DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Substances Generally Recognized as Safe
Final Rule

Docket No. FDA-1997-N-0020 (formerly 97N-0103)

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

Economics Staff
Office of Planning
Office of Policy, Planning, and Legislation
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I. Introduction and Summary

A. Introduction

For this final regulatory impact analysis, we use the following terms: "GRAS substance" refers to a substance not subject to premarket approval as a food additive under the Federal Food, Drug, and Cosmetic Act (FD&C Act) because the substance is generally recognized as safe (GRAS) under the conditions of its intended use in food for humans or animals under Section 201(s) of the FD&C Act (21 U.S.C. 321(s)) and the criteria for eligibility for classification as GRAS in 21 CFR 170.30 or 21 CFR 570.30; "GRAS conclusion" refers to a conclusion that a substance is GRAS under the conditions of its intended use within the meaning of Section 201(s) of the FD&C Act and the criteria for eligibility for classification as GRAS in 21 CFR 170.30 or 21 CFR 570.30; and "GRAS petition" refers to a GRAS affirmation petition that had been provided for under 21 CFR 170.35(c) or 21 CFR 570.35(c).

The final rule amends certain criteria in the regulations related to the GRAS provision of the FD&C Act, and replaces a voluntary GRAS petition process with a voluntary GRAS notification procedure. A substance must be GRAS or otherwise excepted from the definition of a food additive before adding it to human or animal food without approval as a food additive. Once you conduct a review of safety information and of general recognition of safety by qualified experts, and if you reach a GRAS conclusion, you can decide to submit a GRAS notice to us for our evaluation. We clarify the procedure that you can follow to notify us of your GRAS conclusion, the type of documentation we expect you to submit with a GRAS notice to support your GRAS conclusion, and how we will respond to your notice.

B. Summary of Costs and Benefits

The final rule will eliminate the petition process to affirm a substance is GRAS under the conditions of its intended use and replace the petition process with a GRAS notification procedure. The level of effort required by a firm to reach a conclusion that a substance is GRAS under the conditions of its intended use remains unchanged by the final rule. We estimate that from 350 to 480 notifiers may voluntarily decide to participate in the GRAS notification procedure and submit on average from 60 to 75 GRAS notices each year. These notifiers will incur one-time administrative costs to read and understand the rule and revise their standard operating procedures. In addition, from 40 to 45 firms with outstanding GRAS affirmation petitions may also incur one-time costs to prepare and submit a GRAS notice. Because the final rule will require that notifiers submit more information to support their GRAS conclusion than they currently provide with their notices, we include annual incremental costs for this additional information.

We estimate that over 10 years with a 7 percent discount rate, the present value of the total costs of the final rule range from $0.9 million to $3.3 million; with a 3 percent discount rate, the present value of the total costs range from $0.9 million to $3.4 million. The annualized costs of the rule range from $0.1 million to $0.4 million with a 7 percent discount rate and range from $0.1 million to $0.5 million with a 3 percent discount rate. We do not quantify the benefits of the final rule, but assume that firms will spend the same level of effort for a GRAS petition and a GRAS notice to reach a GRAS conclusion. Thus, firms will voluntarily participate in the GRAS notification procedure when they expect to receive a non-negative private benefit. Clarifying the information we expect from firms that reach a GRAS conclusion will allow us to complete our evaluation of a GRAS notice within the timelines specified in the final rule. We anticipate that the more timely evaluation of GRAS notices, compared to the rulemaking process for GRAS

petitions, will create an incentive for firms to submit GRAS notices. The net benefit of the final rule will depend on the quantity of GRAS notices submitted and the difference in the values firms assign to a GRAS notice and a GRAS petition.

In table 1, we provide the Regulatory Information Service Center/Office of Information and Regulatory Affairs Consolidated Information System accounting information.

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	Annualized Monetized $millions/year					7%		
						3%		
	Annualized Quantified					7%		
						3%		
	Qualitative	The final rule will reduce the delay to evaluate industry submissions on GRAS substances.						
Costs	Annualized Monetized $millions/year	$0.3	$0.1	$0.4	2014	7%	10 years	
		$0.3	$0.1	$0.5	2014	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%		
						3%		
	From/To	From:			To:			
Effects	State, Local or Tribal Government: No effect Small Business: No effect Wages: No effect Growth: No effect							

II. Final Regulatory Impact Analysis

We have examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct us to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). We have developed a comprehensive Economic Analysis of Impacts that assesses the impacts of the final rule. We believe that this final rule is not a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. The final rule replaces the voluntary GRAS petition process with a voluntary GRAS notification procedure. Similar to the petition process, we expect that profit-maximizing firms will only submit the GRAS notice when the private benefits equal or exceed the costs of the GRAS notice, regardless of the size of the firm. Because small firms face the same voluntary business decision as large firms, we certify that the final rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $144 million, using the most current (2014) Implicit Price Deflator for the Gross

Domestic Product. This final rule will not result in an expenditure in any year that meets or exceeds this amount.

A. Background and Need for Regulation

In 1997, we published a proposed rule that would amend our regulations regarding GRAS substances for use in human food or in food for animals. At that time, firms could voluntarily participate in a GRAS petition process. Of the 93 GRAS petitions (for substances intended for use in human food) that we filed between 1972 and 1996, we completed rulemaking for 24 of those petitions[1]. Because this process requires notice and comment rulemaking, the time to review and issue regulations in response to these petitions ranged from 1.4 years to 19.8 years and averaged 7.9 years.

In the proposed rule, we invited interested persons who determine[2] that a use of a human food substance is GRAS to notify us of those determinations as described in the proposed rule (62 FR 18938 at 18954; the "Interim Pilot program"). Shortly after publication of the proposed rule, we began accepting and evaluating GRAS notices for human food substances. By the end of 2015, we had filed over 600 GRAS notices and sent 474 GRAS "no questions letters", 17 "insufficient basis letters", and 97 "cease to evaluate letters." We make this information publicly available on our website in a GRAS Inventory. In 2010, we published a notice in the Federal Register (2010 notice) reopening the comment period for the proposed rule to update comments because of the length of time that had elapsed since the publication of the proposed rule and because we had identified a number of issues within the scope of the proposed rule that may require further clarification. In June of that same year, we also launched an Interim Pilot

[1] We note that some of these GRAS petitions came to completion through issuance of a food additive regulation rather than a GRAS affirmation regulation.
[2] We note that the final rule refers to GRAS "conclusions" rather than "GRAS determinations."

program for animal food substances similar to the one for human food substances (75 FR 31800). By the end of 2015, we had sent 7 GRAS "no questions letters", 5 "insufficient basis letters", and 6 "cease to evaluate letters" for GRAS notices for substances intended for use in animal food.

The final rule will replace the voluntary GRAS petition process with the voluntary GRAS notification procedure and we are therefore ending our Interim Pilot program. The rule will provide more clarity to firms considering whether a substance is GRAS under the conditions of its intended use and considering submitting GRAS notices to us. Our GRAS petition process required notice and comment rulemaking, a time-consuming process that created a disincentive for firms to participate. We judge that the GRAS notification procedure provides a strong incentive for firms to voluntarily participate in our program, and allows us to respond to GRAS notices in a timely manner.

B. Comments

The agency received several public comments to the 1997 proposed rule and to the 2010 notice reopening the comment period for the proposed rule. Most comments address specific aspects of the proposed rule or responded to specific questions we asked. A few of these comments quote parts of the preliminary regulatory impact analysis (PRIA) or address broad issues raised in the PRIA. However, none of the comments on the PRIA provide sufficient information that we can use to revise our preliminary analysis. We group comments by general topic: Potential costs savings of a GRAS notification procedure; the value of a GRAS notice; and potential incentives or disincentives of the GRAS notification procedure.

Comment 1) Some commenters agree with our statement in the PRIA that the companies spend the same effort to gather information that supports their GRAS conclusions for a GRAS notice and a GRAS petition, and thus the cost savings from the rule would be modest. Other

commenters stated that the GRAS notification procedure would take less time than the GRAS petition process, decreasing costs for both us and industry. One commenter noted that by setting regulatory deadline for our responses to GRAS notices, the proposed rule would reduce uncertainty and eliminate the long delays associated with the GRAS petition process.

Response 1) The GRAS petition process required rulemaking, a lengthy and time consuming process. Comparing the GRAS notification procedure to the GRAS petition process, we note that companies must devote the same level of effort to generate information sufficient to reach a GRAS conclusion. Of the 93 GRAS petitions (for substances intended for use in human food) that we filed between 1972 and 1996, we completed rulemaking for 24 of those petitions. The time to complete rulemaking for those 24 GRAS petitions ranged from 1.4 years to 19.8 years and averaged 7.9 years. Results from our Interim Pilot program for human food show that, on average, we sent "no questions letters," "cease to evaluate letters," and "insufficient basis letters" for GRAS notices in 200 days after we filed a notice. Although we can't quantify the value of faster decisions, we expect that companies benefit from the much faster GRAS notification procedure. Moreover, the final rule specifies reasonable timelines for our responses to GRAS notices based on our real-world experience with the Interim Pilot programs.

Comment 2) Some commenters assert that food manufacturers would place less value on a GRAS notice than a GRAS petition and would not participate in the program.

Response 2) Companies can use a food substance that is GRAS under the conditions of its intended use without notifying us; the final rule does not change this. The final rule will replace the GRAS petition process with the GRAS notification procedure. We disagree that companies place less value on the GRAS notification procedure. Even though some companies may prefer the GRAS petition process over the GRAS notification procedure, we see no

evidence that the GRAS notification procedure creates a disincentive for companies to participate. Moreover, from 1998 through 2015, we filed over 600 GRAS notices for human food substances in our Interim Pilot program. Such a large number of notices demonstrates that notifiers gain some private benefit from GRAS notices and that notifiers value the GRAS notification procedure and consider it a viable and cost-effective alternative to the GRAS petition process.

Comment 3) One comment expressed concern that the GRAS notification procedure would hurt consumer confidence in food products.

Response 3) We disagree that the GRAS notification procedure would hurt consumer confidence, because the rule doesn't change the statutory eligibility criteria for classification of a substance as generally recognized as safe for its intended use in human or animal food. Notifiers may still use a substance they conclude is GRAS without FDA evaluation or concurrence. The success of the voluntary GRAS notification procedure has actually encouraged notifiers to submit GRAS notices to us, increasing our awareness of the composition of our food supply and the dietary exposure to GRAS substances. In addition, notified substances include substances that are intended to address food safety problems (e.g., antimicrobial substances and substances intended to reduce acrylamide formation) and public health issues (e.g., substances that would reduce levels of sodium chloride in food). We conduct a substantive evaluation of the GRAS notices that we receive to evaluate the basis for the notifier's GRAS conclusion. We strive to make the process transparent and have posted information about the human and animal GRAS inventories on our website. We will continue to make this information accessible to food manufacturers and consumers.

Comment 4) Some commenters stated that the more timely GRAS notification procedure, including a regulatory timeframe for FDA to complete its evaluation of a GRAS notice, creates an incentive for firms to participate. Some commenters supported the GRAS notification procedure, but expressed concern that the success of the program depends on our timely response to notices.

Response 4) We agree that the timely evaluation of GRAS notices will create an incentive for companies to participate. In the final rule we clarify the information we expect notifiers to submit in support of their GRAS conclusions. Removing uncertainty about our expectations and setting realistic timelines for our evaluation of GRAS notices will further encourage companies to participate in the GRAS notification procedure.

C. Baseline

In the proposed rule, we invited interested persons who determine that a human food substance is GRAS under the conditions of its intended use to participate in the Interim Pilot program. We explained that we would administer the notices as described in the proposed rule (i.e., we would acknowledge receipt of the notice, respond in writing to the notifier, and make publicly accessible a copy of all GRAS exemption claims and our response). We filed the first GRAS notice for human food substances in 1998. By the end of 2015, we had filed over 600 GRAS notices for substances intended for use in human food and sent response letters for about 95 percent of these GRAS notices. Table 2 shows a breakdown of the response letters by response time for GRAS notices for substances intended for use in human food. We sent more than 60 percent of these response letters within 180 days; we sent more than 85 percent of these response letters within 270 days. Even though we sent 17 insufficient basis letters since 1998, we have not sent any of these letters since 2011.

Table 2. Response Letters for GRAS Notices for Substances Intended for Use in Human Food by Response Time[1] and Type of Letter

	Response Time from 1 Day to 90 Days	Response Time from 91 Days to 180 Days	Response Time from 181 Days to 270 Days	Response Time More than 270 Days	Total Number of Letters by Type[2]	Percent of Letters by Type
Cease to evaluate letters	41	33	8	15	97	16%
Insufficient basis letters	2	10	1	4	17	3%
No questions letters	20	268	129	57	474	81%
Total Number of Letters by Response Time	63	311	138	76	588	100%
Percent of Letters by Response Time	11%	53%	23%	13%	100%	

[1]Response time for "cease to evaluate letters" equals the number of days between the date we filed the GRAS notice and the date we stopped evaluating the GRAS notice; for the other two types of response letters, response time equals the number of days between the date we filed the GRAS notice and the date of our response letter to the GRAS notice.
[2]We count the response letter for GRN13 as an "insufficient basis letter".
Numbers may not sum due to rounding.

We established an Interim Pilot program for substances intended for use in animal food in 2010 and filed the first GRAS notice for a substance intended for use in animal food in December 2010. By the end of 2015, we had filed 18 GRAS notices. Table 3 shows a breakdown of the response letters by response time for GRAS notices for substances intended for use in animal food. We sent about 28 percent of these response letters within 270 days; we sent more than 95 percent of these response letters within 360 days. Moreover, we have not sent any insufficient basis letters since 2012.

Table 3. Response Letters for GRAS Notices for Substances Intended for Use in Animal Food by Response Time[1] and Type of Letter

	Response Time from 1 Day to 180 Days	Response Time from 181 Days to 270 Days	Response Time from 271 Days to 360 Days	Response Time More than 360 Days	Total Number of Letters by Type	Percent of Letters by Type
Cease to evaluate letters	1	3	2		6	33%
Insufficient basis letters			5		5	28%
No questions letters	1		5	1	7	39%
Total Number of Letters by Response Time	2	3	12	1	18	100%
Percent of Letters by Response Time	11%	17%	67%	6%	100%	

[1]Response time for "cease to evaluate letters" equals the number of days between the date we filed the GRAS notice and the date we stopped evaluating the GRAS notice; for the other two response letters, response time equals the number of days between the date we filed the GRAS notice and the date of our response letter to the GRAS notice.

D. Costs of the Rule

The final rule will eliminate the petition process to affirm that a substance is GRAS under the conditions of its intended use and replace the GRAS petition process with a GRAS notification procedure. The level of effort required by a firm to reach a GRAS conclusion remains unchanged by the final rule. Once firms reach their GRAS conclusions, they can voluntarily decide to submit a GRAS notice to us. However, when a firm decides to submit a GRAS notice to us, the firm must follow the requirements specified in the final rule. Because the final rule will require some additional reporting compared to current practices for GRAS notices (e.g., a certification statement, and identification of any information that the notifier

views as confidential), we estimate incremental annual costs for these additional requirements. In addition to annual costs, notifiers will incur one-time costs to read and understand the rule, and to revise their standard operating procedures (SOPs). Some firms have outstanding GRAS petitions, for which we will be closing the docket. We anticipate that if these firms decide to submit a GRAS notice they will use the information from their GRAS petition in their GRAS notice. We include one-time costs for these firms to prepare and submit a GRAS notice for the substance in their GRAS petition.

1. Who is affected by the Final Rule?

Using the North American Industry Classification System (NAICS), the government classifies firms by their primary type of business operation. Firms most likely to submit a GRAS notice fall into three basic industries. These include Food Manufacturing (NAICS code 311000), Basic Chemical Manufacturing (NAICS code 325100), and Other Chemical Product and Preparation Manufacturing (NAICS code 325900). Based on GRAS notices we filed during our two Interim Pilot programs, as shown in table 4, we estimate that from 350 to 480 notifiers will incur costs to comply with the final rule.

Table 4. Estimated Number of Affected Notifiers

	Lower Bound Estimate	Upper bound Estimate
Number of Human Food Substance Notifiers	340	460
Number of Animal Food Substance Notifiers	10	20
Total Number of Affected Notifiers	350	480

2. Unit Costs

We use 2014 occupation specific wages from the US Bureau of Labor Statistics for these three industries to calculate the average hourly wage for managers and clerical employees. We selected types of employees likely to perform the actions required by the final rule. For

managers, we used the average hourly wages for business and financial operations (occupation 13-0000) and compliance officers (occupation 13-1041) as proxies; for clerical workers, we used hourly wages for general office clerks (occupation 43-9061). As shown in table 5, the average hourly wage for managers equals $66.60 with a 100-percent overhead; the average hourly wage for clerical employees shown in table 6 equals $32.26 with a 100-percent overhead.

Table 5. Average Hourly Wages for Managers

Occupation	**NAICS Code**	**Average Hourly Wage**	**Loaded Average Hourly Wage**
Compliance Officers	311000	$29.04	$58.08
Business and Financial Operations	311000	$29.75	$59.50
Compliance Officers	325100	$39.44	$78.88
Business and Financial Operations	325100	$36.44	$72.88
Compliance Officers	325900	$33.04	$66.08
Business and Financial Operations	325900	$32.09	$64.18
Total Average Hourly Wage		**$33.30**	**$66.60**

Table 6. Average Hourly Wages for Clerical Workers

Occupation	**NAICS Code**	**Average Hourly Wage**	**Loaded Average Hourly Wage**
Office Clerks General	311000	$14.71	$29.42
Office Clerks General	325100	$17.51	$35.02
Office Clerks General	325900	$16.17	$58.34
Total Average Hourly Wage		**$16.13**	**$32.26**

3. One-time costs

For all affected notifiers, we expect that they will spend time reading and understanding the requirements of the final rule and revising SOPs for preparing and submitting GRAS notices.

Based on the length of the final rule and using average reading speed ranging from 200 to 250 words per minute as recommended by the Department of Health and Human Services, it will take about 5.4 to 6.8 hours for one person to read and understand the rule. Due to the number of provisions in the final rule, we anticipate that 2 or 3 managers will perform this task. As shown in table 7, each affected notifier will incur a one-time cost to read and understand the rule that range from about $720 to $1,350.

Table 7. Cost to Read and Understand the Final Rule

	Lower Bound Estimate	**Upper bound Estimate**
Number of Hours	5.4	6.8
Number of Managers	2	3
Hourly Wage[1]	$66.60	$66.60
Cost to Read and Understand the Final Rule	$720.24	$1,350.45

[1] Source: Tables 5 and 6.

We anticipate that notifiers will revise their SOPs to conform to the requirements of the final rule. We estimate that notifiers will spend from 10 hours to 60 hours to perform this task. Because revising and writing SOPs require effort from both clerical workers and managers, we use a weighted average hourly wage of about $58.00 (25 percent for clerical workers and 75 percent for managers). As shown in table 8, each notifier will incur a one-time cost to revise and write SOPs that range from about $580 to $3,480.

Table 8. Cost to Revise Standard Operating Procedures

	Lower Bound Estimate	Upper bound Estimate
Number of Hours	10	60
Weighted Average Hourly Wage[1]	$58.02	$58.02
Cost to Revise SOPs	$580.15	$3,480.90

[1] Source: Tables 5 and 6. Average weighted wage of $58.02 = (0.25 x 32.26 + .75 x $66.60).

Firms with outstanding GRAS petitions may choose to submit GRAS notices and incorporate the information previously included in their petitions. To account for the additional effort by these firms, we include the one-time cost to prepare and submit a GRAS notice for up to 45 outstanding GRAS petitions for substances intended for use in human food. As shown in table 9, we estimate that notifiers will spend between 170 and 190 hours divided evenly between clerical workers and managers. With a weighted average wage of $49.43 (50 percent for clerical workers and 50 percent for managers), the one-time cost to prepare and submit a GRAS notice will range from about $8,400 to $9,150 for each outstanding GRAS petition.

Table 9a. Estimated Number of Outstanding GRAS Petitions

	Lower bound	Upper bound
GRAS petitions for substances intended for use in human food	40	45

Table 9b. Cost to Prepare a GRAS Notice for an Outstanding GRAS Petition

Number of Hours	170	175	180	185
Weighted Average Hourly Wage[1]	$49.43	$49.43	$49.43	$49.43
Cost to Prepare a GRAS Notice	$8,403.10	$8,650.25	$8,897.40	$9,144.55

[1] Source: Tables 5 and 6. Average weighted wage of $49.43 = (0.5 x 32.26 + 0.5 x $66.60).

4. Annual Costs

In addition to these one-time costs, the final rule will require that firms submit some additional information to support their GRAS conclusion with their notices. Some examples of the type of additional information we expect firms to submit include a certification statement or identification of any information that the notifier views as confidential. We estimate that notifiers will submit between 60 and 75 GRAS notices each year, 40 to 50 GRAS notices for

substances intended for use in human food and 20 to 25 GRAS notices for substances intended for use in animal food. Although uncertain, we estimate that notifiers will spend between 5 more hours and 20 more hours to prepare and submit each GRAS notice than they currently spend. With a weighted average wage of $49.43 (50 percent for clerical workers and 50 percent for managers), notifiers will incur incremental costs that range from $250 to $990 for each GRAS notice submitted annually.

5. Total Costs of the Final Rule

Annual costs range from $0.01 million to $0.07 million with an average of $0.04 million. The one-time costs range from $0.8 million to $2.7 million with an average one-time cost of $1.8 million. Over 10 years with a 7 percent discount rate, the present value of the total costs of the final rule range from $0.9 million to $3.3 million; with a 3 percent discount rate, the present value of the total costs range from $0.9 million to $3.4 million. The annualized costs of the rule range from $0.1 million to $0.4 million with a 7 percent discount rate, and range from $0.1 million to $0.5 million with a 3 percent discount rate.

E. Benefits of the Rule

Although we lack sufficient data to quantify the benefits of the final rule, we include a qualitative discussion of the expected benefits. Notifiers have voluntarily participated in the Interim Pilot program for substances intended for use in human food since 1998; notifiers have voluntarily participated in the Interim Pilot program for substances intended for use in animal food since 2010. By the end of 2015, we had filed over 600 GRAS notices for substances intended for use in human food and 18 GRAS notices for substances intended for use in animal food. The response to these programs suggests that notifiers consider the voluntary GRAS notification procedure a viable alternative to the voluntary GRAS petition process.

Through the GRAS notices we have already received, we have increased our awareness of the composition of the nation's food supply and the dietary exposure to GRAS substances, which helps us to ensure the safe use of substances added to food. The ongoing submission of GRAS notices provides evidence that our response to a GRAS notice can support the marketing of a food substance by the regulated industry. Notified substances include substances that are intended to address food safety problems (e.g., antimicrobial substances and substances intended to reduce acrylamide formation) and public health issues (e.g., substances that would reduce levels of sodium chloride in food). In addition, the letters we issue responding to GRAS notices demonstrate that we inform notifiers of any scientific or regulatory issues that call into question a notifier's conclusion of GRAS status, and stakeholders have ready access to those letters. As discussed in Response 81 of the preamble, we intend to increase the transparency of our response letters when a notifier asks us to cease to evaluate a GRAS notice.

In the years since we published the proposed rule, we have in part focused resources on postmarket actions with respect to the GRAS program, such as issuing a declaratory order announcing our final determination that there is no longer a consensus among qualified experts that partially hydrogenated oils are GRAS for any use in human food, as well as issuing warning letters regarding the use of caffeine as an added ingredient in alcoholic beverages. We also have taken other important public health actions with respect to substances used in food on the basis of the GRAS provision of the FD&C Act. For example, we recently announced an initiative to establish voluntary short-term and long-term goals for sodium reduction in a variety of identified categories of foods to address the excessive intake of sodium in the current population and promote improvements in public health (81 FR 35363, June 2, 2016). In addition, we recently held a public meeting in which we invited public comment on what should be included, changed,

or even excluded from our guidance entitled "Guidance for Industry and Other Stakeholders: Toxicological Principles for the Safety Assessment of Food Ingredients" (79 FR 64603, October 30, 2014); that guidance is intended to help interested parties understand our expectations regarding how to determine which toxicity studies are appropriate and regarding the design, conduct, and reporting of the results of toxicity studies and applies to assessing the safety of GRAS substances.

The final rule clarifies the criteria that notifiers must use when they consider whether a substance is GRAS under the conditions of its intended use. Making our expectations more clear will reduce uncertainty about the procedure and encourage notifiers to continue their participation in the voluntary GRAS notification procedure. Making our expectations more clear also will help notifiers prepare GRAS notices and will allow us to complete our evaluation within the timelines specified in the final rule.

Based on the response to the Interim Pilot programs, we assume that industry benefits from a more timely evaluation under the voluntary GRAS notification procedure than under the voluntary GRAS petition process. For example, during the Interim Pilot program for human food substances, we took an average of 200 days after filing a notice to send 588 response letters; we took an average of 7.9 years to complete rulemaking for 24 GRAS petitions. As expected with any pilot program, the Interim Pilot program for substances intended for use in human food evolved over time as parties discovered more efficient ways to comply with the program.

Although the Interim Pilot program for animal food has existed for a much shorter time than the program for human food, we see similar time savings with the GRAS notification procedure. Under this Interim Pilot program, we took an average of 276 days after filing a notice to send 18 response letters; we took an average of 4.9 years to complete rulemaking for the 3

previous GRAS petitions. We assume that notifiers will voluntarily participate in the GRAS notification procedure when the notifier expects to receive some benefit from the participation. The final rule clarifies our expectations about the information notifiers should submit with a GRAS notice for a substance intended for use in animal food. We expect that by removing some uncertainty that may have discouraged participation by notifiers in the animal food industry, the final rule will encourage participation of notifiers in the GRAS notification procedure for substances intended for use in animal food.

F. Distributional Effects

We estimate that the final rule will have no distributional effects.

G. International Effects

Foreign notifiers who voluntarily choose to submit GRAS notices to us must comply with the same requirements as domestic notifiers. Based on the GRAS notices filed since 1998, about 45 percent of the notifiers come from foreign establishments located in 29 countries. Table 10 shows a distribution of foreign notifiers by country; notifiers from Japan, Canada, The Netherlands and China represent about 50 percent of all foreign notifiers. Because the final rule will not change the incentives for foreign notifiers to submit GRAS notices to us, we anticipate that the final rule will have no international effects.

Table 10. Number and Share of Foreign Notifiers by Country

Country	Number of Foreign Notifiers	Share of Foreign Notifiers	Country	Number of Foreign Notifiers	Share of Foreign Notifiers
Japan	34	20%	South Korea	3	2%
Canada	27	16%	Hong Kong	2	1%
The Netherlands	14	8%	Sweden	2	1%
China	11	6%	Thailand	2	1%

Germany	10	6%	USA and China	2	1%
Spain	9	5%	Chile	1	1%
United Kingdom	7	4%	Iceland	1	1%
Australia	6	4%	Ireland	1	1%
France	5	3%	Italy	1	1%
India	5	3%	Luxembourg	1	1%
Israel	5	3%	Mexico	1	1%
Denmark	4	2%	Peru	1	1%
Belgium	3	2%	Singapore	1	1%
Finland	3	2%	Switzerland	1	1%
New Zealand	3	2%	The Netherlands and Germany	1	1%
Norway	3	2%	USA and Germany	1	1%

H. Uncertainty

The final rule replaces the voluntary GRAS petition process with a voluntary GRAS notification procedure. The incentives to voluntarily participate in the GRAS notification procedure remain unchanged. Firms will participate when they expect to receive a private benefit. For our final regulatory impact analysis, we base our estimates on the number of firms that submitted GRAS notices since 1998 and the number of GRAS petitions currently outstanding. To account for uncertainty, we used ranges for the number of affected firms and the incremental burden of the final rule once firms voluntarily decide to submit a GRAS notice.

As shown in table 11, the number of GRAS notices filed for substances intended for use in human food varies year to year, but on average has increased over time. The total number of notices strongly suggests that firms will continue to participate in the GRAS notification procedure for substances intended for use in human food.

Table 11. Number of GRAS Notices for Human Food Substances Filed by Filing Year

Filing Year	**Number of Notices Filed**	**Filing Year**	**Number of Notices Filed**

1998	12	2007	20
1999	23	2008	36
2000	30	2009	36
2001	28	2010	55
2002	26	2011	45
2003	23	2012	41
2004	20	2013	43
2005	26	2014	69
2006	30	2015	51

In comparison to GRAS notices for substances intended for use in human food, we had filed fewer than 20 GRAS notices by the end of 2015 for substances intended for use in animal food, with more than half of these filed in 2011. In addition, as shown in table 12, we filed no GRAS notices in 2015. The final rule clarifies our expectations and the type of information notifiers should include in their GRAS notices. This will remove some uncertainty that may have discouraged firms from submitting GRAS notices for substances intended for use in animal food in the past. Although uncertain, we expect that the number of GRAS notices for animal food substances will increase as firms gain experience with the GRAS notification procedure.

Table 12. Number of GRAS Notices for Animal Food Substances Filed by Filing Year

Filing Year	**Number of Notices Filed**
2010	2
2011	11
2012	1
2013	1
2014	3
2015	0

I. Analysis of Regulatory Alternatives to the Rule

Although we received no comments on the regulatory alternatives discussed in our preliminary regulatory impact analysis, several comments suggested that we retain the GRAS

affirmation petition process in addition to the GRAS notification procedure. Commenters suggested that they could use our GRAS affirmation to promote their substances in certain markets. This alternative would come with substantial costs—because the GRAS affirmation petition process requires rulemaking, which can take many years —without generating any social benefits. Although we lack information to estimate the costs and benefits of this alternative, we expect that the net social costs of this alternative would greatly exceed the net social costs of the final rule.

III. Final Regulatory Flexibility Analysis

The Regulatory Flexibility Act requires a Regulatory Flexibility Analysis (RFA) unless the Agency can certify that the final rule would have no significant impact on a substantial number of small entities. The Small Business Administration (SBA) establishes thresholds for small entities by North American Industry Classification System (NAICS); the SBA considers small any entity below these thresholds.

The final rule will affect all small entities that voluntarily participate in the GRAS notification procedure. We expect that this will primarily affect entities in the food manufacturing and chemical manufacturing industries. For manufacturing industries, SBA uses employment size to determine firm size. The threshold number of employees varies from 500 employees to 1,250 employees depending on the particular manufacturing sector. Although this may overestimate the number of small entities affected by the final rule, we use 500 employees as the cut-off between small and large entities. As shown in tables 13 and 14, we consider at least 98 percent of the food manufacturing establishments and 98 percent of chemical manufacturing establishment as small. However, the rule will not affect a substantial number of entities in these industries.

Table 13. Food Manufacturing Establishments by Employment Size (NAICS 311)

	Fewer than 20 Employees	20 to 99 Employees	100 to 499 Employees	500 or more Employees	Industry Total	Percent of Small
Number of Establishments	17,458	5,017	2,618	526	25,619	98%
Total value of shipments ($ mil)	$33,335	$140,709	$344,067	$221,162	$739,272	
Average per Establishment Value of Shipments ($ mil)	$1.9	$28.0	$131.4	$420.5	$28.9	

Source: 2012 Economic Census of the United States, EC1231SG2: Manufacturing: Summary Series: General Summary: Industry Statistics for Subsectors and Industries by Employment Size: 2012

Table 14. Chemical Manufacturing Establishments by Employment Size (NAICS 325)

	Fewer than 20 Employees	20 to 99 Employees	100 to 499 Employees	500 or more Employees	Industry Total	Percent of Small
Number of Establishments	7,851	3,888	1,367	211	13,317	98%
Total value of shipments and receipts for services ($ mil)	$29,370	$154,230	$336,760	$264,939	$785,300	
Average per Establishment Receipts ($m mil)	$3.7	$39.7	$246.3	$1,255.6	$59.0	

Source: 2012 Economic Census of the United States, EC1231SG2: Manufacturing: Summary Series: General Summary: Industry Statistics for Subsectors and Industries by Employment Size: 2012

We expect that profit-maximizing firms will only submit the GRAS notice when the private benefits equal or exceed the costs of preparing and submitting the GRAS notice, regardless of the size of the firm. Affected notifiers will incur one-time costs to read and understand the final rule and revise their SOPs. We estimate that these costs range from $1,300 to $4,830 for each notifier. Some notifiers will incur annual reporting costs ranging from $250 to $1,000. Even with our upper bound cost estimate, the per notifier annualized costs equal less than $1,700. This accounts for less than 0.3 percent for the smallest manufacturing establishments that employ fewer than 5 employees. Because affected notifiers will incur

minimal costs compared to their annual revenues, we certify that the final rule will not have a significant economic impact on a substantial number of small entities.