Substances Generally Recognized as Safe (GRAS): Notification Procedure

0910-0342

SUPPORTING STATEMENT

Terms of Clearance: None.

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 exemption from the definition of "food additive," and thus from the premarket approval requirement, for uses of substances that are GRAS by qualified experts. In the Federal Register of April 17, 1997 (62 FR 18938) (the 1997 proposed rule), FDA published a proposed rule that would establish a voluntary procedure whereby manufacturers would notify FDA about a view that a particular use (or uses) of a substance is not subject to the statutory premarket approval requirements based on a determination that such use is GRAS. The proposed regulations (proposed 21 CFR 170.36 (§ 170.36) and 21 CFR 570.36 (§ 570.36)) provide a standard format for the voluntary submission of a notice. The notice would include a detailed summary of the data and information that support the GRAS determination, and the notifier would maintain a record of such data and information. FDA would make the information describing the subject of the GRAS notice, and the agency's response to the notice, available in a publicly accessible file; the entire GRAS notice would be publicly available consistent with the Freedom of Information Act (FOIA) and other Federal disclosure statutes. In the Federal Register of December 28, 2010 (75 FR 81536) (the GRAS reopener), FDA announced the reopening of the comment period for the 1997 proposed rule. The agency requested that comments be submitted by March 28, 2011.

FDA is requesting an extension of the approval of the information collection, including approval of new FDA Form 3667, developed to facilitate the submission process of GRAS notices submitted to the Agency's Center for Food Safety and Applied Nutrition (CFSAN). A draft of new Form FDA 3667, entitled "Generally Recognized as Safe (GRAS) Notice," and is available at: http://www.fda.gov/downloads/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodIngredientsandPackaging/RegulatorySubmissions/UCM199312.pdf. The form, and elements that would be prepared as attachments to the form, may be submitted in electronic format via the Electronic Submission Gateway (ESG), or may be submitted in paper format, or as electronic files on physical media with paper signature page. CFSAN expects that most if not all businesses filing GRAS notices in the next three years will choose to take advantage of the option of electronically submitting their GRAS notice. Thus, the burden estimate in Table 1, Line 1 is based on the expectation of one hundred percent (100%) participation in the electronic submission process. FDA's Center for Veterinary Medicine (CVM) continues to comply with the GRAS Pilot Program procedures announced on June 4, 2010 (75 FR 31800) that instructs participants to provide GRAS notices in letter format to the agency. While FDA does not expect proposed Form FDA 3667 to reduce reporting time for notifiers, the Agency does expect the form to help expedite the Agency's review of the information being submitted.

GRAS notices submitted to CFSAN include the following information on Form FDA 3667 and in attachments to the form:

A. Introductory Information About the Submission
   - Whether the GRAS notice submission is a new GRAS notice, or an amendment or supplement to a previously transmitted GRAS notice;
   - Whether the notifier has determined that all files provided in an electronic transmission are free of computer viruses;
   - The date of the notifier's most recent meeting with FDA before transmitting a new GRAS notice; and
   - The date of any correspondence, sent to the notifier by FDA, relevant to an amendment or supplement the notifier is transmitting;

B. Information About the Notifier
   - The name of and contact information for the notifier, including the identity of the contact person and the company name (if applicable); and
   - The name of and contact information for any agent or attorney who is authorized to act on behalf of the notifier.

C. General Administrative Information
   - The name of the substance that is the subject of the GRAS notice submission;
   - The format of the submission (i.e., paper, electronic, or electronic with a paper signature page);
   - The mode of transmission of any electronic submission (i.e., ESG or transmission on physical media such as CD-ROM or DVD);
   - Whether the notifier is referring us to information already in our files;
   - The statutory basis for the notifier's determination of GRAS status;
   - Whether the notifier has designated in its submission any information as trade secret or as confidential commercial or financial information; and
   - Whether the notifier has attached a redacted copy of some or all of the submission.

D. Intended Use
   - The intended conditions of use of the notified substance.

E. Identity
   - Information that identifies the notified substance. For example, there may be a chemical name and formula and a standardized registry number.

F. Checklist of Other Elements Not Completed Directly on Form FDA 3667
   - Any additional information about identity not previously covered;
   - Method of manufacture;
   - Specifications for food-grade material;
   - Dietary exposure;
   - Self-limiting levels of use;
   - Common use in food before 1958 (if applicable);
   - Comprehensive discussion of the basis for the determination of GRAS status; and
   - Bibliography.

Form FDA 3667 also requires the signature of a responsible official (or agent or attorney) and a list of attachments.

FDA requests OMB approval of new Form FDA 3667 and approval of the information collections for GRAS notification procedures set forth in proposed §§ 170.36 and 570.36, which describe the

information that FDA considers important in evaluating whether a notice provides a sufficient basis for a GRAS determination and the proposed recordkeeping requirements.

2. Purpose and Use of the Information Collection

The information is used by FDA to evaluate whether the notice provides a sufficient basis for a conclusion of GRAS status and whether information in the notice or otherwise available to FDA raises issues of public health significance that lead the agency to question whether use of the substance is GRAS.

Description of Respondents: The respondents to this collection of information are manufacturers of substances used in food and feed. Respondents are from the private sector (for-profit businesses).

3. Use of Improved Information Technology and Burden Reduction

As noted above, FDA has recently developed new Form FDA 3667, which interested persons may use to transmit their GRAS notice to CFSAN. GRAS notices submitted to CVM continue to be in letter format. Therefore, the agency estimates that approximately 70% of submissions will be made electronically, while 30% will continue to be submitted in letter format under the established pilot procedures over the next three years.

4. Efforts to Identify Duplication and Use of Similar Information

No duplication of Federal regulations is likely. 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. Both USDA/FSIS (64 FR 72167; December 23, 1999) and FDA (65 FR 51758; August 25, 2000) have amended their regulations to harmonize and improve the efficiency of the procedures used by USDA/FSIS and FDA with respect to reviewing and approving the use of substances in meat and poultry. In general, USDA/FSIS evaluates food substances as to their suitability for specified uses in meat or poultry products. When USDA/FSIS receives a request to evaluate the suitability of a substance for use in meat or poultry products, USDA/FSIS consults with FDA about the regulatory status of the substance. When FDA receives a GRAS notice that includes a use in meat or poultry products, FDA consults with USDA/FSIS and provides to the notifier feedback from USDA/FSIS about the suitability of the substance for use in meat or poultry products. If USDA/FSIS informs FDA that the use of the substance in meat or poultry products requires rulemaking under the statutes that FSIS implements, FDA provides that information to the notifier. FDA and USDA have now signed a Memorandum of Understanding regarding these procedures (http://www.fsis.usda.gov/OA/topics/mou_fda.htm).

5. Impact on Small Businesses or Other Small Entities

FDA estimates that ten percent (10 %) of respondents are small businesses. The proposed notification procedures are no more burdensome for small businesses than for large. The proposed requirements are the minimum requirements to provide a sufficient basis for a conclusion of GRAS status. FDA's GRAS notices minimize the burden on all businesses, including small businesses, by providing that the notifier submit a detailed summary of the data and information, rather than the data and information itself, that are the basis for the conclusion of GRAS status. 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 has provided a Small Business Guide on the agency's website at http://www.fda.gov/oc/industry/.

6. Consequences of Collecting the Information Less Frequently

Data collection occurs occasionally. The data in a GRAS notification are submitted only once and therefore cannot be collected less frequently.

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

The proposed GRAS notification program would require that records be retained for more than three years. Under the proposal, notifiers would supply a detailed summary of the information that provides the basis for a conclusion of GRAS status rather than the information itself. As a result, FDA proposed to require that the notifier retain the information that forms the basis for the conclusion of GRAS status and sign a statement that such information is available for FDA review and copying at reasonable times or will be sent to FDA upon request. There are no other special circumstances associated with this collection of information.

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

In accordance with 5 CFR 1320.8(d), FDA published a 60-day notice for public comment in the Federal Register of January 18, 2012 (77 FR 2552). No comments were received.

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

FDA proposed that a particular section (i.e., the "GRAS exemption claim") of a notice be immediately available for public disclosure on the date the notice is filed. FDA also proposed that all remaining data and information in a notice will become available for public disclosure, in accordance with 21 CFR part 20, on the date of receipt of the notice. The general recognition standard signifies that neither the proposed use of the substance nor the critical information needed to establish its safety are confidential. Therefore, FDA presumes that a notice will not contain any information that is protected from public disclosure. Moreover, because a GRAS substance may be marketed without prior approval, FDA presumes that, in most cases, submission of a notice will not reflect the notifier's plans about the timing of commercialization, which is arguably confidential commercial information (21 CFR 20.61(b)), because a notifier may market a substance at any time before or after notifying FDA. FDA makes the information in the GRAS exemption claim and the agency's response to the notice accessible to the public through an electronic inventory of GRAS notices posted on the agency's Web site at http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=grasListing.

FDA believes that, in most cases, neither the existence of a GRAS notice, nor most or all of its content, would satisfy the criteria for exemption from disclosure. However, 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

submitter 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

Description of Respondents: The respondents to this collection of information are manufacturers of substances used in food and feed.

12 a. Annualized Hour Burden Estimate

FDA estimates the burden of this collection of information as follows:

Table 1.--Estimated Annual Reporting Burden[1]

21 CFR Section	FDA Form No. [2]	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
170.36 (CFSAN)	FDA 3667[3]	40	1	40	150	6,000
570.36 (CVM)	N/A	20	1	20	150	3,000
Total						9,000

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Only CFSAN uses Form FDA 3667. CVM continues to comply with the GRAS Pilot Program procedures announced on June 4, 2010 (75 FR 31800).
[3] Form FDA 3667 may be submitted electronically via the ESG.

Table 2.--Estimated Annual Recordkeeping Burden[1]					
21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
170.36(c)(v) (CFSAN)	40	1	40	15	600
570.36(c)(v) (CVM)	20	1	20	15	300
Total					900

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

As noted, CFSAN estimates that all of the future Form FDA 3667 submissions will be made electronically via the ESG. While FDA does not charge for the use of the ESG, FDA requires respondents to obtain a public key infrastructure (PKI) certificate in order to set up the account. This can be obtained in-house or outsourced by purchasing a public key certificate that is valid for 1 year to 3 years. The certificate typically costs from $20-$30.

Both CFSAN and CVM receive submissions that are intended by the submitter to be GRAS notices. Not all of the submissions received contain sufficient information to be filed by the agency as GRAS notices. In the December 28, 2010, GRAS reopener, FDA requested comment on its GRAS submission filing decision process and described its current preliminary review process of GRAS submissions (75 FR 81536, at 81543). Therefore, the agency is basing the following estimates on the number of GRAS notices that have been filed by the relevant Center.

In the 1997 proposed rule, FDA estimated that CFSAN would file approximately 50 GRAS notices per year and that the Center for Veterinary Medicine (CVM) would file approximately 10 GRAS notices per year. Approval for the GRAS notification program was granted by OMB on June 16, 1997, under OMB control number 0910-0342. In 2009, FDA's estimate of the annual number of GRAS notices that will be filed by CFSAN and CVM was revised downward from the original PRA approval, based on the actual number of GRAS notices filed by CFSAN from 1998 to 2008. In 2009, FDA sought and OMB approved an estimate that CFSAN would file 25 GRAS notices and CVM would file 5 GRAS notices. On June 4, 2010 CVM announced the beginning of a GRAS Pilot Program (75 FR 31800). This notice stated that the revised estimate in the 2009 PRA approval reflected FDA's best judgment at the time as to the number of notices CVM will file annually through this pilot program.

For purposes of this revision, CFSAN and CVM are re-evaluating their estimates of the annual number of GRAS notices that will be received by CFSAN and CVM in the next three years, 2012 through 2015. CFSAN filed 365 GRAS notices during the 13-year period from 1998 through 2010, for an average of approximately 28 GRAS notices per year. However, recent years have seen an increase in the number of GRAS notices filed, with 36 notices filed in both 2008 and 2009 and 55 notices in 2010. Based on an approximate average from the last three years, FDA is revising its estimate of the annual number of GRAS notices filed by CFSAN to be 40 or less. CFSAN expects that most if not all businesses filing GRAS notices in the next three years will choose to take advantage of the option of electronically submitting their GRAS notice. We expect participation to be 100% thus the estimate in Table 1 is based on the burden of that experience. FDA also is

revising its estimate of the annual number of GRAS notices submitted to CVM. As noted, on June 4, 2010 CVM announced the beginning of a GRAS Pilot Program. From June 2010 to October 2011, CVM filed 13 GRAS notices. Based on this experience, FDA is revising its estimate of the annual number of GRAS notices filed by CVM to be 20 or less.

In the 1997 proposed rule, FDA estimated that the notification procedures would require 150 hours per response for the reporting burdens and 15 hours per response for the recordkeeping burdens for both proposed sections (§§ 170.36 and 570.36). FDA is retaining these estimates for this request. The availability of the form, and the opportunity to provide the information in electronic format, could reduce this estimate. However, as a conservative approach for the purpose of this analysis, FDA is assuming that the availability of the form and the opportunity to submit the information in electronic format will have no effect on the average time to prepare a GRAS notification.

12 b. Annualized Cost Burden Estimate

FDA estimates the annualized burden hour cost to respondents for this collection of information to be approximately $872,784. FDA estimates a respondent's average wage to be that of a Federal government employee at the GS-13/Step-2 rate for the Washington-Baltimore locality pay area for the year 2012, which is $44.08 per hour. To account for overhead, this cost is increased by 100 percent, which is $88.16 per hour. Thus, the annual wage cost for completion and submission of GRAS notifications is approximately $872,784 (9,900 hours x $88.16 per hour). In addition, while FDA does not charge for the use of the ESG, FDA requires respondents to obtain a public key infrastructure (PKI) certificate in order to set up the account. This can be obtained in-house or outsourced by purchasing a public key certificate that is valid for 1 year to 3 years. The certificate typically costs from $20-$30.

13. Estimates of Other Total Annual Cost Burden to Respondents and Record Keepers

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

14. Annualized Cost to Federal Government

FDA is estimating that the agency 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 is expected to be devoted to processing the notices submitted to CVM. Based on an average cost of $168,090 per fully supported position ($84,045 increased by 100 percent to account for overhead), the cost of processing GRAS notifications would be $1,176,630 per year ($168,090 x 7).

15. Explanation for Program Changes or Adjustments

FDA is requesting an extension of approval for this ICR, for which there is an increase in burden. The burden change is due to an adjustment based on the number of GRAS notices received by the agency from 2008 to 2011. Specifically, responses under 21 CFR 170.36 increased from 25 to 40, (an increase of 15 responses) and caused the associated annual hour burden to increase by 2,475 hours. We are characterizing the increase as an adjustment because it is based on an increase in the number of GRAS notices submitted to CFSAN, caused by an increase in the number of firms submitting such notices. Similarly, responses under 21 CFR 570.36 increased from 5 to 20 (an increase of 15 responses) and caused the associated annual hour burden to increase by 2,475 hours.

We are characterizing the increase as an adjustment because it is based on an increase in the number of GRAS notices submitted to CVM, caused by an increase in the number of firms submitting such notices. In total, the annual responses increased by 30 and the hour burden increased by 4,950.

As described in Q1, FDA is also requesting approval of a new form: FDA Form 3667. Although the form is new, it merely creates a template for reporting; the information is identical to what respondents were previously required to provide to FDA. Therefore, we do not believe that the new form will have any effect on the burden of this collection.

16. Plans for Tabulation and Publication and Project Time Schedule

FDA proposed to make readily accessible to the public the information in a section of the notice called the "GRAS exemption claim" and the agency's response to the notice. At this time, FDA is making this information accessible through an electronic inventory of GRAS notices, available at http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=grasListing.

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

There are no reasons why display of the expiration date for OMB approval of the information collection would be inappropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.