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August 16, 2005

*BY ELECTRONIC AND REGULAR MAIL*

Marcia L. Moore  
Center for Food Safety and Applied Nutrition  
Food and Drug Administration  
5100 Paint Branch Pkwy.,  
College Park, MD 20740, 301-436-2397,

Re: Threshold Working Group Draft Report (June 2005), *Approaches to Establish Thresholds for Major Food Allergens and for Gluten in Food* (Docket No. 2005N-0231)

Dear Ms. Moore:

The Grocery Manufacturers Association (GMA) submits these written comments on the aforementioned June 2005 draft report on establishing allergen thresholds prepared by the Threshold Working Group (hereinafter the Draft Report), which was the subject of the July 13-15 meeting of the Food Advisory Committee (FAC). GMA is the world's largest association of food, beverage and consumer product companies. GMA's member companies employ more than 2.5 million workers in all 50 states and have total sales of approximately 680 billion dollars.

GMA and its member companies have been actively involved in the allergen issue. Indeed, GMA played an instrumental role in the industry-developed allergen labeling guidelines that have resulted in many food packages bearing plain English names of the major allergens<sup>1</sup>. The majority of the GMA member companies voluntarily adopted these labeling practices well before the Food Allergy Labeling and Consumer Protection Act (FALCPA).

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<sup>1</sup> Food Allergen Labeling Guidelines  
<http://www.gmabrands.com/publicpolicy/docs/whitepaper.cfm?DocID=770&>

2005N-0231

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GMA commends the Food and Drug Administration (FDA) for its efforts in developing the data and information that are needed to implement FALCPA. GMA also commends FDA for convening the Food Advisory Committee (FAC) on allergen thresholds and for the agency's efforts in preparing the Draft Report. GMA appreciates the agency's transparency in identifying the various methods that should be explored for establishing allergen thresholds.

The establishment of allergen thresholds is integral to the effective application of FALCPA. FALCPA subjects incidental additives, such as processing aids, to the allergen labeling requirements. This provision becomes problematic when the allergenic protein in a food is present at such low levels that it does not pose a risk to human health. For example, typical uses of soy lecithin—a commonly used processing aid—result in soy protein levels in foods well under 10 parts per million (ppm) and many uses result in levels in the parts per billion and parts per trillion ranges.

FALCPA will fail the food allergic community if it results in allergen labeling of foods with inconsequential levels of protein from major allergens. The labeling of such foods would needlessly remove additional products from the selection of food allergic consumers. FALCPA also would lead to confusion in situations when a food label is revised to declare a major allergen that is present at insignificant levels, particularly when the food allergic consumer has been eating the product safely for years without incident. By establishing thresholds, FDA would prevent the over labeling of the many food products that currently are being enjoyed and consumed without incident.

GMA offers the following comments on the various approaches for establishing thresholds under consideration by FDA.

## **I. Comments on Draft Report Provisions on Food Allergens**

### **A. Statutorily-Derived Approach**

GMA concurs with the agency assessment that it would be appropriate to develop interim thresholds using a statutorily-derived approach. FALCPA specifically excludes highly refined oils from the definition of major allergen. At the time Congress passed FALCPA, the literature contained numerous references to the presence of detectable levels of protein in highly refined oils. Crevel et al. (2000) published a literature review on the levels of protein in various oils. Crevel notes “published values vary widely, depending on the type and source of the oil as well as

the methodology used for extraction and analysis.” 2/ Crevel reported that the Leatherhead Food Research Association in the United Kingdom had unpublished data revealing levels of up to 48 ppm in refined peanut oil.

FALCPA exempts highly refined oils from the major allergen definition regardless of the level of protein in the product. Congress exempted highly refined oils from the definition of major allergen at a time when the literature contained reports of detectable levels of protein in refined oils, such as 48 ppm of protein in refined peanut oil. If Congress had intended to include all products with detectable levels of protein in the definition of “major allergen,” it would not have exempted highly refined oils, which contain detectable levels of protein as reported in the literature.

The legislative history also establishes Congressional intent that ingredients with insignificant levels of allergens should not be subject to the allergen labeling requirements. During legislative discussions, the Senate Committee reporting the bill out of Committee to the full Senate expressly stated that it “encourages FDA to adopt a reasonable standard for determining whether a food ingredient “does not contain an allergenic protein” ... for example, ingredients containing allergenic proteins below [a future] established threshold would be eligible for the notification procedure.” 3/ The Senate Committee further directed FDA to provide “guidance to industry on the information that would be useful for making a determination that foods that contain protein derived from one of the eight food allergens do not cause an allergic response that poses a risk to human health” and create a “process ...that minimizes the burden on the food manufacturer.” 4/

GMA believes the language of FALCPA and the legislative history support the establishment of a statutorily-based threshold until sufficient data are available to conduct a safety or risk assessment approach. GMA does not believe it is necessary, however, as explained in the Draft Report, to set the threshold level on the basis of the “average protein” level in highly refined oils. FALCPA exempts all highly refined oils from the definition of major allergen regardless of the level of

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2/ Crevel, R.W.R. et al., *Allergenicity of Refined Vegetable Oils*, 38 Food and Chemical Toxicology, 385, 389 (2000).

3/ S. Rep. No. 108-226 at p.7 (2004).

4/ *Id.*

protein in the oil. Because the published literature contained reports of up to 48 ppm of protein in refined peanut oils at the time Congress passed FALCPA, it would be reasonable to establish the statutorily based threshold at 48 ppm. GMA, however, believes that 10 ppm would be a more reasonable level for a threshold based on the statutorily-derived approach.

The food industry has long taken the position, on the basis of advice from leading experts, that an allergenic protein that is present at levels below 10 ppm in the finished food should not be subject to ingredient labeling because such levels are unlikely to trigger a response in food allergic consumers. GMA collected data on food allergic complaints from various member companies that did not label the presence of soy lecithin and fish gelatin when present at levels below 10 ppm. The data summarized in the chart below reveal similar levels of consumer complaints in the control products, which did not contain any allergens, and the products with undeclared soy lecithin and fish gelatin.

<b>Product</b>	<b>Complaints per Million Units/Packages</b>	<b>Complaints Per Million Servings</b>
Control	0.058	0.05500
Soy Lecithin	0.077	0.00700
Fish Gelatin	0.001	0.00002

The data generated by GMA identified an absence of credible complaints when consuming food products with very low levels of undeclared soy lecithin and fish gelatin. Given the prevalence of food allergies in this country and the significant number of units and servings sold, a higher incident of allergic consumer complaints would have been expected if the products had a high enough level of allergenic protein to trigger an adverse reaction. The absence of credible consumer complaints to products with very low levels of undeclared major allergens provides further support for the establishment of 10 ppm as an interim level based on the statutorily-derived approach.

GMA concurs with the Draft Report assessment that thresholds established under the statutorily-derived approach should be viewed as “interim levels.” As more data become available, the statutorily-derived threshold should be replaced with a method based on a safety or risk assessment approach as recommended in the Draft Report.

## **B. Method of Analysis Derived Approach**

GMA does not support the use of a method of analysis approach when setting thresholds for major allergens. We question the utility of this approach because commercially-available methods of analysis have not been developed for all of the major allergens. Indeed, the peanut method is the only method that has been validated. Moreover, the analytical approach can be complicated by the development of increasingly more sensitive analytical methods, which could result in a continually changing threshold level. Limits of detection well below 1 ppm could easily be obtained through advances in analytical technology.

In the event the agency ultimately decides to use the methods of analysis approach, GMA concurs with Draft Report recommendations that such thresholds should be considered interim and replaced with thresholds that are established under the safety or risk assessment approaches.

## **C. Safety Assessment Approach**

GMA believes it would be appropriate to establish thresholds on the basis of the safety assessment approach outlined by the agency. We question, however, whether it is appropriate to use an uncertainty factor of 100, with a 10-fold factor to account for intraspecies differences and another 10-fold factor to account for severity of the response and sensitivity of the population. GMA concurs with the FAC recommendations that it is not possible to set one uncertainty factor that can be applied across all studies. The scientific community must evaluate each study independently, identify its strengths and weaknesses, and make an informed assessment of the uncertainty factor, if any, that should be applied in a study. Indeed, an uncertainty factor may not be necessary when evaluating studies involving a sufficient number of patients with various sensitivities when there are no symptoms reported at the lowest tested doses and objective symptoms reported at higher doses.

Another issue that must be considered in any safety assessment is the scientific standard that will be used by the agency when developing the threshold. FALCPA does not specifically address this issue in the context of thresholds. FALCPA does recognize, however, that an ingredient should be exempt from the major allergen definition under the petition process if the petitioner can demonstrate that the use of the ingredient "does not cause an allergic response that poses a risk to human health." GMA believes it is reasonable for FDA to adopt this standard when determining whether there are sufficient data to support the establishment of thresholds under the safety assessment.

GMA also believes it is appropriate, as recommended in the Draft Report, to use the first objective symptom when determining the lowest observed adverse effect level (LOAEL) or the no observed adverse effect level (NOAEL). Because subjective responses are not the type of responses that “pose a risk to human health,” objective symptoms should be used when setting NOAELS and LOAELS. GMA does not believe, as suggested during the FAC deliberations, that the uncertainty factor should be increased to accommodate the first subjective symptom. The scientific community should evaluate each study and make an informed decision on whether the first subjective symptom in the study is indicative of a true allergic response or a psychologically-induced response. In instances when a subject reports a first subjective response at a very low level and there is no evidence of an objective response until a significantly higher level, it would be seemingly inappropriate to use the first subjective response as the basis for the uncertainty factor.

GMA also believes FDA should consider approaches such as that used by the American Academy of Pediatrics (AAP) in setting a threshold for hypoallergenic infant formulas. The AAP determined that infant formulas can be labeled hypoallergenic if it is documented under double-blind, placebo-controlled conditions that, at a minimum, there is 95 percent certainty that 90 percent of the cow’s milk allergic population will not react. <sup>5/</sup> This approach could be used, modified as necessary for specific allergens and populations, to address thresholds for other allergens.

#### **D. Risk Assessment Approach**

GMA concurs with the agency assessment that there are insufficient data and information at this time to set thresholds using the risk-assessment approach. As more data become available, GMA believes it would be appropriate for the agency to set allergen thresholds using either the safety or risk assessment approaches.

## **II. Comments on Draft Report Provisions on Gluten**

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<sup>5/</sup> Policy Statement on Hypoallergenic Infant Formulas, American Academy of Pediatrics Committee on Nutrition, PEDIATRICS Vol. 106 No. 2, pp. 346-349 (Aug. 2000) (accessed on Aug. 16, 2005 at <http://aappolicy.aappublications.org/cgi/content/full/pediatrics;106/2/346>).

GMA supports the Draft Report recommendations on establishing threshold levels for gluten for purposes of establishing definitions for gluten free and offers the following brief comments.

**A. Method of Analysis Approach**

GMA believes it would be appropriate to set the gluten threshold based on the method of analysis approach, although we question whether any products would qualify for the claim given the commingling of gluten and non-gluten containing grains. Corn, wheat, soybeans, oats and other grains are grown on the same farms in the United States and farmers use the same combines to harvest, wagons to transport, and grain bins to store these various grains. The grain elevators receiving the grains also may use the same catch basin and augers to transport different types of grains. The grains then can be transported in containers by truck and rail that are used to transport other grains. There are many opportunities for gluten and non-gluten containing grains to be commingled. Indeed, the USDA grade standards specifically recognize that up to 10 percent of "other grains" can be found in corn, soybeans, wheat and canola and that up to 25 percent of "other grains" can be found in oats and barley. 6/

While the milling industry may try to separate unwanted grains during the milling process, it simply is not possible with the current technology to separate all wheat from oats, corn, soybeans and other grains. The flours milled from non-gluten containing grains and the products made from such flours, therefore, can be expected to have very low levels of gluten. GMA, therefore, suspects that very few products would be eligible for a gluten-free claim if the threshold is based on the analytical method.

If FDA chooses to use the method of analysis as the basis for defining gluten free, GMA believes that such a position would be consistent with agency precedent on the use of "free." FDA has taken the position that the term "free," when used outside the context of nutrient content claims, should be limited to products with no detectable levels of the substance. For example, FDA takes the position that "alcohol free" only may be used in instance when a product contains "no detectable alcohol." 7/ GMA similarly believes it would be appropriate for FDA

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6/ See., e.g., 7 CFR §§ 810.401(corn), 810.1001(oats), 810.1601(soybeans) and 810.2202(wheat).

7/ FDA Compliance Policy Guide, Sec. 510.400, Dealcoholized Wine and Malt Beverages--Labeling (CPG 7101.04) (March 1995).

to define “gluten free” for use on products that contain no detectable levels of gluten. Very few products, however, likely would qualify for such a claim. GMA would encourage FDA to set the threshold for gluten free claims on the basis of the safety or risk assessment approach as soon as the data are available.

**B. Safety Assessment Approach**

GMA supports the use of the safety assessment approach when setting thresholds for gluten. For the same reasons discussed in more detail above, GMA believes that FDA should consider the objective rather than subjective response when setting LOAELS and NOAELS. GMA also believes it would be inappropriate to set a single uncertainty factor for all studies. FDA must evaluate the quality of the underlying study and set the uncertainty factor on the basis of the study design.

**C. Risk Assessment Approach**

GMA concurs with the agency assessment that there are insufficient data and information at this time to set thresholds using the risk-assessment approach. As more data become available, GMA believes it would be appropriate for the agency to set gluten thresholds using either the safety or risk assessment approaches.

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GMA appreciates the opportunity to comment on this very important issue. The FALCPA labeling requirements become effective on January 1, 2006. We urge FDA to establish, in as expeditious a manner as possible, thresholds for major allergens. The industry needs this information so it will know whether it will be necessary to label major allergens when they are present at minor and inconsequential levels.

In conclusion, GMA believes the statutorily derived method is appropriate for the establishment of interim threshold levels for major allergens and urges the agency to adopt an interim threshold as soon as possible. For the reasons noted above, GMA believes that 10 ppm is an appropriate statutorily-derived threshold. GMA agrees with the Draft Report recommendation that interim thresholds should be replaced using the safety or risk assessment approach as the relevant data become available.

GMA believes the method of analysis approach may be appropriate for setting interim levels for “gluten free”, but questions whether any products would

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qualify given the commingling of grains. GMA also supports the risk and safety assessments for setting thresholds on gluten free.

If you have any questions on this or other matters, please contact us.

Sincerely,

A handwritten signature in black ink that reads "Alison Kretser". The signature is written in a cursive style with a large, sweeping flourish at the end.

Alison Kretser  
Sr. Director, Scientific and Nutrition Policy