$60,716,118
Total cost of submissions of certain information for substances that were already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule	**$29,775,281**	**$3,581,666**	**$106,958,771**

e. Total One-time Costs

We estimate that the total one-time costs of the proposed rule are approximately $37.6 million (= $5.1 million + $2.68 million + $13.38 million + $16.4 million), with a lower bound of $7.1 million (= $3.1 million + $382.95 thousand + $1.85 million + $1.7 million) and an upper bound of $121.6 million (= $7.8 million + $6.89 million+ $46.24 million + $60.7 million). Table 13Table 13 summarizes these costs.

Table 13. Total One-time Costs of the Proposed Rule (2024 dollars)

	Primary	Low	High
Cost of reading and understanding the rule (industry)	$5,193,869	$3,136,338	$7,765,782
Cost of revising standard operating procedures (industry)	$2,680,663	$382,952	$6,893,134
Cost of preparing and submitting submissions of certain information (industry)	$13,379,750	$1,853,145	$46,242,653
Cost of reviewing submissions of certain information (FDA)	$16,395,531	$1,728,521	$60,716,118
Total one-time costs of the proposed rule	**$37,649,813**	**$7,100,955**	**$121,617,687**

2. Annual Costs

a. Costs of Preparing and Submitting GRAS Notices for New Substances or New Uses of Substances That Would Have Been the Subject of an Independent Conclusion of GRAS Status

If the proposed rule is finalized, food manufacturers would be required to submit to FDA GRAS notices for new substances or new uses of substances introduced into interstate commerce under the GRAS provision of the FD&C Act after the effective date of a final rule (new GRAS notices). Such new substances or new uses of substances would not otherwise be the subject of a GRAS notice voluntarily submitted to FDA, as they would have been purported to be GRAS based on an independent conclusion. However, if the proposed rule is finalized, GRAS notices would be required for such substances unless an exemption applies. We use the average number of GRAS submissions between 1998 and 2024 and the percent of GRAS notice submissions to estimate the annual number of substances purported to be GRAS based on an independent

conclusion that are not currently submitted to FDA, yielding an estimate of approximately 77 GRAS substances or uses of substances (= (50.3 / (1 - 60.44%)) - 50.3) annually that would require submission of a GRAS notice under a final rule, with a lower bound of 38 (= (50.3 / (1 - 43.31%)) - 50.3) substances or uses of substances and an upper bound of 115 (= (50.3 / (1 - 69.62%)) - 50.3) substances or uses of substances. We assume that the time burden to manufacturers of preparing a GRAS notice is approximately 180 hours, with a lower bound of 70 hours and an upper bound of 190 hours, and that submissions will be prepared by management and clerical staff. We request comment on this assumption. Drawing on BLS wage data (Ref. 9; Ref. 10), we estimate a fully-loaded composite wage rate for food manufacturing and chemical manufacturing managers and clerical staff of approximately $65.59. We request comment on these estimates. To estimate the annual cost of preparing and submitting such GRAS notices, we multiply the estimated annual number of substances or uses of substances introduced into interstate commerce for use in food that would require a GRAS notice by the time burden of preparing a GRAS notice and the composite hourly wage rate, to yield an annual cost of submitting future GRAS notices of approximately $908.2 thousand (= 76.9 x 180 hours x $65.59), with a lower bound of $428.9 thousand (= 38.5 x 170 hours x $65.59) and an upper bound of $1.4 million (= 115.4 x 190 hours x $65.59).

To estimate the additional cost of translation for some foreign manufacturers, we multiply the estimated number of substances introduced into interstate commerce based on an independent conclusions of GRAS status by the percent of GRAS notices submitted by notifiers in non-English speaking countries (38.4 percent), the time burden of translation (33.3 hours, with a lower bound of 20 hours and an upper bound of 50 hours), and the hourly wage of technical writers ($88.14). We estimate that the one-time costs of translation for such GRAS notices is

approximately $87.5 thousand (= 76.92 x 38.43% x 33.33 hours x $88.78), with a lower bound of $26.2 thousand (= 38.46 x 38.43% x 20 hours x $88.78) and an upper bound of $196.8 thousand (= 115.38 x 38.43% x 50 hours x $88.78).

The total annual costs of preparing and submitting new GRAS notices is approximately $1.1 million (= $908.2 thousand + $68.1 thousand + $87.5 thousand) in 2024 dollars, with a lower bound of $476.5 thousand (= $428.9 thousand + $21.4 thousand + $26.2 thousand) and an upper bound of $1.8 million (= $1.44 million + $143.79 thousand + $196.83 thousand) in 2024 dollars. These costs are summarized at Table 14.

Table 14. Total Annual Costs of Preparing and Submitting New GRAS Notices (2024 dollars)

	Primary	Low	High
Average number of GRAS submissions submitted 1998-2024	50.3	50.3	50.3
Percent of all GRAS substances that are submitted	60.44%	60.44%	60.44%
Number of independent conclusions of GRAS status not submitted to FDA	76.9	38.5	115.4
Time burden of full GRAS notice (hours)	180	170	190
Hourly wage rate	$65.59	$65.59	$65.59
Cost to submit new GRAS notices	$908,169.23	$428,857.69	$1,437,934.62
Percent that will resubmit	7.5%	5%	10%
Number of resubmissions	5.77	1.92	11.54
Cost of FDA re-review	$68,112.69	$21,442.88	$143,793.46
Percent of submissions not in English	38.43%	38.43%	38.43%
Approximate number of words in GRAS notice submission	30,000	30,000	30,000
Time burden of reading (hours)	2.22	2.00	2.50
Reading/translation multiplier	15	10	20
Time burden of translating GRAS notice submission (hours)	33.33	20	50
Hourly wage of technical writers	$88.78	$88.78	$88.78
Cost of translation per GRAS notice	$2,959.33	$1,775.60	$4,439.00
Total cost of translation	$87,482.45	$26,244.73	$196,835.50
Total cost of preparing and submitting new GRAS notices	**$1,063,764**	**$476,545**	**$1,778,564**

Note: Time burden of full GRAS notice is drawn from the 2016 GRAS FRIA (Ref. 8).

b. Costs of Reviewing New GRAS Notices

Under the proposed rule, if finalized, FDA will review GRAS notice submissions from manufacturers of new substances or new uses of substances introduced into interstate commerce that would otherwise not have been submitted under the voluntary program based on an independent conclusion of GRAS status. We estimate that FDA will receive approximately 77 such submissions annually, with a lower bound of 39 submissions and an upper bound of 115 submissions. We assume that submissions will be reviewed by the appropriate FDA staff and estimate a composite wage rate for one GS13-5 level employee of $124.77 (= $129,759 / 40 / 52 * 2) and one GS14-5 level employee of $151.91 (= $157,982 / 40 / 52 * 2) in the Washington-Baltimore-Arlington metropolitan area, doubled for benefits and overhead (Ref. 12). We estimate that the time burden of reviewing a GRAS notice submission is approximately 35 percent of the time burden of preparing and submitting a GRAS notice, yielding a per submission FDA time burden of approximately 63 hours (= 180 hours x 35%), with a lower bound of 59.5 (= 170 hours x 35%) hours and an upper bound of 66.5 hours (= 190 hours x 35%).

We multiply the number of new GRAS notice submissions by the composite hourly wage of FDA reviewers and the time burden of review to yield a cost of initial GRAS notice review of approximately $1.3 million (= 76.923 x $276.674 x 63 hours), with a lower bound of $633.2 thousand (= 38.462 x $276.674 x 59.5 hours) and an upper bound of $2.3 million (= 115.385 x $276.674 x 66.5 hours).

We expect that some GRAS notice submissions may not be complete or may otherwise not be adequate such that FDA cannot issue a No Questions letter. In such cases, manufacturers would resubmit notices for FDA review. We estimate that approximately 7.5 percent, or 6 GRAS notices (= 76.9 x 7.5%) would be resubmitted, with a lower bound of 2 GRAS notices (= 38.5 x 5%) and an upper bound of 12 GRAS notices (= 115.4 x 10%). We multiply the number of

resubmissions by the time burden of reviewing GRAS notices and the FDA composite wage rate to yield an annual re-review cost of approximately $100.6 thousand (= 5.77 x 63 hours x $276.674), with a lower bound of $31.7 thousand (= 1.92 x $276.674 x 59.5 hours) and an upper bound of $212.3 thousand (= 11.54 x 66.5 hours x $276.674). The estimated annual costs of reviewing new GRAS notices is approximately $1.4 million (= (76.923 x $276.674 x 63 hours) + (5.769 x $276.674 x 63 hours)) in 2024 dollars, with a lower bound of $633.2 thousand (= (38.462 x $276.674 x 59.5 hours) + (1.92 x $276.674 x 59.5 hours)) and an upper bound of $2.3 million (= (115.385 x $276.674 x 66.5 hours) + (11.54 x $330.583 x 66.5 hours)). These costs are summarized in Table 15.

Table 15. Total Annual Costs of Reviewing New GRAS Notices (2024 dollars)

	Primary	Low	High
Number of new GRAS notices	76.9	38.5	115.4
Composite hourly wage of FDA reviewers	$276.67	$276.67	$276.67
Time burden to reviewers (hours)	63.0	59.5	66.5
Cost of initial review	$1,340,804.96	$633,157.90	$2,122,941.18
Percent that will be resubmitted	7.5%	5%	10%
Number of resubmissions	5.77	1.92	11.54
Cost of FDA re-review	$100,560.37	$31,657.89	$212,294.12
Total annual cost of reviewing new GRAS notices	**$1,441,365**	**$664,816**	**$2,335,235**

3. Total Costs

One-time costs incurred in the year after the rule is finalized include reading and understanding the rule and revising standard operating procedures. Other one-time costs include preparing and submitting certain information for substances that were already used in food before the effective date of a final rule, for companies that choose to submit this information during the limited time for such submissions instead of a GRAS notice. We estimate that total one-time costs of the proposed rule are approximately $37.6 million (= $5.19 million + $2.68

million + $13.38 million + $16.4 million) in 2024 dollars, with a lower bound of $7.0 million (= $3.14 million + $382.95 thousand + $1.85 million + $1.73 million) and an upper bound of $121.6 million (= $7.8 million + $6.89 million + $46.24 million + $60.72 million). Annually recurring costs include preparing, submitting, and reviewing GRAS notices for new substances or new uses of substances. We estimate that total recurring costs of the proposed rule are approximately $2.5 million (= $1.1 million + $1.4 million), with a lower bound of $1.1 million (= $476.5 thousand + $664.8 thousand) and an upper bound of $4.1 million (= $1.8 million + $2.3 million). These costs are summarized in Table 16.

Table 16. Total Costs of the Proposed Rule (2024 dollars)

	Primary	Low	High
Reading and understand the rule (one-time)	$5,193,868.63	$3,136,337.86	$7,765,782.09
Revising standard operating procedures (one-time)	$2,680,663.37	$382,951.91	$6,893,134.38
Preparing and submitting certain information for substances that were already used in food before the effective date of a final rule, for companies that choose to submit this information during the limited time for such submission instead of a GRAS notice (one-time)	$13,379,750.48	$1,853,144.58	$46,242,653.10
Reviewing submissions certain information for substances that were already used in food before the effective date of a final rule, for companies that choose to submit this information during the limited time for such submission instead of a GRAS notice (one-time)	$13,379,750.48	$1,853,144.58	$46,242,653.10
Preparing and submitting new GRAS notices (annual)	$1,063,764.37	$476,545.31	$1,778,563.58
Reviewing new GRAS notices (annual)	$1,441,365.33	$644,815.79	$2,335,235.30
Total one-time costs of the proposed rule	**$37,649,813**	**$7,100,955**	**$121,617,687**
Total recurring costs of the proposed rule	**$2,505,130**	**$1,141,361**	**$4,113,799**

Table 17 presents the 10-year stream of estimated costs of the proposed rule, as well as the present value and annualized value of costs, discounted at 3 and 7 percent over 10 years in 2024 dollars. We estimate that the present value of the costs of the proposed rule is

approximately $57.9 million, with a lower bound of $16.6 million and an upper bound of $153.2 million, discounted at a 3 percent in 2024 dollars. At a 7 percent discount rate, the present value of costs is approximately $52.8 million, with a lower bound of $14.7 million and an upper bound of $142.6 million. The annualized costs of the proposed rule are approximately $6.8 million, with a lower bound of $1.9 million and an upper bound of $18.0 million, discounted at 3 percent. At a 7 percent discount rate, annualized costs are approximately $7.5 million, with a lower bound of $2.1 million and an upper bound of $20.3 million.

Table 17. 10-year Stream, Present Value, and Annualized Costs of the Proposed Rule (2024 dollars)

	Primary	Low	High
Year 1	$40,145,942.77	$8,242,316.51	$125,731,486.18
Year 2	$2,505,129.70	$1,141,361.10	$4,113,798.88
Year 3	$2,505,129.70	$1,141,361.10	$4,113,798.88
Year 4	$2,505,129.70	$1,141,361.10	$4,113,798.88
Year 5	$2,505,129.70	$1,141,361.10	$4,113,798.88
Year 6	$2,505,129.70	$1,141,361.10	$4,113,798.88
Year 7	$2,505,129.70	$1,141,361.10	$4,113,798.88
Year 8	$2,505,129.70	$1,141,361.10	$4,113,798.88
Year 9	$2,505,129.70	$1,141,361.10	$4,113,798.88
Year 10	$2,505,129.70	$1,141,361.10	$4,113,798.88
Net present value of costs (3%)	$57,922,481	$16,630,179	$153,166,963
Net present value of costs (7%)	$52,781,724	$14,652,850	$142,554,992
Annualized costs (10 years, 3%)	**$6,790,282**	**$1,949,654**	**$17,955,841**
Annualized costs (10 years, 7%)	**$7,514,930**	**$2,086,236**	**$20,296,624**

G. Analysis of Regulatory Alternatives to the Proposed Rule

1. Extended Submission Period for Submission of Certain Information for Substances that were Already Used in Food Before the Effective Date of a Final Rule

With this alternative to the proposed rule, manufacturers of substances that are already in interstate commerce before the effective date of a final rule based on an independent conclusion of GRAS status would have up to 3 years after the publication of the final rule to submit this certain information to FDA. The additional flexibility of this alternative would decrease costs to affected manufacturers of purported GRAS substances. We equally divide the one-time costs (i.e., those incurred only in the year after publication of the final rule) of the proposed rule to manufacturers across the 3 years after the effective date of the final rule. These estimates suggest that some manufacturers may submit when the rule becomes effective, while others may take advantage of the added flexibility and submit 2 to 3 years after the publication of the final rule.

Under this regulatory alternative, we estimate the annualized costs of the proposed rule are approximately $6.1 million, with a lower bound of approximately $1.7 million and an upper bound of approximately $17.0 million, discounted at 3 percent over 10 years in 2024 dollars. At a 7 percent discount rate, estimated costs are approximately $6.6 million, with a lower bound of approximately $1.8 million and an upper bound of approximately $18.6 million. These estimates are summarized in Table 18.

Extending the submission period for submission of certain information for substances that were already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule would lead to potential reductions in the benefits discussed in Section E. That is, while the information would still be provided, the delay would reduce the amount of time that the potential benefits could be realized.

Table 18. Regulatory Alternative to the Proposed Rule: Extended Submission Period (2024 dollars)

	Primary	Low	High
Primary annualized costs (10 years, 3%)	$6,790,282	$1,949,564	17,955,841
Primary annualized costs, (10 years, 7%)	$7,514,930	$2,086,236	$20,296,624
Alternative annualized costs, (10 years, 3%)	**$6,095,036**	**$1,698,571**	**$16,992,836**

Alternative annualized costs, (10 years, 7%)	**$6,562,847**	**$1,774,256**	**$18,638,256**

2. Require Submission of a GRAS Notice for All Substances Already Introduced into Interstate Commerce Based on an Independent Conclusion of GRAS Status Before the Effective Date of a Final Rule

With this alternative to the proposed rule, manufacturers of substances already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule would be required to submit a full GRAS notice. We estimate that the time burden to manufacturers of submitting a GRAS notice for a substance already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule would be equal to the time burden of submitting a GRAS notice for a new substance or a new use of a substance. This additional requirement would increase costs to affected manufacturers and increase costs to FDA in order to review additional submissions.

Under this regulatory alternative, we estimate the annualized costs of the proposed rule are approximately $21.5 million, with a lower bound of approximately $4.9 million and an upper bound of approximately $52.7 million, discounted at 3 percent over 10 years in 2024 dollars. At a 7 percent discount rate, estimate costs are approximately $24.8 million, with a lower bound of approximately $5.6 million and an upper bound of approximately $61.0 million. These estimates are summarized in Table 19.

This alternative could lead to increases in potential benefits. A full GRAS notice provides substantially more information than what the proposed rule is requesting from manufacturers of substances already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule. As information asymmetries form the basis

of the potential benefits associated with the proposed rule, this alternative could generate larger benefits.

Table 19. Regulatory Alternative to the Proposed Rule: Full GRAS Notice Requirement (2024 dollars)

	Primary	Low	High
Primary annualized costs (10 years, 3%)	$6,790,282	$1,949,564	17,955,841
Primary annualized costs, (10 years, 7%)	$7,514,930	$2,086,236	$20,296,624
Alternative annualized costs, (10 years, 3%)	**$21,546,112**	**$4,919,447**	**$52,729,271**
Alternative annualized costs, (10 years, 7%)	**$24,766,071**	**$5,558,347**	**$60,950,476**

3. Extend Submission Period for Substances Already Introduced into Interstate Commerce Based on an Independent Conclusion of GRAS Status Before the Effective Date of a Final Rule and Require GRAS Notices

With this alternative to the proposed rule, manufacturers of substances already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of a final rule would have 3 years to submit certain information to FDA (i.e., regulatory alternative 1) and would also be required to submit a full GRAS notice (i.e., regulatory alternative 2). Because the decrease in costs from the extended submission period alternative is smaller than the increase in costs from the full GRAS notice submission requirement alternative in absolute value, the combination of these alternatives would be a net cost increase to affected manufacturers.

Under this regulatory alternative, we estimate the annualized costs of the proposed rule are approximately $20.4 million, with a lower bound of approximately $4.6 million and an upper bound of approximately $50.8 million, discounted at 3 percent over 10 years in 2024 dollars. At a 7 percent discount rate, estimate costs are approximately $22.7 million, with a lower bound of approximately $5.0 million and an upper bound of approximately $56.7 million. These estimates are summarized in Table 20.

This alternative would have an ambiguous effect on benefits over 10 years. Although the increased information provided could lead to an increase in benefits, the delayed provision of this information would reduce the amount of time that the potential benefits could be realized.

Table 20. Regulatory Alternative to the Proposed Rule: Extended Submission Period and Full GRAS Notice Requirement (2024 dollars)

	Primary	Low	High
Primary annualized costs (10 years, 3%)	$6,790,282	$1,949,564	17,955,841
Primary annualized costs, (10 years, 7%)	$7,514,930	$2,086,236	$20,296,624
Alternative annualized costs, (10 years, 3%)	**$20,425,257**	**$4,582,794**	**$50,763,281**
Alternative annualized costs, (10 years, 7%)	**$22,710,020**	**$5,024,173**	**$56,690,508**

H. International Effects

In our primary analysis, we estimate costs to affected foreign manufacturers of substances already introduced into interstate commerce based on an independent conclusion of GRAS status before the effective date of the final rule, as well as new substances or new uses of substances introduced into interstate commerce for use in food that would be required to be the subject of a GRAS notice after the effective date of a final rule. If the proposed rule is finalized, we expect foreign manufacturers to incur costs related to reading the rule, revising standard operating procedures, and preparing and submitting GRAS notices for new substances or new uses of substances introduced into interstate commerce under the GRAS provision of the FD&C Act after the effective date of a final rule. For those foreign manufacturers that choose to submit certain information during the limited time for such submissions instead of a GRAS notice, they will also incur costs related to preparing and submitting certain information for substances purported to be GRAS that were already used in food before the effective date of the final rule. We also expect some affected foreign firms to incur costs of translating GRAS notice documentation to English.

We estimate that approximately 47.14 percent of GRAS-notifying entities are outside the U.S. and that 91.21 percent of foreign GRAS-notifying entities are in non-English speaking countries. To consider the effect of the proposed rule on foreign entities, we estimate the costs described in section II.F for 47.14 percent of affected entities. We additionally estimate translation costs for 91.21 percent of affected foreign entities.

The estimated present value of costs to affected foreign entities is approximately $29.2 million, with a lower bound of $8.4 million and an upper bound of $76.5 million, discounted at 3 percent over 10 years in 2024 dollars. At a 7 percent discount rate, the estimated present value of costs is approximately $26.7 million, with a lower bound of $7.4 million and an upper bound of $71.2 million. The estimated annualized costs to affected foreign entities is approximately $3.4 million, with a lower bound of $986.3 thousand and an upper bound of $9.0 million, discounted at 3 percent over 10 years. At a 7 percent discount rate, estimated annualized costs are approximately $3.8 million, with a lower bound of $1.1 million and an upper bound of $10.1 million. These estimates, as well as the estimated 10-year stream of costs are presented in Table 21.

Table 21. Estimated Costs of the Proposed Rule to Affected Foreign Entities (2024$)

	Primary	Low	High
Year 1	$20,458,271.62	$4,344,197.48	$62,710,593.67
Year 2	$2,237,556.35	$555,029.09	$2,066,680.7
Year 3	$2,237,556.35	$555,029.09	$2,066,680.7
Year 4	$2,237,556.35	$555,029.09	$2,066,680.7
Year 5	$2,237,556.35	$555,029.09	$2,066,680.7
Year 6	$2,237,556.35	$555,029.09	$2,066,680.7
Year 7	$2,237,556.35	$555,029.09	$2,066,680.7
Year 8	$2,237,556.35	$555,029.09	$2,066,680.7
Year 9	$2,237,556.35	$555,029.09	$2,066,680.7
Year 10	$2,237,556.35	$555,029.09	$2,066,680.7
Present value, 3% (10 years)	$29,217,495.26	$8,413,314.95	$76,506,791.41

Present value, 7% (10 years)	$26,655,363.21	$7,439,570.91	$71,192,054.95
Annualized, 3% (10 years)	**$3,425,182**	**$986,297**	**$8,968,930**
Annualized, 7% (10 years)	**$3,795,124**	**$1,059,228**	**$10,136,147**

III. **Initial Small Entity Analysis**

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because we estimate that the economic impact of this proposed rule is more than three percent of annual revenue, we find that the proposed rule will have a significant economic impact on a substantial number of small entities. This analysis, as well as other sections in this document and the Preamble of the proposed rule, serves as the Initial Regulatory Flexibility Analysis, as required under the Regulatory Flexibility Act.

A. Description and Number of Affected Small Entities

The data on affected entities comes from the FDA's GRAS Notice Inventory, Animal Food GRAS Notice Inventory (Ref. 2) and Dun & Bradstreet (D&B) firm data. We merge the FDA GRAS Notice Inventory with D&B firm data to identify firm-level characteristics. As discussed in II.D.2, we assume the characteristics of firms manufacturing substances based on an independent conclusion of GRAS status are similar to the firms which have submitted GRAS notices to FDA. Firms across a variety of industries are involved with the production of GRAS substances and submission of GRAS notices. The most common industries of firms which have previously submitted GRAS notices are Pharmaceutical Preparations (NAICS 325412), Perishable Prepared Food Manufacturing (NAICS 311991), Dry, Condensed, and Evaporated

Dairy Product Manufacturing (NAICS 311514), and Industrial Organic Chemicals (NAICS 325199). The Small Business Administration considers firms in these categories small if they do not exceed a certain number of employees: 1,300 employees for Pharmaceutical Preparations, 700 employees for Perishable Prepared Food Manufacturing, 1,000 employees for Dry, Condensed, and Evaporated Dairy Product Manufacturing, and 1,250 employees for Industrial Organic Chemicals Industry (Ref. 13). These small business thresholds are summarized in Table 22.

Table 22. Small Business Administration Size Standards for Industries Affected by the Proposed Rule

NAICS Code	Industry Description	SBA Small Business Threshold (number of employees)
311514	Dry, Condensed, and Evaporated Dairy Product Manufacturing	1,000
311991	Perishable Prepared Food Manufacturing	700
325199	Industrial Organic Chemical Manufacturing	1,250
325412	Pharmaceutical Preparation Manufacturing	1,300

Using FDA's GRAS Notice Inventory, Animal Food GRAS Notice Inventory and D&B data we estimate that approximately 40 percent of domestic GRAS notifiers are small entities, and that there are approximately 210 affected small entities. The mean annual revenue of these small entities is approximately $17.2 million (median annual revenue is approximately $1.2 million). We request comment on data sources, methods, and assumptions for identifying affected small entities.

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

We assume that the costs associated with this proposed rule that are incurred by small entities are proportional to the size of the small-entity product market, and that the proportion of small entities is equal for foreign and domestic firms. We estimate that there are approximately 132 (= 210 firms x 62.9 percent) domestic affected small entities and approximately 78 (= 210

firms x 37.1 percent) foreign affected small entities. We request comments on these assumptions. We therefore estimate that the annualized costs of the proposed rule incurred by affected small entities are approximately $1.7 million (= $6.79 million x 62.86 percent x 40 percent), with a lower bound of $490.2 thousand (= $1.95 million x 62.86 percent x 40 percent) and an upper bound of $4.5 million (= $17.95 million x 62.86 percent x 40 percent), discounted at 3 percent over 10 years in 2024 dollars. At a 7 percent discount rate, annualized costs of the proposed rule incurred by affected small entities are approximately $1.9 million (= $7.5 million x 62.86 percent x 40 percent), with a lower bound of $524.5 thousand (= $2.09 million x 62.86 percent x 40 percent) and an upper bound of $5.1 million (= $20.3 million x 62.86 percent x 40 percent). We divide annualized costs to small entities by the estimated number of affected small entities (132), to yield per entity costs of approximately $12.9 thousand (= $1.71 million / 132), with a lower bound of $3.7 thousand (= $490.2 thousand / 132) and an upper bound of $34.2 thousand (= $4.51 million / 132), discounted at 3 percent over 10 years. At a 7 percent discount rate, per entity costs are approximately $14.3 thousand (= $1.89 million / 132), with a lower bound of $4.0 thousand (= $524.5 thousand / 132) and an upper bound of $38.7 thousand (= $5.1 million / 132).

Using the mean ($17.2 million) and median ($1.2 million) annual revenue for small entities, we estimate the proportion of estimated costs to revenue, alternatively expressing estimated annual costs as a percentage of mean and median revenue. We estimate that costs of the rule as a percentage of mean annual revenue are approximately 0.08 percent (= $12,934 / $17.2 million, with a lower bound of 0.02 percent (= $3,713 / $17.2 million) and an upper bound of 0.2 percent (= $34,202 / $17.2 million), discounted at 3 percent over 10 years. At a 7 percent discount rate, costs as a percentage of mean annual revenue are approximately 0.08 percent (=

$14,314 / $17.2 million), with a lower bound of 0.02 percent (= $3,974 / $17.2 million) and an upper bound of 0.22 percent (= 38,660 / $17.2 million). We estimate that costs of the rule as a percentage of median annual revenue are approximately 1.08 percent (= $12,934 / $1.2 million), with a lower bound of 0.31 percent (= $3,713 / $1.2 million) and an upper bound of 2.85 percent (= $34,202 / $1.2 million), discounted at 3 percent over 10 years. At a 7 percent discount rate, costs as a percentage of mean annual revenue are approximately 1.19 percent (= $14,314 / $1.2 million), with a lower bound of 0.33 percent (= $3,974 / $1.2 million) and an upper bound of 3.22 percent (= $38,660 / $1.2 million). The costs of the proposed rule for affected small entities are summarized in Table 23.

Table 23. Costs of the Proposed Rule for Affected Small Entities (2024 dollars)

	Primary	Low	High
Annualized costs of the proposed rule (3%)	$6,790,281.79	$1,949,563.63	$17,955,840.72
Annualized costs of the proposed rule (7%)	$7,514,930.04	$2,086,236.15	$20,296,623.74
Number of affected domestic small entities	132	132	132
Number of affected foreign small entities	78	78	78
Total number of affected small entities	210	210	210
Percent of small entities that are domestic	62.9%	62.9%	62.9%
Percent of affected entities considered small	40%	40%	40%
Annualized costs of the proposed rule to small entities (3%)	$1,707,270.85	$490,176.00	$4,514,611.38
Annualized costs of the proposed rule to small entities (7%)	$1,889,468.12	$524,539.37	$5,103,151.11
Annualized costs of the proposed rule per small entity (3%)	$12,933.87	$3,713.45	$34,201.60
Annualized costs of the proposed rule per small entity (7%)	$14,314.15	$3,973.78	$38,660.24
Mean annual revenue of small entities	$17,200,000	$17,200,000	$17,200,000
Median annual revenue of small entities	$1,200,000	$1,200,000	$1,200,000
Cost of the rule as a percentage of mean annual revenue (3%)	0.08%	0.02%	0.20%
Cost of the rule as a percentage of mean annual revenue (7%)	0.08%	0.02%	0.22%
Cost of the rule as a percentage of median annual revenue (3%)	1.08%	0.31%	2.85%
Cost of the rule as a percentage of median annual revenue (7%)	1.19%	0.33%	3.22%

IV. **References**

1. U.S. Food and Drug Administration (FDA), Post-market Determinations that the Use of a Substance is not GRAS, available at: https://www.hfpappexternal.fda.gov/scripts/fdcc/index.cfm?set=Postmarket, accessed June 26, 2025.

2. U.S. Food and Drug Administration (FDA), GRAS Notices, available at: https://www.hfpappexternal.fda.gov/scripts/fdcc/cfc/XMLService.cfc?method=downloadxls&set=GRASNotices, accessed June 26, 2025.

3. U.S. Food and Drug Administration (FDA), Current Animal Food GRAS Notices Inventory, available at: https://www.fda.gov/animal-veterinary/generally-recognized-safe-gras-notification-program/current-animal-food-gras-notices-inventory, accessed June 26, 2025.

4. Neltner, T. G., Kulkarni, N. R., Alger, H. M., Maffini, M. V., Bongard, E. D., Fortin, N. D., & Olson, E. D. (2011). Navigating the US food additive regulatory program. *Comprehensive Reviews in Food Science and Food Safety*, 10(6), 342-368.

5. U.S. Census Bureau, CB2200CBPAll Sectors: County Business Patterns, including ZIP Code Business Patterns, by Legal Form of Organization and Employment Size Class for the U.S., States, and Selected Geographies: 2022, available at: https://data.census.gov/table/CBP2022.CB2200CBP, accessed June 26, 2025.

6. Institute of Medicine (US) Subcommittee on Interpretation and Uses of Dietary Reference Intakes; Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. DRI Dietary Reference Intakes: Applications in Dietary Assessment. Washington (DC): National Academies Press (US); 2000. 6, Using the Tolerable Upper Intake Level for Nutrient Assessment of Groups, available at: https://www.ncbi.nlm.nih.gov/books/NBK222879/, accessed June 26, 2025.

7. U.S. Department of Health and Human Services (HHS), "Valuing Time in U.S. Department of Health and Human Services Regulatory Impact Analyses: Conceptual Framework and Best Practices," 2017, available at https://aspe.hhs.gov/reports/valuing-time-us-department-health-human-services-regulatory-impact-analyses-conceptual-framework, accessed June 26, 2025.

8. U.S. Food and Drug Administration (FDA), Substances Generally Recognized as Safe Final Regulatory Impact Analysis, August 17, 2016, available at: https://www.fda.gov/media/99659/download, accessed June 26, 2025.

9. U.S. Bureau of Labor Statistics (BLS), "Occupational Employment and Wages, Industry: Food Manufacturing, May 2024, https://data.bls.gov/oes/#/industry/311000, accessed June 26, 2025.

10. U.S. Bureau of Labor Statistics (BLS), "Occupational Employment and Wages, Industry: Basic Chemical Manufacturing, May 2024, https://data.bls.gov/oes/#/industry/3250A1, accessed June 26, 2025.

11. U.S. Bureau of Labor Statistics (BLS), "Occupational Employment and Wage Statistics (OEWS) Profiles, May 2024, https://data.bls.gov/oesprofile/, accessed June 26, 2025.

12. U.S. Office of Personnel Management (OPM), "2024 General Schedule (GS) Pay Tables" available at: https://www.opm.gov/policy-data-oversight/pay-leave/salaries-wages/2024/general-schedule/, accessed June 26, 2025.

13. U.S. Small Business Administration (SBA), "Table of Small Business Size Standards Matched to North American Industry Classification System Codes," available at: https://www.sba.gov/document/support-table-size-standards, accessed June 26, 2025.