Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced by New Plant Varieties Intended for Food Use

0910-0583

SUPPORTING STATEMENT

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

Since May 29, 1992, when FDA issued a policy statement on foods derived from new plant varieties, FDA has encouraged developers of new plant varieties, including those varieties that are developed through biotechnology, to consult with FDA early in the development process to discuss possible scientific and regulatory issues that might arise (57 FR 22984). The guidance entitled, "Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced by New Plant Varieties Intended for Food Use," continues to foster early communication by encouraging developers to submit to FDA their evaluation of the food safety of their new protein. Such communication helps to ensure that any potential food safety issues regarding a new protein in a new plant variety are resolved early in development, prior to any possible inadvertent introduction into the food supply of material from that plant variety. FDA believes that any food safety concern related to such material entering the food supply would be limited to the potential that a new protein in food from the plant variety could cause an allergic reaction in susceptible individuals or could be a toxin. The guidance describes the procedures for early food safety evaluation of new proteins in new plant varieties, including bioengineered food plants, and the procedures for communicating with FDA about the safety evaluation.

FDA has recently developed a form that interested persons may use to transmit their submission to the Office of Food Additive Safety in the Center for Food Safety and Applied Nutrition. New Form FDA 3666, a draft of which is available at http://www.fda.gov/downloads/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodIngredientsandPackaging/RegulatorySubmissions/UCM199325.pdf, is entitled, "Early Food Safety Evaluation of a New Non-Pesticidal Protein Produced by a New Plant Variety (New Protein Consultation)" and may be used in lieu of a cover letter for a New Protein Consultation (NPC). Form FDA 3666 prompts a submitter to include certain elements of a NPC in a standard format and helps the respondent organize their submission to focus on the information needed for FDA's safety review. 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. The information is used by FDA to evaluate the food safety of a specific new protein produced by a new plant variety.

The NPC submitted to FDA includes the following information on Form FDA 3666 and in attachments to the form:

A. Introductory Information About the Submission

- Whether the NPC submission is a new submission, or an amendment or supplement to a previously established NPC;
- Whether the submitter has determined that all files provided in an electronic transmission are free of computer viruses;
- The date of the submitter's most recent meeting (if any) with FDA before transmitting a new NPC submission; and
- The date of any correspondence, sent to the submitter by FDA, relevant to an amendment or supplement the submitter is transmitting.

B. Information About the Submitter

- The name of and contact information for the submitter, 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 submitter.

C. General Administrative Information

- The title of the 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 submitter is referring us to information already in our files;
- Whether the submitter has designated in its submission any information as trade secret or as confidential commercial or financial information; and
- Whether the submitter has attached a redacted copy of some or all of the submission.

D. Information about the New Protein

- The name of the new protein;
- Any requested registry designations for the new protein; and
- The purpose or intended technical effect of the new protein.

E. Information about Genetic Material

- Information about the introduced genetic material (including identity and source).

F. The Scientific Evaluation of the Food Safety of the New Protein

The submitter indicates:

- Whether there is a history of safe use of the new protein in food or feed;
- Whether the submitter has included an assessment of the amino acid similarity between the new protein and known allergens and toxins;
- Whether the submitter has included information about the overall stability of the protein, and the resistance of the protein to enzymatic degradation using appropriate in vitro assays; and
- Whether the submitter has included any other information for FDA to consider in evaluating a NPC.

Form FDA 3666 also requires the signature of a responsible official (or agent or attorney) and a list of attachments.

FDA reviews NPCs under the broad statutory authority of the FDA to protect the public health by ensuring that foods are safe, wholesome, sanitary, and properly labeled found in section 903 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. Section 393), as well as the authority found in the food additive provisions in sections 201(s) and 409 of the act (21 U.S.C. Sections 321(s) and 348) and in the adulterated food provisions in section 402 of the act (21 U.S.C. Section 342).

FDA requests OMB approval of new Form FDA 3666 and extension of approval of the information collection provisions in the guidance entitled, "Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced by New Plant Varieties Intended for Food Use."

2. Purpose and Use of the Information Collection

NPCs are reviewed by FDA scientific personnel to ascertain that the data establish the identity of the specific new proteins in new plant varieties, including bioengineered food plants, and support the developer's determination that the new protein is safe for use in food or feed and is in compliance with all applicable requirements of the the Federal Food, Drug, and Cosmetic Act (FD&C Act).

Description of Respondents: The respondents to this collection of information are developers of new plant varieties intended for food use. Respondents are from the private sector (for-profit businesses, as well as not-for-profit institutions) and from the Federal government.

3. Use of Improved Information Technology and Burden Reduction

As noted above, FDA has recently developed new Form FDA 3666, which interested persons may use to transmit their NPC. The form, and elements that would be prepared as attachments to the form, may be submitted in electronic format via the ESG, or may be submitted in paper format, or as electronic files on physical media with paper signature page. The agency estimates that all of the NPCs (100%) will be submitted electronically in the next three years.

4. Efforts to Identify Duplication and Use of Similar Information

FDA procedures prevent duplicative collection of this information. FDA makes submissions of NPCs, and FDA's responses thereto, easily accessible to the public via the Internet. If a protein has been evaluated in a NPC and no safety concerns are identified, we would not expect an additional NPC to be submitted if the same protein is introduced into another plant species. Also, if a protein has previously been reviewed as part of a biotechnology consultation (approved by OMB under control number 0910-0704) and there were no safety concerns identified, we would not expect the submission of a NPC for such a protein.

FDA continues to work with the U.S. Environmental Protection Agency (EPA) and the U.S. Department of Agriculture (USDA) to eliminate areas of duplicate data collection and evaluation. Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136 et seq.), EPA has authority to regulate all pesticides, regardless of how they are made or their mode of action. FDA's NPC applies to non-pesticidal proteins and is not duplicative with EPA responsibilities.

Many plants developed using recombinant DNA (rDNA) technology are considered "regulated articles" under regulations of USDA's Animal and Plant Health Inspection Service (APHIS) (7 CFR Part 340), which regulates the introduction of certain "genetically engineered" plants into the environment. A developer must obtain authorization from APHIS to field test such crops and, depending on the nature of the crop, a developer files either a permit application or a notification. In contrast, FDA requests a submission of data and information concerning the food safety of a specific new protein produced in a new plant variety. Therefore, although a submission to APHIS would include some information, such as the name of the company and the identity of the protein, which would be included in the information requested by FDA in a NPC, the submission is not duplicative.

5. Impact on Small Businesses or Other Small Entities

FDA estimates that five percent (5 %) of respondents are small businesses. Most of respondent companies are multinationals with hundreds of millions of dollars in annual sales and do not meet the criteria for a small business. However, at least one of the companies that have consulted with FDA would meet the small entity definitions.

FDA's NPC minimizes the reporting burden on all businesses, including small businesses, by providing that the developer submit a summary of data and information, rather than the data and information itself. There is no burden to the developer for developing the data and information that underlie the new protein evaluation because they would have already generated such data and information to ensure that the protein is safe and is in compliance with all applicable requirements of the FD&C Act. 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 NPC are submitted only once for each specific new protein and therefore cannot be collected less frequently.

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

There are no 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 May 15, 2012 (77 FR 28602). No comments were received.

9. Explanation of Any Payment or Gift to Respondents

FDA does not provide any payment or gifts to respondents.

10. Assurance of Confidentiality Provided to Respondents

FDA believes that, in most cases, neither the existence of a NPC, nor most or all of its content, would satisfy the criteria for exemption from disclosure. However, Information submitted to FDA in a NPC may contain trade secret and commercial confidential information. As a result, all files are maintained in a secured area. Form FDA 3666, 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 NPC, 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 act and would be protected from disclosure under the Freedom of Information Act (FOIA) under sections 552(a) and (b) (5 U.S.C. 552(a) and (b)). At this time, we do not proactively disclose the submission of a NPC until after the submitter completes the consultation procedure. After the consultation is complete, we place on the FDA Internet site the redacted copy of the NPC and an electronic version of the agency response to the submitter (http://www.fda.gov/Food/Biotechnology/Submissions/default.htm).

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 developers of new plant varieties intended for food use.

12 a. Annualized Hour Burden Estimate

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

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

Category	FDA Form No. [2]	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
First four data components	Form FDA 3666	20	1	20	4	80
Two other data components	Form FDA 3666	20	1	20	16	320
Total						400

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Form FDA 3666 may be submitted electronically via the ESG.

The estimated number of annual responses and average burden per response are based on FDA's experience with early food safety evaluations submitted in the past 3 years. Completing an early food safety evaluation for a new protein from a new plant variety is a one-time burden (one

evaluation per new protein). Based on its experience over the past 3 years, FDA estimates that approximately 20 developers will choose to complete an early food safety evaluation for their new plant protein, for a total of 20 responses annually. Many developers of novel plants may choose not to submit an evaluation because the field testing of a plant containing a new protein is conducted in such a way (e.g., on such a small scale, or in such isolated conditions, etc.) that cross-pollination with traditional crops or commingling of plant material is not likely to be an issue. Also, other developers may have previously communicated with FDA about the food safety of a new plant protein, for example, when the same protein was expressed in a different crop.

The early food safety evaluation for new proteins includes six main data components. Four of these data components are easily and quickly obtainable, having to do with the identity and source of the protein. FDA estimates that completing these data components will take about 4 hours per NPC. FDA estimates the reporting burden for the first four data components to be 80 hours (4 hours x 20 responses).

Two data components ask for original data to be generated. One data component consists of a bioinformatics analysis which can be performed using publicly available databases. The other data component involves "wet" lab work to assess the new protein's stability and the resistance of the protein to enzymatic degradation using appropriate in vitro assays (protein digestibility study). The paperwork burden of these two data components consists of the time it takes the company to assemble the information on these two data components and include it in a NPC. FDA estimates that completing these data components will take about 16 hours per NPC. FDA estimates the reporting burden for the two other data components to be 320 hours (16 hours x 20 responses). Thus, FDA estimates the total annual hour burden for this collection of information to be 400 hours.

FDA expects that most if not all businesses filing NPCs in the next three years will choose to take advantage of the option of electronic submission via the ESG. Thus, the burden estimates in Table 1 are based on the expectation of one hundred percent (100%) participation in the electronic submission process. The opportunity to provide the information in electronic format could reduce the agency's previous estimates for the time to prepare each submission. However, as a conservative approach for the purpose of this analysis, FDA is assuming that the availability of new Form FDA 3666 and the opportunity to submit the information in electronic format will have no effect on the average time to prepare a submission.

As requested in part III of Form FDA 3666, section 5, this submission may incorporate by reference information from a previous submission to FDA (biotechnology notification file (BNF), new protein consultation, generally recognized as safe (GRAS) notice, GRAS affirmation petition, food additive petition, and food master file). These collections of information have been approved by OMB under the following control numbers: biotechnology consultation procedures are approved under OMB Control No. 0910-0704; new protein consultations are approved under this collection, OMB Control No. 0910-0583; GRAS notices and affirmation petitions are approved under OMB Control No. 0910-0342; and, food additive petitions and food master files are approved under OMB Control No. 0910-0016.

12 b. Annualized Cost Burden Estimate

Gathering the information for the NPC and providing it to the agency requires a team of professional employees, which may include toxicologists, chemists, and lawyers. FDA estimates

that the average hourly wage for these employees would be equivalent to a GS-14/Step-1 level in the locality pay area of Washington-Baltimore in 2012, approximately $50.41/hour. Doubling this wage to account for overhead costs, FDA estimates the average hourly cost to respondents to be $100.82/hour. Thus, the overall estimated cost incurred by the respondents is $40,328 (400 burden hours x $100.82/hour = $40,328). 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 Costs to Respondents and/or Recordkeepers/Capital Costs

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

14. Annualized Cost to Federal Government

FDA estimates that the staffing burden for review of a NPC is 80 hours per submission. We estimate that we will receive approximately 20 NPCs annually. Thus, we estimate 1,600 hours will be needed to review NPC submissions annually. FDA estimates the annual cost to the Federal government to be 1,600 hours at rate of $55.46/hour, the GS-13/Step-10 rate for the Washington-Baltimore locality pay area for the year 2012 (1,600 hours x $55.46/hour = $88,736). To account for overhead, this cost is increased by 100%, making the total estimated annual cost to the Federal government $177,472.

15. Explanation for Program Changes or Adjustments

The current approval for this information collection expired July 31, 2012. FDA seeks to reinstate the collection to reflect that, although there is no change in the reporting burden, the agency has developed new form FDA 3666 to facilitate processing of the voluntary submissions. At this time, the agency is not collecting the information, but awaits OMB review and approval of Form FDA 3666, and therefore believes that we are not in violation of the PRA.

16. Plans for Tabulation and Publication and Project Time Schedule

No statistics from the information obtained from this data collection will be published. However, as noted above in Section 10, we do not proactively disclose the submission of a NPC until after the submitter completes the consultation procedure. After the consultation is complete, we place on the FDA Internet site the redacted copy of the NPC and an electronic version of the agency response to the submitter (http://www.fda.gov/Food/Biotechnology/Submissions/default.htm).

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.