Substances Generally Recognized as Safe (GRAS) Notification Procedures

OMB Control No. 0910-0342
RIN 0910-AH15

Terms of Clearance: *In accordance with the terms of 5 CFR 1320, this ICR is approved for a period of three years. OMB notes that the Supporting Statement claims that the new form will be more efficient than the existing form, but it does not calculate a reduction in the burden on the public or a reduction in Agency processing time. Please examine this as the form is in use and consider updating these figures, as appropriate, when resubmitting to OMB.*

Response: Consistent with the rulemaking, Form FDA 3667 provides a standardized format for information being submitted to the agency. While we do not calculate a reduction in burden to respondents, we believe the standardized format will facilitate agency review of information being submitted so that a GRAS determination can be made.

A. Justification

1. Circumstances Making the Collection of Information Necessary

Section 409 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 348) establishes a premarket approval requirement for "food additives." Section 201(s) of the FD&C Act (21 U.S.C. 321) provides an exclusion to the definition of "food additive," and thus from the premarket approval requirement, for uses of substances that are GRAS by qualified experts. The Food and Drug Administration (FDA, the agency, or we) has issued a final rule implementing regulations that clarify the criteria for when the use of a substance in food for humans or animals is not subject to the premarket approval requirements of the FD&C Act because the substance is GRAS under the conditions of its intended use. The regulations also replace the voluntary GRAS affirmation petition process with a voluntary notification procedure under which any person may notify us of a conclusion that a substance is GRAS under the conditions of its intended use. Food additives that are not GRAS must obtain premarket approval. The clarified criteria for GRAS status should help stakeholders draw more informed conclusions about whether the intended conditions of use of a substance in food for humans or animals complies with the FD&C Act, and the notification procedure will enable stakeholders to be aware of whether we have questioned the basis of a conclusion of GRAS status.

As explained in the regulations, a GRAS notice must include the following:

PART NO.	INFORMATION TO BE INCLUDED
1	Signed statements and a certification
2	The identity, method of manufacture, specifications, and physical or technical effect of the notified substance
3	Dietary exposure to the notified substance
4	Self-limiting levels of use in circumstances where the amount of the notified substance that can be added to human food or animal food is limited because the food containing levels of the notified substance above a particular level would become unpalatable or technologically impractical

PART NO.	INFORMATION TO BE INCLUDED
5	The history of consumption of the substance for food use by a significant number of consumers (or animals in the case of animal food) prior to January 1, 1958, if a conclusion of GRAS status is based on common use of the substance in food prior to 1958
6	A narrative that provides the basis for the notifier's conclusion of GRAS status, including why the scientific data, information, methods, and principles described in the notice provide a basis for the conclusion that the notified substance is generally recognized, among qualified experts, to be safe under the conditions of its intended use
7	A list of the generally available data, information, and methods the notifier cites in the GRAS notice

Accordingly, FDA is requesting OMB approval of the information collection provisions associated with applicable regulations in parts 170 and 570 as revised by our final rule of August 17, 2016 (81 FR 54960) regarding the notification procedures for GRAS substances. These regulations implement the GRAS provision of section 201(s) of the FD&C Act in part 170 and part 570 for human food and animal food, respectively. We are also requesting approval of Form FDA 3667 entitled, "*Generally Recognized As Safe (GRAS) Notice*."

2. Purpose and Use of the Information Collection

The information submitted to us in a GRAS notice is necessary to allow us to administer efficiently the FD&C Act's various provisions that apply to the use of substances added to food, specifically with regard to whether a substance is GRAS under the conditions of its intended use or is a food additive subject to premarket review. We will use the information collected through the GRAS notification procedure to complete our evaluation within the timelines specified in the final rule.

Description of Respondents: Respondents to the collection of information are manufacturers of substances used in human food and animal food. As estimated in the Final Regulatory Impact Analysis (FRIA), we estimate there are 480 such respondents: approximately 340 to 460 notifiers for human food and approximately 10 to 20 notifiers for animal food.

3. Use of Improved Information Technology and Burden Reduction

We acknowledge that technology may not be available to every notifier and, thus, the regulations do not require the submission of an electronic copy. Instead, the regulations final provide that a notifier may submit a GRAS notice either in an electronic format that is accessible for our evaluation or on paper (see § 170.210(b)). Based on our review, we estimate 70% of submissions will be made electronically, while 30% will continue to be submitted in letter format.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection. Under the Meat and Poultry Inspection Acts, the United States Department of Agriculture's Food Safety and Inspection Service (USDA/FSIS) has regulatory authority for meat and poultry. FDA and USDA have signed a Memorandum of Understanding that provides for a coordinated evaluation process with FSIS when the intended conditions of use of a notified substance include use in a product or

products subject to regulation by USDA under statutes that it administers (75 FR 81536 at 81541-81542).

5. Impact on Small Businesses or Other Small Entities

We estimate ten percent (10%) of respondents are small businesses; however the regulations are applicable to all respondents. FDA aids small businesses in complying with its requirements through the Agency's Regional Small Business Representatives and through the scientific and administrative staffs within the Agency. FDA also provides a Small Business Guide on the Agency's website at http://www.fda.gov/oc/industry/.

6. Consequences of Collecting the Information Less Frequently

GRAS notifications are submitted only once.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

The information collection requirements are consistent with 5 CFR §1320.5, excepting extended retention of GRAS notification records. We believe this extended retention period is necessary because, under the regulations, notifiers submit a summary of information that provides the basis for a conclusion of GRAS status rather than the information itself. Although the rule does not specify any timeframe to retain the data and information that support the conclusion of GRAS status, preservation of the data and information that are the basis for the conclusion of GRAS status represents prudent practice for those who claim an exclusion from a statutory requirement regardless of whether the person subsequently notifies FDA.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In compliance with the Paperwork Reduction Act of 1995 (44 U.S.C. 3506(c)(2)(B)), FDA solicited public comment on the information collection provisions in its proposed rule of April 17, 1997 (62 FR 18938). In 2010, we reopened the comment period for the proposed rule to update comments and to solicit comment on specific issues (75 FR 81536, December 28, 2010). While some comments were received suggesting specific modifications and different approaches and questioning the utility of the information, no comments suggested that we modify burden estimates. All comments received in response to the rulemaking may be found in the Agency docket, FDA-1997-N-0020 (formerly 97N-0103), and are addressed in the agency's final rule that published August 17, 2016 (81 FR 54960).

9. Explanation of Any Payment or Gift to Respondents

FDA does not provide any payments or gifts to respondents.

10. Assurance of Confidentiality Provided to Respondents

In accordance with our public information regulations in § 20.85 (Disclosure to other Federal government departments and agencies), we can share confidential commercial information with another Federal agency pursuant to a written agreement that the record will not be further disclosed. The amended MOU between FDA and USDA's FSIS now provides for FDA to share with FSIS confidential commercial information in a submission such as a GRAS notice. We generally cannot share trade secret information with other Federal agencies under section 301(j) of the FD&C Act (21 U.S.C. 331(j)), and therefore we would need the notifier's authorization to share this information with FSIS. For efficiency in administering the coordinated evaluation of a GRAS notice with FSIS, we have added a requirement for a notifier who submits a GRAS notice that we would send to FSIS to include in part 1 of the GRAS notice a statement as to whether the notifier: (1) Authorizes us to send any trade secrets to FSIS; or (2) asks us to exclude any trade secrets from the copy of the GRAS notice that we will send to FSIS (see § 170.225(c)(11)). Under the provisions that make the coordinated evaluation of a GRAS notice with FSIS explicit, we will exclude any trade secrets unless the notifier has authorized us to send trade secret information to FSIS (see § 170.270). These provisions will enable us, with the notifier's authorization, to share a GRAS notice that includes trade secret information with FSIS without first redacting the GRAS notice to remove the trade secret information and, thus, will reduce the time it takes for us to provide FSIS with a copy of the GRAS notice. These provisions also will clarify the notifier's expectations regarding whether we should share trade secret information with FSIS and, thus, require us to redact the trade secret information from the copy we send to FSIS when consistent with the notifier's express wishes.

Information submitted to FDA in a GRAS notice may contain trade secret and commercial confidential information. As a result, all files are maintained in a secured area. Form FDA 3667, its instructions, and related guidance, provide instructions for assisting FDA with protecting confidential information. A notifier may choose to provide a redacted copy of the GRAS notice, identifying that information that the submitter views as trade secret or as confidential commercial or financial information.

Only information that is releasable under the agency's regulations in 21 CFR part 20 would be released to the public. This information is also safeguarded by Section 301(j) of the FD&C Act and would be protected from disclosure under FOIA under sections 552(a) and (b) (5 U.S.C. 552(a) and (b)).

11. Justification for Sensitive Questions

This information collection does not involve any questions that are of a personally sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

FDA estimates the burden of this information collection as follows:

12 a. Annualized Hour Burden Estimate

One-Time Reporting Burden

Table 1 shows the estimated one-time reporting burden associated with the final rule. We expect that all respondents to the information collection will spend time reading and understanding the requirements of the final rule and revising standard operating procedures for preparing and submitting GRAS notices. As noted, we estimate that approximately 340 to 460 notifiers (for human food) and approximately 10 to 20 notifiers (for animal food) will be affected by the final rule. We use the upper-bound estimates of 460 and 20 respondents as shown in rows 1 and 2. We estimate that it will take from 20 to 80 hours for respondents to perform this action. We use the upper-bound estimate of 80 hours as shown in rows 1 and 2. Of the 480 affected respondents, some will have outstanding GRAS petitions. Firms with outstanding GRAS petitions regarding substances intended for use in human food may choose to submit GRAS notices and incorporate the information included in their petition. As estimated in the Final Regulatory Impact Analysis, up to 45 petitions (for human food) will be submitted as GRAS notices and incorporated. We use the upper-bound estimate of 45 as shown in row 3. To account for the additional effort by these firms, we include the one-time burden to prepare and submit a GRAS notice for all outstanding petitions. Because there are no outstanding GRAS petitions regarding substances intended for use in animal food, we do not account for any burden for the submission of a GRAS notice that incorporates a GRAS petition regarding a substance intended for use in animal food. We estimate that respondents will spend between 170 and 190 hours to submit GRAS notices for each outstanding petition and have used, therefore, an average estimate of 185 hours as shown in row 3.

Table 1 – Estimated One-time Reporting Burden[1]

Activity; 21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Notifier's review of final rule and revision of procedures for preparing and submitting GRAS notices for human food; 170.210 through 170.270	460	1	460	80	36,800
Notifier's review of final rule and revision of procedures for preparing and submitting GRAS notices for animal food; 570.210 through 570.270	20	1	20	80	1,600
Prepare and submit GRAS notice for an outstanding GRAS petition; 170.285	45	1	45	185	8,325
TOTAL			525		46,725

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

Recurring Reporting Burden

Table 2 shows the estimated recurring annual reporting burden associated with the information collection. As previously discussed, the rulemaking replaces 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 for its intended use remains unchanged by the final rule. However, the regulations require that firms submit some additional information to support the conclusions found within their notices. The additional information might include an amendment (§§ 170.260 and 570.260); a supplement (§§ 170.280 and 570.280); a request for FDA to cease to evaluate a GRAS notice (§§ 170.260 and 570.260); an incorporation into a GRAS notice (§§ 170.215 and 570.215); and, information required when the intended conditions of use of a notified substance includes use in a product subject to regulation by FSIS, including authorization to us to share any trade secrets with FSIS (§ 170.270). Because the amount of additional information may vary, we estimate that respondents will spend between 155 and 170 hours to prepare and submit each notice. Using the upper-bound figure of 170 hours, we therefore estimate that the 50 notifiers for human food and 25 notifiers for animal food will expend 12,750 hours annually as shown, respectively, in rows 1 and 2.

Table 2 – Estimated Annual Reporting Burden[1]

Activity; 21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
GRAS notification procedure for human food;170.210 through 170.270	50	1	50	170	8,500
GRAS notification procedure for animal food; 570.210 through 570.270	25	1	25	170	4,250
TOTAL			75		12,750

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

Recordkeeping

The rulemaking does contain recordkeeping requirements. We believe that documentation used by respondents in support of a conclusion of GRAS status is information that is collected and retained as a part of usual and customary business practices for a firm engaged in the manufacture of substances used in human food and animal food. While the regulations do not specify a timeframe to retain the data and information that support the conclusion of GRAS status, preservation of the data and information that are the basis for the conclusion of GRAS status represents prudent practice for those who claim an exclusion from a statutory requirement regardless of whether the person subsequently notifies FDA. Accordingly, no estimated burden is provided for these activities (5 CFR 1320.3(b)(2)).

This final rule also refers to other currently approved collections of information found in FDA regulations. These collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR 25.32(i) are approved under OMB control number 0910-0541. The collections of information in 21 CFR 10.33 are approved under OMB control number 0910-0191.

12 b. Annualized Cost Burden Estimate

As estimated in the Final Regulatory Impact Analysis, the total annualized cost burden is $9,953.49 to $14,965.90, as calculated below.

Activity	Lower Bound Estimate	Upper bound Estimate
Cost to Read and Understand the Final Rule	$720.24	$1,350.45
Cost to Revise SOPs	$580.15	$3,480.90
Cost to Prepare a GRAS Notice for an outstanding petition	$8,403.10	$9,144.55
Incremental costs for additional information	$250.00	$990.00
Total	$9,953.49	$14,965.90

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no capital, start-up, operating, or maintenance costs associated with this information collection.

14. Annualized Cost to Federal Government

FDA estimates it will direct approximately 4 full time equivalent positions (FTE's) to the GRAS notification procedure for human foods. Due to the smaller number of notices anticipated for animal food, only 3 FTE are expected to be devoted to processing the notices submitted to CVM. Based on an average cost of $172,000 per fully supported position ($86,000 increased by 100 percent to account for overhead), the cost of processing GRAS notifications would be $1,204,000 per year ($172,000 x 7).

15. Explanation for Program Changes or Adjustments

The information collection includes a one-time burden of **525 responses and 46,725 hours** to reflect current rulemaking. Upon its next request for renewal of the information collection the agency expects this burden to have been realized. Meanwhile, the annual reporting burden reflects an adjustment of **15 additional responses and 2,850 additional hours**. We attribute the increase to an increase in the number of respondents to the information collection.

16. Plans for Tabulation and Publication and Project Time Schedule

The final rule specifies that we will make the following readily accessible to the public: (1) A list of filed GRAS notices, including the information described in certain of the signed statements that are included in Part 1 of a GRAS notice (i.e., § 170.225(c)(2) through (c)(5)); and (2) The text of any letter that we issue under § 170.265(b)(1) (our response to a GRAS notice based on our evaluation of the notice), § 170.265(b)(3) (a letter if we grant a request that we cease to evaluate a GRAS notice), or § 170.265(c) (a subsequent letter that we send about a GRAS notice). (See § 170.275(b).) We are not specifying that the mechanism for us to do so is through an "Inventory" because the procedure we used to make this information readily accessible to the

public evolved over time during the Interim Pilot program, and may continue to evolve.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

Display of OMB expiration date is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.