**Substantiation for Dietary Supplement Claims Made Under Section 403(r)(6) of the Federal Food, Drug, and Cosmetic Act**

**0910-0626**

**SUPPORTING STATEMENT**

**Terms of Clearance:** None.

## A. Justification

### 1. Circumstances Making the Collection of Information Necessary

Section 403(r)(6) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 343(r)(6)) requires that a manufacturer of a dietary supplement making a nutritional deficiency, structure/function, or general well-being claim have substantiation that the claim is truthful and not misleading. Under section 403(r)(6)(A) of the FD&C Act, such a statement is one that "claims a benefit related to a classical nutrient deficiency disease and discloses the prevalence of such disease in the United States, describes the role of a nutrient or dietary ingredient intended to affect the structure or function in humans, characterizes the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function, or describes general well-being from consumption for a nutrient or dietary ingredient."

The guidance document entitled, "Substantiation for Dietary Supplement Claims Made Under Section 403(r)(6) of the Federal Food, Drug, and Cosmetic Act," provides FDA's recommendations to manufacturers about the amount, type, and quality of evidence they should have to substantiate a claim under section 403(r)(6). The guidance does not discuss the types of claims that can be made concerning the effect of a dietary supplement on the structure or function of the body, nor does it discuss criteria to determine when a statement about a dietary supplement is a disease claim. The guidance document is intended to assist manufacturers in their efforts to comply with section 403(r)(6). The guidance document can be found at http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/DietarySupplements/ucm073200.htm#pra.

FDA is requesting OMB approval of the voluntary information collection provisions contained in the guidance document entitled, "Substantiation for Dietary Supplement Claims Made Under Section 403(r)(6) of the Federal Food, Drug, and Cosmetic Act."

### 2. Purpose and Use of the Information Collection

Dietary supplement manufacturers collect the necessary substantiating information for their product as required by section 403(r)(6). The guidance provides information to manufacturers to assist them in doing so. The recommendations contained in the guidance are voluntary. Dietary supplement manufacturers will only need to collect information to substantiate their product's

nutritional deficiency, structure/function, or general well-being claim if they choose to place a claim on their product's label.

*Description of Respondents*: The respondents to this collection of information are manufacturers of dietary supplements sold in the United States. Respondents are from the private sector (for-profit businesses).

**3. Use of Improved Information Technology and Burden Reduction**

The guidance does not specifically prescribe the use of automated, electronic, mechanical, or other technological techniques or other forms of information technology as necessary for use by dietary supplement manufacturers. Companies are free to use whatever forms of information technology that may best assist them in voluntarily developing substantiation information as recommended in the guidance.

The agency estimates that one-hundred percent (100%) of the substantiating information will be maintained electronically in the next three years.

**4. Efforts to Identify Duplication and Use of Similar Information**

This guidance will not result in a duplicative collection of information. The standard discussed in the guidance for substantiation of a claim on the labeling of a dietary supplement is consistent with standards set by the Federal Trade Commission (FTC) for dietary supplements and other health related products that the claim be based on competent and reliable scientific evidence. The FDA and FTC are the only Federal agencies that require respondents to develop substantiation information. Since both agencies use the same standard, if a firm has already collected data to satisfy FTC, then that information can be used or modified for this use. Therefore, there is no duplication.

**5. Impact on Small Businesses or Other Small Entities**

FDA estimates that ninety percent (90 %) of respondents are small businesses. FDA recognizes that some dietary supplement manufacturers are small businesses, and has kept their particular needs in mind throughout the development of this guidance document. Dietary supplement manufacturers making a nutritional deficiency, structure/function, or general well-being claim are required by section 403(r)(6) of the FD&C Act to have substantiation that the claim is truthful and not misleading. There is no known way to reduce the burdens on a small business choosing to place a claim on their product's label. FDA notes, however, that the recommended information collection contained in the guidance is voluntary. 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. There are no consequences to Federal program or policy activities if the information is not collected or is collected less frequently. Under section 403(r)(6) of the FD&C Act, a manufacturer of a dietary supplement cannot make a nutritional deficiency, structure/function, or general well-being claim on a dietary supplement product if it does not have substantiation that the claim is truthful and not misleading.

**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 the Federal Register of June 3, 2011 (76 FR 32215), FDA published a 60-day notice requesting public comment on the proposed extension of this collection of information. FDA received five letters in response to the notice, each containing multiple comments. Several comments were generally supportive of the necessity of the information collection provisions of the guidance. Additional comments were outside the scope of the four collection of information topics on which the notice solicits comments, and will not be discussed in this document.

(Comment 1) Several comment letters noted the accuracy of FDA's estimate of the burden hours, which ranges from 44 to 120 hours per claim depending upon the nature of the claim.

(Response) FDA agrees. As discussed in this notice, if the product is one of several on the market making a particular claim for which there is adequate publicly available and widely established evidence supporting the claim, then the time to gather supporting data will be minimal; if the product is the first of its kind to make a particular claim or the evidence supporting the claim is less publicly available or not widely established, then gathering the appropriate scientific evidence to substantiate the claim will be more time consuming.

(Comment 2) One comment stated that FDA incorrectly estimated that there are no capital costs associated with developing information that meets the guidance's recommendations to manufacturers about the amount, type, and quality of evidence they should have to substantiate a claim under section 403(r)(6) of the FD&C Act. The comment argued that FDA did not fully consider that manufacturers invest significant capital resources in subscriptions to scientific journals and libraries to gain access to full-text scientific literature, consultants to develop appropriate wording for claims, and legal review of claims.

(Response) FDA disagrees. The comment mischaracterizes the significant costs associated with hiring consultants, obtaining reference materials, and securing legal review of a notification as capital costs. For purposes of information collection requests under the Paperwork Reduction Act, capital costs are costs for equipment, machinery, and construction that, if not for FDA's request or requirement, the respondent would not incur. This includes: Buying new software and new computer equipment; monitoring, sampling, drilling and testing equipment; record storage facilities; the cost of purchasing or contracting out information collection services; and, postage

costs to mail in a report. Capital costs do not include costs to achieve regulatory compliance with requirements not associated with the information collection. Subscriptions to scientific journals and libraries to gain access to full-text scientific literature, hiring consultants to develop appropriate wording for claims, and legal review of claims are costs associated with developing information that the manufacturer uses to satisfy itself that it has met the guidance's recommendations to manufacturers about the amount, type, and quality of evidence they should have to substantiate a claim under section 403(r)(6) of the FD&C Act; thus, these costs are not capital costs because they are costs associated with achieving regulatory compliance with requirements of the FD&C Act, not costs associated specifically with equipment, machinery, and construction needed to retain appropriate substantiating evidence. FDA notes that it has added a reference to these costs as "Costs to Respondent" in section 12 (b) of the supporting statement component of the Information Collection Request that it has submitted to OMB.

(Comment 3) One comment suggested that, to enhance the quality, utility and clarity of the information as well as minimize the burden of collection on manufacturers, FDA explore options for electronic submission and a digital, interactive database so the information can be easily reviewed, collated, analyzed and reported.

(Response) FDA notes that dietary supplement manufacturers making a nutritional deficiency, structure/function, or general well-being claim are required by section 403(r)(6) of the FD&C Act to have substantiation that the claim is truthful and not misleading. There is no requirement in the FD&C Act or recommendation in the guidance document that manufacturers submit the substantiation information to FDA. The information is retained by the manufacturers in their records. The guidance does not specifically prescribe the use of automated, electronic, mechanical, or other technological techniques or other forms of information technology as necessary for use by dietary supplement manufacturers. Companies are free to use whatever forms of information technology that may best assist them in developing substantiation information.

(Comment 4) One comment stated that FDA should provide clarity on what type of evidence is needed to substantiate a traditional use claim. The comment argued that Canada, the European Union, and Australia recognize traditional use evidence to support appropriate claim statements. The comment stated that several authoritative labeling standards monographs for herbal products specify traditional use claim statements, such as Health Canada Natural Health Products Directorate (NHPD) monographs, European Medicines Agency (EMA) European Community Herbal Monographs, and World Health Organization (WHO) Monographs on Selected Medicinal Plants. The comment recommended that FDA allow such monographs as acceptable pieces of evidence to substantiate a traditional use claim. The comment concluded that FDA's acceptance of label claim statements listed in appropriate monographs and clear guidance on other types of evidence that could be used to substantiate traditional use claims would significantly reduce the burden of collecting such information.

(Response) FDA disagrees that traditional use evidence is sufficient to meet the substantiation standard of competent and reliable scientific evidence applied by FDA in "Guidance for Industry: Substantiation for Dietary Supplement Claims Made Under Section 403(r)(6) of the

Federal Food, Drug, and Cosmetic Act." A claim based on historical or traditional use is not a claim that is substantiated by scientific evidence. Claims permitted by foreign and international monographs do not always have to be substantiated by scientific studies but may be acceptable if, in some cases, they are accompanied by disclosures that they claim is not scientifically established or are deemed appropriate merely by their history of use for a particular intended use. Therefore, FDA does not believe that these monographs are adequate to meet the substantiation standard applied by FDA.

(Comment 5) One comment suggested that FDA should identify monographs that are already recognized in other countries as substantiation for claims made for products that are manufactured in strict conformity to these monographs. The comment identified two specific compendia of monographs and recommended that FDA recognize these monographs as "constituting in and of themselves substantiation for a pre-existing widely established claim that may be made for a dietary supplement under section 403(r)(6) of the FD&C Act, so long as the claim is not a drug claim and is significantly similar to the use or purpose described in a monograph, and the conditions and level of use of the ingredient(s) that is the basis of the claim is within the dosage range described in the monograph."

(Response) FDA disagrees that foreign or other third-party monographs assure that a claim is substantiated by competent and reliable scientific evidence, which is the standard applied by FDA. Claims that may be permitted by foreign and international monographs do not always have to be substantiated by scientific studies but may be acceptable if substantiated, in whole or in part, by evidence not deemed adequate for a claim made for a dietary supplement in the United States, such as animal data or traditional medicinal use. Therefore, FDA does not believe that these monographs are adequate to meet the substantiation standard applied by FDA

(Comment 6) One comment argued that FDA overestimated the burden of the information collection by overestimating the number of respondents. The comment noted that FDA's website contains a list of notifications submitted in compliance with the requirements of 21 CFR 101.93 (a)(1) and stated that their review of the notices submitted between December 2007 and August 2010 indicates that the Agency has received an average of approximately 1,600 to 1,650 annually during this time, not the 2,001 per year estimated by FDA.

(Response) FDA disagrees that it has overestimated the number of respondents and stands by the estimate of 2,001 annual respondents for the next 3 years. The number of such notifications received by FDA in any given year can vary quite widely (by up to 300). In addition, the number of firms keeping records in anticipation of submitting a notification may be greater than the number of notification submitted. Thus, FDA believes retaining the estimate of 2,001 from the prior submission is appropriate.

**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**

Information that is trade secret or confidential 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)), and by part 20 of the agency's regulations (21 CFR part 20).

## 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

### 12 a. Annualized Hour Burden Estimate

*Description of Respondents*: The respondents to this collection of information are manufacturers of dietary supplements sold in the United States. Respondents are from the private sector (for-profit businesses).

FDA estimates the burden for this information collection as follows:

Table 1. – Estimated Annual Recordkeeping Burden[1]

| Claim type | No. of Recordkeepers | No. of Records per Recordkeeper | Total Annual Records | Average Burden per Recordkeeping (in Hours)[2] | Total Hours |
|---|---|---|---|---|---|
| Widely known, established | 667 | 1 | 667 | 44 | 29,348 |
| Pre-existing, not widely established | 667 | 1 | 667 | 120 | 80,040 |
| Novel | 667 | 1 | 667 | 120 | 80,040 |
| Total | | | | | 189,428 |

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Burden estimates of less than 1 hour are expressed as a fraction of an hour in the format "[number of minutes per response]/60".

Dietary supplement manufacturers will only need to collect information to substantiate their product's nutritional deficiency, structure/function, or general well-being claim if they chose to place a claim on their product's label. Gathering evidence on their product's claim is a one-time burden, in which they collect the necessary substantiating information for their product as required by section 403(r)(6) of the FD&C Act.

The standard discussed in the guidance for substantiation of a claim on the labeling of a dietary supplement is consistent with standards set by the FTC for dietary supplements and other health-related products that the claim be based on competent and reliable scientific evidence. This evidence standard is broad enough that some dietary supplement manufacturers may only need to collect peer-reviewed scientific journal articles to substantiate their claims; other dietary supplement manufacturers whose products have properties that are less well-documented may have to conduct studies to build a body of evidence to support their claims. It is unlikely that a dietary supplement manufacturer will attempt to make a claim when the cost of obtaining the evidence to support the claim outweighs the benefits of having the claim on the product's label. It is likely that manufacturers will seek substantiation for their claims in the scientific literature.

The time it takes to assemble the necessary scientific information to support their claims depends on the product and the claimed benefits. If the product is one of several on the market making a particular claim for which there is adequate publicly available and widely established evidence supporting the claim, then the time to gather supporting data will be minimal; if the product is the first of its kind to make a particular claim or the evidence supporting the claim is less publicly available or not widely established, then gathering the appropriate scientific evidence to substantiate the claim will be more time consuming.

FDA assumes that it will take 44 hours to assemble information needed to substantiate a claim on a particular dietary supplement when the claim is widely known and established. FDA believes it will take closer to 120 hours to assemble supporting scientific information when the claim is novel or when the claim is pre-existing but the scientific underpinnings of the claim are not widely established. These are claims that may be based on emerging science, where conducting literature searches and understanding the literature takes time. It is also possible that references for claims made for some dietary ingredients or dietary supplements may primarily be found in foreign journals and in foreign languages or in the older, classical literature where it is not available on computerized literature databases or in the major scientific reference databases, such as the National Library of Medicine's literature database, all of which increases the time of obtaining substantiation.

In the Federal Register of January 6, 2000 (65 FR 1000), FDA published a final rule on statements made for dietary supplements concerning the effect of the product on the structure or function of the body. FDA estimated that there were 29,000 dietary supplement products marketed in the United States (65 FR 1000 at 1045). Assuming that the flow of new products is 10 percent per year, then 2,900 new dietary supplement products will come on the market each year. The structure/function final rule estimated that about 69 percent of dietary supplements have a claim on their labels, most probably a structure/function claim (65 FR 1000 at 1046). Therefore, we assume that supplement manufacturers will need time to assemble the evidence to substantiate each of the 2,001 claims (2,900 x 69 percent) made each year. If we assume that the 2,001 claims are equally likely to be pre-existing widely established claims, novel claims, or pre-existing claims that are not widely established, then we can expect 667 of each of these types of claims to be substantiated per year. Table 1 of this document shows that the annual burden hours associated with assembling evidence for claims is 189,428 (the sum of 667 x 44 hours, 667 x 120 hours, and 667 x 120 hours).

### 12b. Annualized Cost Burden Estimate

FDA estimates that the average hourly wage for the employee collecting information for substantiation would be equivalent to a GS-12/Step-1 level in the locality pay area of Washington-Baltimore in 2011, approximately $35.88/hour. Doubling this wage to account for overhead costs, FDA estimates the average hourly cost to respondents to be $71.76/hour. Thus, the overall estimated cost incurred by the respondents is $13,593,353.28 (189,428 burden hours x $71.76/hr = $13,593,353.28). Several comment letters filed in response to the June 3, 2011 Federal Register notice noted that firms experience costs associated with hiring consultants to develop appropriate wording for claims, paying for full-text scientific literature and obtaining legal review of claims. The comments did not provide data supporting specific burden hours or hourly wage rates associated with consultants or legal reviewers. As a result, the agency will analyze these costs for possible inclusion in its next information collection request for this collection.

## 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 the Federal Government

FDA's review of the retained records would generally occur only as part of a regulatory action if FDA were to allege that a claim is unsubstantiated. FDA estimates that its review of the retained records would take 80 hours per action. FDA estimates the hourly cost for review and evaluation to be $59.30 per hour, the GS-15/Step-1 rate for the Washington-Baltimore locality pay area for the year 2011. To account for overhead, this cost is increased by 100 percent, making the total cost $118.60 per hour. Thus, FDA estimates the cost to the Federal Government for the review of records to be $9,488 per review ($118.60/hour x 80 hours). FDA estimates that it would review on average 2 records per year. Thus, FDA estimates that the total annual cost to the Federal Government would be $18,976 ($9,488 x 2 reviews).

## 15. Explanation for Program Changes or Adjustments

The burden estimate for the subject ICR was inadvertently placed in the wrong table as reporting. This error has been corrected and the burden rightfully recorded and place in the burden table as recordkeeping. The burden estimate has remained unchanged since the last extension request.

Although there was no change in the total estimated burden of this collection, the number of responses increased from 1,334 to 2,001 (this reflects the correction of an error). CFSAN has made an adjustment by adding a new IC to more accurately reflect the burden table estimate. In 2008, FDA published 60-day and 30-day Federal Register notices containing a reporting burden table with three lines. Unfortunately, the ICRAS/ROCIS submission in 2008 contained only two ICs. IC #1 correctly reported the first line of the burden table, but IC # 2 incorrectly reported the

second and third lines of the burden table compressed into one IC. This was an error because it caused the number of responses to be underreported at 667, instead of 1,334 (667 x 2). To correct this error, we have added a new IC # 3, which causes the number of responses to increase from 1,334 to 2,001. A more detailed explanation for these changes follows.

For IC#1 -- In 2008, we estimated that 667 respondents will spend 44 hours each for a total burden of 29,348 hours. This IC was correct and remains unchanged in 2011.

For IC # 2 -- In 2008, the burden table estimated that 667 respondents will spend 120 hours each for a total burden of 80,040 hours, but the IC reported that 667 respondents will spend 240 hours each for a total burden of 160,080. This error has been corrected for 2011 by correctly reporting the number of responses at 667 and the hours per response at 120 each, thereby reducing the total hours for IC # 2 from 160,080 to 80,040, a reduction of 80,040 hours. The 80,040 hours are now reported in IC # 3. The number of responses remains at 667.

For IC # 3 -- For 2011, we have created a new IC to correctly report the 80,040 reporting burden hours previously reported in IC # 2. This IC estimates that 667 respondents will spend 120 hours each for a total burden of 80,040 hours. This new IC adds 667 responses, thereby correcting the 2008 error underreporting responses.

**16. Plans for Tabulation and Publication and Project Time Schedule**

The agency has no plans for publication of information from this information collection.

**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.