ZUCKERMAN SPAEDER LLP
ATTORNEYS AT LAW
1201 CONNECTICUT AVENUE, N.W.
WASHINGTON, D.C. 20036-2638
(202) 778-1800
FACSIMILE (202) 822-8106

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WILLIAM B. SCHULTZ
(202) 778-1820
WSCHULTZ@ZUCKERMAN.COM

October 4, 2001

Dockets Management Branch
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

Dear Sir or Madam:

Please find attached a Petition we have submitted to the FDA on behalf of the Center for Science in the Public Interest ("CSPI") regarding the labeling and manufacturing of foods containing allergenic substances.

The CSPI petition urges FDA to require the declaration of allergenic foods on ingredient labels, and to establish good manufacturing practices ("GMP's") to prevent the inadvertent introduction of allergenic ingredients into non-allergenic foods. This petition addresses the same issues that were raised in a recent petition filed with FDA by nine State Attorneys General. Docket No. 00P-1322.

If you have any questions concerning this Petition, please call Bill Schultz at (202) 778-1820 or Carlos Angulo at (202) 778-1811.

Thank you for your attention to this matter.

Sincerely,

William B. Schultz

William B. Schultz
Carlos T. Angulo

Attachment

00P-1322

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FOOD AND DRUG ADMINISTRATION

Petition for Rules Regarding The Labeling and Manufacture of Foods Containing Allergenic Substances	)	**Docket No. _____**

Submitted on Behalf of the Center for Science in the Public Interest

October 4, 2001

I. Introduction

This petition is submitted on behalf of the Center for Science in the Public Interest ("CSPI") and requests action by the Food and Drug Administration ("FDA") regarding allergenic food substances.[1] Specifically, CSPI requests that the FDA Commissioner amend Title 21 of the Code of Federal Regulations to provide adequate notice and protection to individuals with food allergies through (1) the imposition of labeling requirements for food allergens, and (2) the establishment of "Good Manufacturing Practices" ("GMPs") aimed at preventing the inadvertent introduction of such allergens into non-allergenic foods.

CSPI is a nonprofit education and advocacy organization with 800,000 members that focuses on, among other things, improving the safety and nutritional quality of our food supply. CSPI seeks to promote health through educating the public about nutrition and works to ensure that advances in science are used for the public good. CSPI represents its members and citizens' interests before legislative, regulatory, and judicial bodies.

FDA has concluded that "the undeclared presence of allergens in foods is a serious public health issue." 66 Fed. Reg. 38591-92 (July 25, 2001). Consistent with the Agency's conclusion, CSPI strongly believes that the public health requires the Agency to mandate the declaration of allergenic foods on ingredient labels. Such requirements will supply consumers suffering from

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[1] The foods most commonly recognized as allergenic and that cause the majority of serious reactions are: (1) peanuts; (2) milk; (3) eggs; (4) fish; (5) soybeans; (6) crustacea; (7) tree nuts; and (8) wheat. 66 Fed. Reg. 38591, 38592 (July 25, 2001). These eight foods are the focus of the May 26, 2000 Attorneys General petition on food allergens (*infra* p. 3), and of FDA's food allergen awareness efforts. *Id.* Thus, references in this petition to "food allergens" or "allergenic substances" are also to these eight allergens. Nonetheless, other foods, including strawberries, apples, carrots, parsnips, celery, hazelnuts, potatoes, and kiwi, can also cause serious allergic reactions (http://wwww.allergylearninglab.com/about/food/index.html?id+4195215 (June 21, 2001)). Also, some food additives, such as sulfites and carmine, can cause serious allergic or non-allergic reactions. CSPI therefore urges FDA to review whether ingredients other than the

food allergies with the information they need to make informed choices about what foods they eat and to avert the potentially fatal consequences of consuming foods to which they are allergic. The public health also requires that food manufacturers follow stringent manufacturing practices to ensure that food allergens are not *inadvertently* added to non-allergenic foods.

In a petition submitted on May 26, 2000, Attorneys General from the States of New York, Maryland, Michigan, Wyoming, Ohio, Tennessee, Connecticut, Vermont, and Massachusetts urged FDA to adopt by regulation specific requirements that the eight major food allergens be declared on food labels and to establish GMPs to prevent the unintentional inclusion of those allergens in foods. Docket No. 00P-1322. CSPI strongly supports most of the specific regulatory changes urged in the Attorneys General petition. This petition further demonstrates that FDA has the legal authority to implement these requested regulations.

This petition is submitted pursuant Section 4(d) of the Administrative Procedure Act, 5 U.S.C. § 553(e), 21 C.F.R. § 10.30, and Sections 201(n), 402, 403(a), 403(i), 409(c), and 721(b) of the Federal Food Drug and Cosmetic Act ("FFDCA"), 21 U.S.C. §§ 321(n), 342, 343(a), 343(i), 348, and 379e(b). As we demonstrate below, the Agency has ample authority under the FFDCA both to require the declaration of allergenic substances on food labels and to establish the requested GMPs.

II. Action Requested

The Attorneys General petition sets forth, at pp. 4-11, specific amendments to Title 21, Code of Federal Regulations, requiring the declaration of food allergens on ingredient labels and

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eight major allergens should also be regulated in the manner suggested in this and the Attorneys General petitions.

establishing GMPs aimed at preventing the inadvertent introduction of allergens into non-allergenic foods. CSPI supports all the specific regulatory recommendations of the State Attorneys General[2] except the recommendation that foods that contain or may contain an allergenic substance display an allergen insignia on the product package (Attorneys General petition at 5-6). CSPI is concerned that this allergen insignia will overshadow other important nutritional and health information on the food label.[3]

III. Statement of Factual Grounds

The Attorneys General petition, at pp. 14-23, comprehensively sets forth the factual basis for the requested amendments to the FDA's regulations. The facts set forth in that petition support beyond dispute FDA's own conclusion that the undeclared presence of food allergens is a serious public health issue. CSPI supplements that statement of facts as follows.

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[2] At the August 13, 2001, public hearing on allergens, it was suggested that some of the current specific food standard regulations, 21 C.F.R. §§ 130 *et seq.*, would have to be amended to comply with a requirement that allergens be declared using their common names (tr. 60-61). There is, however, a general requirement that the ingredients for these standardized foods be labeled in accordance with the general food labeling regulations set forth in 21 C.F.R. Part 101. 21 C.F.R. § 130.3(e). This general requirement is repeated for specific products that contain an allergen, such as macaroni products, 21 C.F.R. § 139.110(g), or mayonnaise, 21 C.F.R. § 169.140(f). Thus, the requested changes to part 101 will extend to these standardized foods.

[3] On July 26, 2001, CSPI submitted a separate citizens petition to FDA regarding the establishment of format requirements for ingredient lists. In that petition, CSPI discussed the relevance of ingredient labeling to the problem of food allergens and urged the adoption of more readable ingredient lists. We incorporate that petition by reference.

Approximately four million Americans,[4] including up to six percent of all American children,[5] are allergic to one type of food or another. As mentioned, at note 1, eight food substances are most commonly recognized as allergenic, and account for the great majority of serious allergic reactions. They are (1) peanuts; (2) milk; (3) eggs; (4) fish; (5) soybeans; (6) crustacea; (7) tree nuts; and (8) wheat.

Food allergies are a serious public health threat for five reasons. First, there is currently no medical treatment available to prevent allergic reactions to food. The only method to manage a food allergy is strictly to avoid the offending food. 66 Fed. Reg. 38591-92 (July 25, 2001). And some current labeling requirements prevent consumers with food allergies from identifying the foods they need to avoid.

Second, the reaction to food allergens can be extremely severe. Some individuals with food allergies run a high risk of suffering a severe allergic reaction known as anaphylaxis. Anaphylaxis is a swift and violent reaction that simultaneously affects various organ systems, including the skin, upper and lower respiratory system, cardiovascular system, eye, uterus, and bladder. Death can occur even if epinephrine is administered within minutes.[6] And, indeed, as many as 150 Americans per year die as a

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[4] Raymond Formanek, "Food Allergies: When Food Becomes the Enemy," *FDA Consumer Magazine*, July-August 2001 (on-line at http://www.fda.gov/fdca/features/2001/401_food.html.).

[5] *Id.*

[6] S. Allan Bock, M.D., Anne Munoz-Furlong, and Hugh A. Sampson, M.D., "Fatalities Due to Anaphylactic Reactions to Foods," 107 *J. Allergy Clin Immunology* 1: 191-193 (2001) at 192.

result of reactions to food allergens.[7] There is no question that the public health consequences of a failure to declare allergens on food labels can be extreme.

Third, the amount of an allergenic food that is needed in some cases to cause a severe reaction is minimal. For example, consumption of as little as one-fifth to one five-thousandth of a teaspoon of an allergenic food can cause death.[8] Thus, what may appear to be an insignificant amount of a food substance to a non-allergic individual is in fact a potentially fatal measure of the substance for someone who is allergic. This discrepancy underscores the importance of labeling. An allergy sufferer – or the parent of an allergy sufferer – cannot rely on the subjective determination of a non-allergy sufferer as to whether a particular substance is included in a food. Labeling provides an objective measure that enables the consumer to identify when a food has any amount of that substance, no matter how apparently insignificant to the untrained eye or palate.

Fourth, allergic reactions to food can occur in a variety of situations – in restaurants, other public eating places, neighbors' homes, and schools, as well as at home. Without proper vigilance on the part of both consumers who have food allergies and those who prepare food, food-induced anaphylaxis can strike at any time, and in a wide range of settings.

Fifth, food allergens are often inadvertently added to non-allergenic foods through "cross-contamination," which occurs when allergenic substances migrate from equipment, utensils, and packaging material into foods that are intended to be allergen-

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[7] Formanek, *supra* n.4.

[8] Audrey T. Hingley, "Food Allergies: Rare but Risky," *FDA Consumer Magazine*, December 1993, at pp. 27-31. *See also* Hourihane JO'B *et al.*, "An evaluation of the sensitivity of subjects with peanut allergy to very low doses of peanut protein: a randomized, double-blind, placebo-controlled food challenge study," *J. Allergy Clin. Immunology* 1997; 100:596-600.

free.[9] For example, in a bakery that manufactures cookies with nuts and without nuts on the same production line, traces of nuts may appear in the cookies that are supposed to be allergen-free. And because a very small amount of a food allergen is sufficient to cause a reaction, even the most incidental degree of cross-contamination can be fatal. Thus, it is not enough to address the problem of food allergens through labeling, which is intended to identify for consumers foods that intentionally contain allergens. Protection against the *inadvertent* introduction of allergens into foods is also necessary.

IV. Statement of Legal Grounds

The facts clearly demonstrate that the problem of food allergens requires an aggressive response on the part of the FDA. It is equally clear that FDA has authority under the FFDCA to require the label declaration of food allergens, and to establish GMPs designed to avoid cross-contamination.

A. The FFDCA Confers Broad Authority on FDA to Effectuate the Important Public Policy Goals of the Statute.

The general purpose of the FFDCA (21 U.S.C. § 301, *et seq.*) is to "protect unwary customers in vital matters of health . . . ." *United States v. 216 Cartoned Bottles, More or Less, of . . . Sudden Change*, 409 F.2d 734, 741 (2d Cir. 1969). Given the Act's broad remedial purpose, courts have construed the statute liberally. *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 798 (1969) (applying "the well-accepted principle that remedial

[9] Fred R. Shank, Ph.D., "Label Declaration of Allergenic Substances in Foods," *FDA Notice to Manufacturers* (June 10, 1996) ("FDA Notice"), at 3.

legislation such as the [FFDCA] is to be given a liberal construction consistent with the Act's overriding purpose to protect the public health . . ."); *216 Cartoned Bottles*, 409 F.2d at 741 ("[T]he Act . . . must be given a liberal construction to effectuate [its] high purpose."). The FFDCA confers authority on FDA to enforce the provisions of the statute by regulation (21 U.S.C. § 371(a)), and this regulatory authority, too, is "broad." *Cosmetic, Toiletry and Fragrance Ass'n v. Schmidt*, 409 F.Supp. 57, 64 (D.D.C. 1976) (upholding FDA Commissioner's authority to require warning statements on aerosolized food, drug, and cosmetic products). Finally, in evaluating the exercise of FDA's regulatory authority, courts accord great deference to the Agency's decisions, especially where they implicate the evaluation of scientific data within the Agency's technical expertise. *International Fabricare Inst. v. U.S. EPA*, 972 F.2d 384, 389 (D.C. Cir. 1992). *See also Community Nutrition Institute v. Young*, 476 U.S. 974, 981-82 (1986) (noting that "the FDA has been delegated broad discretion by Congress in any number of areas" and deferring to Agency expertise).

B. The Agency May Require the Declaration of Allergenic Substances on Ingredient Labels.

Several provisions of the FFDCA provide FDA with authority to require the labeling of allergenic foods in order to effectuate the statute's goal of protecting the public health. These are discussed below.

1. FDA May Require Labeling Pursuant to its Authority to Enforce the Prohibition on Misbranded Foods in Section 403(a) of the FFDCA.

The FFDCA prohibits the introduction into interstate commerce of any food or drug that is misbranded (21 U.S.C. § 331(a)), and, as noted above, FDA has broad authority to issue regulations to enforce this prohibition. 21 U.S.C. § 371(a). This authority permits the Agency to require the declaration of allergenic substances -- including (as discussed below in section IV.B.3) spices, flavorings, colors and "incidental" additives -- on food labels.

Section 403 of the FFDCA (21 U.S.C. § 343) sets forth the different ways in which a food product may be misbranded. Under section 403(a), a food is deemed to be misbranded if "its labeling [is] false or misleading in any particular . . . ." 21 U.S.C. § 343(a)(1).[10] Under FFDCA section 201(n) (21 U.S.C. § 321(n)), labeling of an article (including a food product) is "false or misleading" if it "fails to reveal [material] facts . . . with respect to consequences which may result from the use of the article to which the labeling or advertising relates . . . under such conditions of use as are customary or usual." The statute could not be clearer: the failure of a food label to provide material information regarding the potential adverse consequences of eating a food, no less than affirmative misrepresentations, can cause a food to be falsely or misleadingly labeled, and therefore misbranded. *See United States v. 62 Packages of Marmola Prescription Tablets*, 48 F.Supp. 878, 884 (W.D. Wisc. 1948) ("There is nothing indefinite or ambiguous about [21 U.S.C. § 321(n)].") FDA has adhered to this unambiguous language, confirming that "a food label is misleading if it does not disclose consequences that may result from consumption of the food." 61 Fed. Reg. 48102, 48106 (September 12, 1996). *See also* Frederick H. Degnan, "The Food Label and the Right to Know," 52 *Food Drug L.J.* 49, 51 (1997) (noting that "[t]he clear import of [21 U.S.C. § 321(n)] . . . is that labeling may be misleading not only because of what it says but because of what it fails to say" and that FDA has consistently "required declarations identifying the presence of ingredients possessing the potential to cause adverse reactions in consumers with sensitivities to such ingredients.")

That a food label can be misbranded because of the absence of material information, just as if the label included incorrect information, is of course consistent with the FFDCA's general

[10] A parallel provision concerning the false or misleading labeling of drugs and medical devices appears at 21 U.S.C. § 352(a).

goal of protecting "unwary customers in vital matters of health . . .". *216 Cartoned Bottles*, 409 F.2d at 741 (2d Cir. 1969). More specifically, "[m]isbranding was one of the chief evils Congress sought to stop when it enacted [the FFDCA]." *United States v. 45/194 Kg. Drums of Pure Vegetable Oil,* 961 F.2d 808, 812 (9th Cir. 1992). FDA and the courts have recognized that these important policy goals require the *inclusion* of material information regarding the consequences of using a product no less than the *exclusion* of false information about the product, so that consumers have available all the information, both positive and negative, necessary to inform their purchasing decisions. *See Henley v. FDA*, 77 F.3d 616, 621 (2d Cir. 1996) (noting that FDA construes 21 U.S.C. § 321(n) to mean that if consumers of oral contraceptives are not fully informed of the benefits and risks in the use of such products, such oral contraceptives are misbranded under the FFDCA); *V.E. Irons v. United States*, 244 F.2d 34, 40 (1st Cir. 1957) (whether label is "false or misleading" depends on its effect on consumers).

In the area of food safety, FDA relies primarily on nutrition and ingredient labeling, rather than on warning labels, to alert "unwary customers" to the risks of particular foods. *See* 53 Fed. Reg. 51065, 51076-78 (December 19, 1988) (disclaiming need for warning labels on foods containing sulfites in light of ingredient-labeling requirement for sulfites). The Agency recognizes ingredient labeling to be a particularly appropriate response where, as in the case of foods containing allergenic substances, the use of certain ingredients is potentially harmful to only a subset of the entire population. *Id.* at 51077 ("The agency has traditionally relied on ingredient labeling of food as the best means of ensuring that a subpopulation of sensitive individuals will be able to avoid certain food ingredients that are of no safety concern to the general population.") FDA's reliance on ingredient labeling in the food-safety context makes it

imperative for a food label to list ingredients that are recognized to have adverse health effects on consumers of that product. Food allergens are such ingredients.

In sum, (1) the general purpose of the FFDCA; (2) the Act's definition of "false or misleading" to encompass the exclusion of material information; (3) FDA's reliance on ingredient labeling to inform consumers of potentially harmful effects of consuming certain foods; and (4) the broad factual record concerning the threat posed by food allergens to millions of Americans all lead to one conclusion. If allergenic ingredients are not declared on food labels, the label lacks material information regarding the consequences of eating that food. The label is therefore "false or misleading," and the food product "misbranded," under the FFDCA. It is clearly within the Agency's authority to issue regulations to enforce the FFDCA's misbranding prohibition (21 U.S.C. § 371(a)), and therefore clearly within its authority to require the declaration of food allergens on ingredient labels.

2. The Agency May Require the Declaration of Allergenic Substances Pursuant to its Authority to Regulate Food Additives Under Section 409 of the FFDCA.

Section 409 of the FFDCA governs the FDA's authority to regulate the use of food additives. This section provides an alternative basis for a requirement that allergenic foods – including (as discussed below) spices, flavorings, and incidental additives -- be declared on ingredient labels.

Subject to certain exceptions, food additives are defined in the FFDCA as any substance that is a component of or otherwise is expected to affect the characteristics of food. 21 U.S.C. § 321(s). The eight allergens that are the focus of this petition often take the form of relatively minor components of other foods and therefore qualify at the threshold as food additives. However, a food substance that otherwise meets the definition of "food additive" in 21 U.S.C. § 321(s) is only deemed to be an additive subject to FDA regulation if it is not "generally

recognized . . . to be safe under the conditions of its intended use . . . ." 21 U.S.C. § 321(s). This so-called GRAS exception was enacted as part of the 1958 Food Additives Amendment to the FFDCA. The exception was in part designed to exempt from the FDA regulatory regime applicable to food additives those natural ingredients -- for example, starch -- that are commonly used in foods, but that over the course of time have been perceived as having no adverse health effects on consumers. *See Fmali Herb, Inc. v. Heckler*, 715 F.2d 1385, 1388-89 (9th Cir. 1983) (discussing legislative history of GRAS provisions). It is critical, however, to recognize that the mere fact that a food has been in common use for a long period of time is not sufficient in and of itself to make that food GRAS. Rather, "'common use in food' merely describes one form of evidence that may be introduced by a proponent for the purpose of meeting the ultimate standard, which is whether the ingredient is safe for human consumption." *Id.* at 1389.

The eight principal food allergens, no matter how long they have been in use as components of food, cannot meet that ultimate standard. The evidence is unequivocal. 29,000 people per year are rushed to hospital emergency rooms because of allergic reactions to foods.[11] Studies place the number of "severe" reactions to these allergens at anywhere from 950 to 2,500 per year. *See* Attorneys General petition at 14 (citing studies). And, as noted earlier, 150 Americans per year are estimated to die as a result of these reactions. "It is generally recognized that GRAS requires a fairly high level of scientific consensus." Lars Noah and Richard Merrill, "Starting from Scratch?: Reinventing the Food Additive Approval Process", 78 *B.U. L. Rev.* 329, 352 (1998)) ("Noah & Merrill"). *See also Cutler v. Hayes*, 818 F.2d 879, 894 (D.C. Cir. 1987) ("For a drug to be generally recognized as effective, there must be expert consensus founded upon substantial evidence") (internal quotations, citations omitted). The only consensus that

[11] Bock, *supra* n. 6 at 193.

appears to exist with respect to food allergens is that they are generally recognized as *unsafe* for a significant sector of the population.

Sections 409(c) and (d) of the FFDCA authorize, and in the case of section 409(c) *requires*, FDA to issue regulations prescribing the conditions under which a food additive must be used if that additive is to be permitted to remain on the market.[12] 21 U.S.C. §§ 348(c), (d). Such regulations may include "any directions or other labeling or packaging requirements for such additive deemed necessary by [the Agency] to assure the safety of . . . use [of the additive]." 21 U.S.C. § 348(c)(1). Clearly, therefore, if food manufacturers -- both domestic and foreign selling in this country -- do not all voluntarily include allergen information on food labels, the Agency may (indeed, must) require the declaration of food allergens if those allergens are to be kept on the market.

Even if food allergens have been accorded GRAS status by FDA, and are therefore currently exempted from the food additive regulatory process, FDA may still require label information regarding these foods.

First, FDA has made clear that "[n]ew information may at any time require reconsideration of the GRAS status of a food ingredient." 21 C.F.R. § 170.30(l). And indeed, revocation of GRAS status is not extraordinary. *See, e.g., Saccharin and its Salts; Removal from Generally Recognized as Safe List; Provisional Regulation Prescribing Conditions of Safe Use*, 36 Fed. Reg. 12109 (June 25, 1971) (proposing to revoke saccharin's GRAS status and substitute a provisional food additive regulation); *Cyclamic Acid and Its Salts*, 34 Fed. Reg. 17063

[12] Section 409(c) governs the Secretary's authority to issue regulations in response to a food additive petition. 21 U.S.C. § 348(c). Section 409(d) governs the Secretary's authority to issue on his or her own initiative regulations governing the use of food additives. 21 U.S.C. § 348(d).

(October 21, 1969) (revoking cyclamate's GRAS status).[13] As the Attorneys General petition notes, at page 14, the studies revealing the risks of food allergens are of relatively recent vintage and furnish the Agency with ample authority to revisit its prior conclusion that a consensus existed as to the safety of these substances.[14]

Second, even if a food retains its GRAS status, FDA regulations permit the Agency to regulate uses of that food as a condition of continued GRAS status. *See* 21 C.F.R. § 170.30(j); Noah & Merrill at 358 ("GRAS substances are not exempt from all FDA controls. For instance, users must comply with any specific usage limitations in a GRAS affirmation regulation.") (Citing 21 C.F.R. § 170.30.) Thus, FDA could require a food allergen to be declared on food labels as a condition of that allergen's continued GRAS status.

In short, whether a particular food allergen is determined to be a food additive under FFDCA section 409, or is entitled to GRAS status, FDA has ample authority to regulate uses of that allergen through the imposition of labeling requirements.

It should also be noted that just as FFDCA sections 409(c) and (d), governing food additives, provide FDA with authority to regulate allergenic substances, so too does section 721(b) of the FFDCA, a parallel provision governing *color* additives (21 U.S.C. § 379e(b)). None of the eight allergenic substances that are the focus of this petition is a color additive, but to the extent that FDA identifies color additives that, by virtue of their allergenic qualities,

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[13] FDA need not issue a regulation to remove a food substance from the GRAS list, but need only publish notice in the Federal Register that a substance is not GRAS and is a food additive subject to regulation under FFDCA section 409. 21 U.S.C. § 348. *See* 21 C.F.R. § 170.38.

[14] *See also* Formanek *supra*. n. 4 ("'The prevalence of food allergy is growing and probably will continue along with all allergic diseases'")(quoting Dr. Robert A. Wood, director of pediatric allergy clinic at Johns Hopkins Medical Institutions).

endanger the public health,[15] section 721(b) provides the Agency with authority to require the declaration of such additives. *E.g.*, 21 C.F.R. § 74.705(d)(2) (requiring declaration of the color additive Yellow Dye No. 5).

3. Neither the Exemption for Spices, Flavorings, and Colors Contained in FFDCA Section 403(i) Nor the "Incidental Additive" Exception in FDA's Regulations Limits FDA's Ability to Require Declaration of Food Allergens.

a. Spices, Flavorings, and Colors Exemption

Allergenic substances may appear in foods as spices, flavorings, or colors. For example, "natural flavorings" that contain peanut flour may be used in packaged soup and partially hydrated casein may be found in hot dogs.[16] Although section 403(i) of the FFDCA generally requires that *all* ingredients in foods fabricated from two or more ingredients be declared on the food's label, that section exempts from these requirements spices, flavorings, and colorings, which may be collectively, rather than individually, designated. 21 U.S.C. § 343(i). Clearly, however, the exemption in section 403(i) does not preclude FDA from requiring the declaration under FFDCA section 403(a) of any spices, colors, or flavorings, such as those containing food allergens, that cause adverse health effects in consumers of foods containing those ingredients. Nor does section 403(i) preclude the Agency from requiring the declaration of allergens pursuant

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[15] For example, carmine or cochineal extract (natural colorings in popsicles), saffron, and annatto colorings have been found to trigger allergic reactions in some individuals. Baldwin JL, Chou AH, Solomon WR, "Popsicle-induced anaphylaxis due to carmine dye allergy." *Ann Allergy Asthma Immunol* 1997;79:415-9. Lucas CD, Hallagan JB, Taylor SL. "The role of natural color additives in food allergy." *Adv Food Nutr Res* 2001; 43:195-216. CSPI has petitioned FDA to require labeling of carmine and cochineal extract colorings. *See* CSPI Petition, August 24, 1998.

[16] McKenna C, Klontz KC, "Systemic allergic reaction following ingestion of undeclared peanut flour in a peanut-sensitive woman," *Ann Asthma Imunol.* 1997; 79:234-6; Gern JE, Yang E, Evrard HM, Sampson HA, "Allergic reaction to mil-contaminated 'non-dairy' products," *New Engl J Med* 1991; 324:976-9.

to its authority to regulate food and color additives. Such a reading of section 403(i) would be contrary to established Agency practice, to longstanding rules of statutory construction, and to the overall purpose of the FFDCA.

FDA has routinely required spices, flavorings, and colors to be declared on food labels where it determined that such requirements were necessary as a matter of public health. For example, Agency regulations require that:

- Any monosodium glutamate used as an ingredient in food be declared by its common or usual name, "monosodium glutamate." 21 C.F.R. § 101.22(h)(5).
- Any protein hydrolysate used in foods for its effect on flavor be declared by its specific or common name, not simply designated as "flavor" or "flavoring." 22 C.F.R.§ 101.22(h)(7).
- *All* ingredients, including spices, flavorings, and colorings, contained in foods that purport to be hypoallergenic be declared. 21 C.F.R. § 105.62
- *All* ingredients, including spices, flavorings, and colorings, contained in foods that purport to be for infant use be declared. 21 C.F.R. § 105.65.
- The coloring additive Yellow Dye No. 5 be declared. 21 C.F.R. § 74.705(d)(2).

In requiring ingredient labeling of certain spices, flavorings, and colorings, notwithstanding the section 403(i) labeling exemption, FDA has recognized that section 403(a), 409, and 721, on one hand, and 403(i), on the other, *complement* one another. It is precisely because the FFDCA permits FDA to require the declaration of potentially dangerous food and color additives that it is generally acceptable to exempt spices, flavorings, and colors from coverage under 403(i).

The Agency has made precisely this point in response to arguments that it should eliminate the spices, flavorings and colorings exemption from section 403(i). FDA rejected such arguments, determining that mandatory declaration of all flavorings would make food labels needlessly complicated. The Agency also noted, however, that "[i]f it becomes necessary for public health or other reasons to require the label declaration of any food ingredient that is exempt from required label declaration, the agency can establish such a requirement as it has done for flavorings, colorings, and spices when used in infant foods . . . and hypoallergenic foods and for the color additive FD&C Yellow No. 5 when used in foods generally." 56 Fed. Reg. 28592, 28595 (June 21, 1991). *See also* FDA Notice at 2 ("[o]n a substance-by-substance basis, the agency has required ingredients covered by the [403(i)] exemption to be declared when necessary to protect individuals who experience adverse reactions to the substance . . ."). Even the food industry, which opposes a general repeal of the spices, flavorings, and colors exemption, has "acknowledged that it would be appropriate to require the label declaration of a specific flavoring, coloring, or spice when public health concerns justify such a requirement." 56 Fed. Reg. at 28594-95 (June 21, 1991).

That FDA may require the declaration of food allergens notwithstanding the exemption in section 403(i) is thoroughly consistent with established rules of statutory construction, and with the purpose of the FFDCA. Because sections 403(a), 403 (i), 409, and 721 of the FFDCA are all part of the same statute, they must be together, so as to give effect to the construed FFDCA's overall purpose. *In Re Graven*, 936 F.2d 378 (8th Cir. 1991) (interpreting potentially conflicting provisions of Bankruptcy Code with an eye toward the overall purposes of the Code); *Crandon v. United States*, 494 U.S. 152, 158 (1990) (statutory construction requires examination of "the design of the statute as a whole and . . . its object and policy."). The overall purpose of the

FFDCA is, as noted above, to protect the public health, and courts have long recognized that this broad remedial purpose requires the statute to be given a liberal construction. *An Article of Drug . . . Bacto-Unidisk, supra*; *216 Cartoned Bottles, supra*. It would be thoroughly inconsistent with this liberal interpretation of the FFDCA to essentially exempt from any labeling requirement spices, flavorings, or colorings that have been proven to be dangerous to significant segments of the public.

As noted above, the Agency has already acknowledged that the undeclared presence of allergens in foods is a serious public health issue. 66 Fed. Reg. at 38592. The basic purposes and policy goals of the FFDCA would be completely frustrated if the exemption in section 403(i) were permitted to prevent FDA from addressing this issue. That exemption presents no impediment whatsoever to FDA's ability to require labeling of such additives where, as here, the public health demands it.

b. Incidental Additives Exemption

Nor does the labeling exemption for "incidental additives" (21 C.F.R. § 101.100(a)(3)) pose an obstacle to an allergen labeling requirement. This regulatory exemption -- which has no statutory basis -- requires that the additive be present in the food at insignificant levels, *id.*, and as FDA has recognized, "[c]learly, an amount of a substance that may cause an adverse reaction is not insignificant." *See* FDA Notice at 2; FDA Statement of Policy for Labeling and Preventing Cross-Contact of Common Food Allergens, April 19, 2001 ("April 19 FDA Compliance Policy Guide"). The Agency has further recognized that, given the small amounts of a food allergen that are needed to trigger a reaction, "it is unlikely that such an allergen, when it is present in a food, can be present at an insignificant level." *Id.*

Thus, a food allergen *never* qualifies as an incidental additive under the Agency's regulations and is therefore not exempt from any labeling requirements the Agency may promulgate. *See* April 19 FDA Compliance Policy Guide ("FDA. . . has never considered food allergens eligible for [the incidental additive] exemption."). Moreover, an "incidental additive" must also have no technical or functional effect in the finished food. 21 C.F.R. § 101.100(a)(3). In many cases, a food allergen added as an ingredient *does* have such an effect, and therefore does not qualify for the exemption. *See* FDA Notice at 1 (noting that egg whites added as a binder in breading used on a breaded fish product is not an incidental additive for purposes of 21 C.F.R. § 101.100(a)(3)).[17]

C. FDA May Establish GMPs to Avoid Cross-Contamination of Non-Allergenic Foods Pursuant to its Authority to Enforce the Prohibition Against Adulterated Foods in Section 402 of the FFDCA.

Label declaration requirements for food allergens enable consumers to identify foods that are *intended* to contain allergenic substances. As discussed in the statement of factual grounds, however, the *inadvertent* inclusion of allergens in foods is also a serious problem, due to the potential for "cross-contamination."[18] Thus, the public health requires FDA to establish by

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[17] While food allergens should presumptively be ineligible for the "incidental additive" exemption, it is possible that the amount of an allergen in a particular food may be so insignificant that that allergen will not cause any reaction in those circumstances. CSPI believes that if a manufacturer can prove that the amount of an allergen in its product is below any reasonable threshold for allergenicity, that allergen could be treated as an "incidental additive" that is entitled to a regulatory exemption from labeling requirements.

[18] Examples of reactions due to cross-contamination include two instances of children suffering anaphylaxis due to milk protein in sorbet, and a reaction to peanut antigen contained in gingersnap cookies. Laoprasert N, Wallen NF, Jones RT, Hefle SL, Taylor SL, "Anaphylaxis in milk-allergic children following ingestion of lemon sorbet containing trace quantities of milk," *J Food Prot* 1998;61;1522-4. Jones RT, Squillace DL, Yunginger JW, "Anaphylaxis in a milk-allergic child after ingestion of milk-contaminated kosher-pareve-labeled 'dairy-free' desert," *Ann Allergy* 1992;68:223-7. Kemp SF, Lockey RF, "Peanut anaphylaxis from food cross-contamination," *JAMA* 1996;275:1636-7.

regulation GMPs that will guide manufacturers in their efforts to prevent cross-contamination. Indeed, FDA has recognized that "adhering to GMPs is essential for effective reduction of adverse [allergic] reactions" and that advisory "may contain" labeling is not an appropriate substitute for such adherence. 66 Fed. Reg. 38591, 38592 (July 25, 2001).[19] The FFDCA provides FDA with ample authority to issue these GMPs, just as it provides the Agency with authority to require the label declaration of allergens.

In addition to banning the circulation in interstate commerce of "misbranded" foods, the FFDCA also prohibits the introduction into interstate commerce of foods that are "adulterated." 21 U.S.C. § 331(a). Section 402 (a) (4) of the FFDCA (21 U.S.C. § 342 (a) (4)) defines "adulterated foods" to include foods "prepared, packed, or held under insanitary conditions whereby [they] may have . . . been rendered injurious to health." FDA has recognized that foods containing allergens inadvertently introduced through cross-contamination may be considered "adulterated" under section 402. 66 Fed. Reg. 398591, 38592-93 (July 25, 2001); April 19 FDA Compliance Policy Guide. Moreover, the FFDCA clearly permits the use by FDA of GMPs as a benchmark for determining whether a food product was manufactured in "insanitary" conditions, and FDA has routinely exercised this authority. *See, e.g.,* 21 C.F.R. § 110.5 (criteria for good manufacturing practices "shall apply in determining whether a food . . . has been prepared, packed, or held under insanitary conditions . . . whereby it may have been rendered injurious to health"). The current GMPs do not address the problem of food allergens. However, it is clear that FDA has the authority to adopt GMPs to prevent cross-contamination of non-allergenic foods and thereby to enforce the prohibition of adulterated foods found in the FFDCA.

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[19] As noted below, however, "may contain" labeling may be appropriate where GMPs alone cannot ensure lack of cross-contamination.

Moreover, as discussed above, to the extent that a food allergen is determined to be a "food additive" under section 409 of the FFDCA or "color additive" under FFDCA section 721, FDA must prescribe regulations for its safe use. 21 U.S.C. 348(c)(1)(A); 21 U.S.C. 379(e). And to the extent that a food retains its GRAS status, FDA may impose use limitations as a condition of continued GRAS status. 21 C.F.R. § 370.130(j). Just as such regulations could include labeling requirements, they may also set forth GMPs to prevent the inadvertent introduction of allergenic foods into non-allergenic foods.

Of course, reliance on GMPs presumes that a manufacturer, through the use of the prescribed practices, can prevent the inadvertent introduction of allergens into foods. CSPI recognizes, however, that under some circumstances it may be impossible for a manufacturer to ensure lack of cross-contamination. Under those circumstances, advisory or "may contain" labeling serves to warn consumers of the possibility that an allergen may have been introduced inadvertently into a food. "May contain" labeling, however, should not serve as a substitute for GMPs when the latter may safely guarantee no cross-contamination. Rather, it is only when GMPs are unable to prevent cross-contamination that these "may contain" labeling requirements are appropriate, indeed essential.

V. Conclusions and Recommendations

In light of the overwhelming evidence that food allergens pose substantial health risks to millions of Americans, CSPI urges FDA to establish at the earliest possible date requirements for the label declaration of the eight principal food allergens. CSPI also urges the Agency to establish GMPs and "may contain" labeling to address the problem of inadvertent cross-contamination by allergens of non-allergenic foods.

VI. Environmental Impact

CSPI believes that the action requested in this petition has no significant environmental impact.

VII. Economic Impact

No statement of the economic impact of the requested revisions to the rules is presented because none has been requested by the Commissioner.[20]

VIII. Certification

The undersigned certify that, to their best knowledge and belief, this petition includes all information and views on which the petitioner relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

William B. Schultz
Carlos T. Angulo
Zuckerman Spaeder LLP
1201 Connecticut Avenue, N.W.
Washington, D.C. 20036

Attorneys for Center for Science in the Public Interest

Dated: October 4, 2001

[20] 21 C.F.R. § 10.30(b).

ZUCKERMAN SPAEDER LLP

ATTORNEYS AT LAW

1201 CONNECTICUT AVENUE, N.W.
WASHINGTON, D.C. 20036-2638
(202) 778-1800
FACSIMILE (202) 822-8106

WILLIAM B. SCHULTZ
(202) 778-1820
WSCHULTZ@ZUCKERMAN.COM

October 4, 2001

Bernard A. Schwetz, D.V.M., Ph.D.
Acting Principal Deputy Commissioner
Food and Drug Administration
5600 Fishers Lane, Rm 14-71
Rockville, MD 20857

Dear Dr. Schwetz,

Please find attached a Petition we have submitted to the FDA on behalf of the Center for Science in the Public Interest ("CSPI") regarding the labeling and manufacturing of foods containing allergenic substances.

The CSPI petition urges FDA to require the declaration of allergenic foods on ingredient labels, and to establish good manufacturing practices ("GMP's") to prevent the inadvertent introduction of allergenic ingredients into non-allergenic foods. This petition addresses the same issues raised in a recent petition filed with FDA by nine State Attorneys General. Docket No. 00P-1322. As set forth more fully in its petition, CSPI endorses many of the specific regulatory recommendations of the State Attorneys General. CSPI's petition also makes clear that FDA has the statutory and regulatory authority both to impose labeling requirements for allergenic foods, and to establish GMPs designed to prevent the contamination of non-allergenic foods.

FDA has identified the problem of allergenic foods as a serious public health issue, and we therefore hope the Agency will take prompt and thorough action to address this problem, in line with the recommendations in the CSPI and Attorneys General petitions.

Sincerely,

William B. Schultz

William B. Schultz
Carlos T. Angulo

Attachment

c: William Hubbard, Senior Associate Commissioner
Joseph Levitt, Director of Center for Food Safety and Applied Nutrition
Dan Troy, Chief Counsel

01 5082

FOOD AND DRUG ADMINISTRATION

Petition for Rules Regarding The Labeling and Manufacture of Foods Containing Allergenic Substances	)	**Docket No. _____**

Submitted on Behalf of the Center for Science in the Public Interest

October 4, 2001

I. Introduction

This petition is submitted on behalf of the Center for Science in the Public Interest ("CSPI") and requests action by the Food and Drug Administration ("FDA") regarding allergenic food substances.[1] Specifically, CSPI requests that the FDA Commissioner amend Title 21 of the Code of Federal Regulations to provide adequate notice and protection to individuals with food allergies through (1) the imposition of labeling requirements for food allergens, and (2) the establishment of "Good Manufacturing Practices" ("GMPs") aimed at preventing the inadvertent introduction of such allergens into non-allergenic foods.

CSPI is a nonprofit education and advocacy organization with 800,000 members that focuses on, among other things, improving the safety and nutritional quality of our food supply. CSPI seeks to promote health through educating the public about nutrition and works to ensure that advances in science are used for the public good. CSPI represents its members and citizens' interests before legislative, regulatory, and judicial bodies.

FDA has concluded that "the undeclared presence of allergens in foods is a serious public health issue." 66 Fed. Reg. 38591-92 (July 25, 2001). Consistent with the Agency's conclusion, CSPI strongly believes that the public health requires the Agency to mandate the declaration of allergenic foods on ingredient labels. Such requirements will supply consumers suffering from

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[1] The foods most commonly recognized as allergenic and that cause the majority of serious reactions are: (1) peanuts; (2) milk; (3) eggs; (4) fish; (5) soybeans; (6) crustacea; (7) tree nuts; and (8) wheat. 66 Fed. Reg. 38591, 38592 (July 25, 2001). These eight foods are the focus of the May 26, 2000 Attorneys General petition on food allergens (*infra* p. 3), and of FDA's food allergen awareness efforts. *Id.* Thus, references in this petition to "food allergens" or "allergenic substances" are also to these eight allergens. Nonetheless, other foods, including strawberries, apples, carrots, parsnips, celery, hazelnuts, potatoes, and kiwi, can also cause serious allergic reactions (http://wwww.allergylearninglab.com/about/food/index.html?id+4195215 (June 21, 2001)). Also, some food additives, such as sulfites and carmine, can cause serious allergic or non-allergic reactions. CSPI therefore urges FDA to review whether ingredients other than the

food allergies with the information they need to make informed choices about what foods they eat and to avert the potentially fatal consequences of consuming foods to which they are allergic. The public health also requires that food manufacturers follow stringent manufacturing practices to ensure that food allergens are not *inadvertently* added to non-allergenic foods.

In a petition submitted on May 26, 2000, Attorneys General from the States of New York, Maryland, Michigan, Wyoming, Ohio, Tennessee, Connecticut, Vermont, and Massachusetts urged FDA to adopt by regulation specific requirements that the eight major food allergens be declared on food labels and to establish GMPs to prevent the unintentional inclusion of those allergens in foods. Docket No. 00P-1322. CSPI strongly supports most of the specific regulatory changes urged in the Attorneys General petition. This petition further demonstrates that FDA has the legal authority to implement these requested regulations.

This petition is submitted pursuant Section 4(d) of the Administrative Procedure Act, 5 U.S.C. § 553(e), 21 C.F.R. § 10.30, and Sections 201(n), 402, 403(a), 403(i), 409(c), and 721(b) of the Federal Food Drug and Cosmetic Act ("FFDCA"), 21 U.S.C. §§ 321(n), 342, 343(a), 343(i), 348, and 379e(b). As we demonstrate below, the Agency has ample authority under the FFDCA both to require the declaration of allergenic substances on food labels and to establish the requested GMPs.

II. Action Requested

The Attorneys General petition sets forth, at pp. 4-11, specific amendments to Title 21, Code of Federal Regulations, requiring the declaration of food allergens on ingredient labels and

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eight major allergens should also be regulated in the manner suggested in this and the Attorneys General petitions.

establishing GMPs aimed at preventing the inadvertent introduction of allergens into non-allergenic foods. CSPI supports all the specific regulatory recommendations of the State Attorneys General[2] except the recommendation that foods that contain or may contain an allergenic substance display an allergen insignia on the product package (Attorneys General petition at 5-6). CSPI is concerned that this allergen insignia will overshadow other important nutritional and health information on the food label.[3]

III. Statement of Factual Grounds

The Attorneys General petition, at pp. 14-23, comprehensively sets forth the factual basis for the requested amendments to the FDA's regulations. The facts set forth in that petition support beyond dispute FDA's own conclusion that the undeclared presence of food allergens is a serious public health issue. CSPI supplements that statement of facts as follows.

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[2] At the August 13, 2001, public hearing on allergens, it was suggested that some of the current specific food standard regulations, 21 C.F.R. §§ 130 *et seq.*, would have to be amended to comply with a requirement that allergens be declared using their common names (tr. 60-61). There is, however, a general requirement that the ingredients for these standardized foods be labeled in accordance with the general food labeling regulations set forth in 21 C.F.R. Part 101. 21 C.F.R. § 130.3(e). This general requirement is repeated for specific products that contain an allergen, such as macaroni products, 21 C.F.R. § 139.110(g), or mayonnaise, 21 C.F.R. § 169.140(f). Thus, the requested changes to part 101 will extend to these standardized foods.

[3] On July 26, 2001, CSPI submitted a separate citizens petition to FDA regarding the establishment of format requirements for ingredient lists. In that petition, CSPI discussed the relevance of ingredient labeling to the problem of food allergens and urged the adoption of more readable ingredient lists. We incorporate that petition by reference.

Approximately four million Americans,[4] including up to six percent of all American children,[5] are allergic to one type of food or another. As mentioned, at note 1, eight food substances are most commonly recognized as allergenic, and account for the great majority of serious allergic reactions. They are (1) peanuts; (2) milk; (3) eggs; (4) fish; (5) soybeans; (6) crustacea; (7) tree nuts; and (8) wheat.

Food allergies are a serious public health threat for five reasons. First, there is currently no medical treatment available to prevent allergic reactions to food. The only method to manage a food allergy is strictly to avoid the offending food. 66 Fed. Reg. 38591-92 (July 25, 2001). And some current labeling requirements prevent consumers with food allergies from identifying the foods they need to avoid.

Second, the reaction to food allergens can be extremely severe. Some individuals with food allergies run a high risk of suffering a severe allergic reaction known as anaphylaxis. Anaphylaxis is a swift and violent reaction that simultaneously affects various organ systems, including the skin, upper and lower respiratory system, cardiovascular system, eye, uterus, and bladder. Death can occur even if epinephrine is administered within minutes.[6] And, indeed, as many as 150 Americans per year die as a

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[4] Raymond Formanek, "Food Allergies: When Food Becomes the Enemy," *FDA Consumer Magazine*, July-August 2001 (on-line at http://www.fda.gov/fdca/features/2001/401_food.html.).

[5] *Id.*

[6] S. Allan Bock, M.D., Anne Munoz-Furlong, and Hugh A. Sampson, M.D., "Fatalities Due to Anaphylactic Reactions to Foods," 107 *J. Allergy Clin Immunology* 1: 191-193 (2001) at 192.

result of reactions to food allergens.[7] There is no question that the public health consequences of a failure to declare allergens on food labels can be extreme.

Third, the amount of an allergenic food that is needed in some cases to cause a severe reaction is minimal. For example, consumption of as little as one-fifth to one five-thousandth of a teaspoon of an allergenic food can cause death.[8] Thus, what may appear to be an insignificant amount of a food substance to a non-allergic individual is in fact a potentially fatal measure of the substance for someone who is allergic. This discrepancy underscores the importance of labeling. An allergy sufferer – or the parent of an allergy sufferer – cannot rely on the subjective determination of a non-allergy sufferer as to whether a particular substance is included in a food. Labeling provides an objective measure that enables the consumer to identify when a food has any amount of that substance, no matter how apparently insignificant to the untrained eye or palate.

Fourth, allergic reactions to food can occur in a variety of situations – in restaurants, other public eating places, neighbors' homes, and schools, as well as at home. Without proper vigilance on the part of both consumers who have food allergies and those who prepare food, food-induced anaphylaxis can strike at any time, and in a wide range of settings.

Fifth, food allergens are often inadvertently added to non-allergenic foods through "cross-contamination," which occurs when allergenic substances migrate from equipment, utensils, and packaging material into foods that are intended to be allergen-

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[7] Formanek, *supra* n.4.

[8] Audrey T. Hingley, "Food Allergies: Rare but Risky," *FDA Consumer Magazine*, December 1993, at pp. 27-31. *See also* Hourihane JO'B *et al.*, "An evaluation of the sensitivity of subjects with peanut allergy to very low doses of peanut protein: a randomized, double-blind, placebo-controlled food challenge study," *J. Allergy Clin. Immunology* 1997; 100:596-600.

free.[9] For example, in a bakery that manufactures cookies with nuts and without nuts on the same production line, traces of nuts may appear in the cookies that are supposed to be allergen-free. And because a very small amount of a food allergen is sufficient to cause a reaction, even the most incidental degree of cross-contamination can be fatal. Thus, it is not enough to address the problem of food allergens through labeling, which is intended to identify for consumers foods that intentionally contain allergens. Protection against the *inadvertent* introduction of allergens into foods is also necessary.

IV. Statement of Legal Grounds

The facts clearly demonstrate that the problem of food allergens requires an aggressive response on the part of the FDA. It is equally clear that FDA has authority under the FFDCA to require the label declaration of food allergens, and to establish GMPs designed to avoid cross-contamination.

A. The FFDCA Confers Broad Authority on FDA to Effectuate the Important Public Policy Goals of the Statute.

The general purpose of the FFDCA (21 U.S.C. § 301, *et seq.*) is to "protect unwary customers in vital matters of health . . . ." *United States v. 216 Cartoned Bottles, More or Less, of . . . Sudden Change*, 409 F.2d 734, 741 (2d Cir. 1969). Given the Act's broad remedial purpose, courts have construed the statute liberally. *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 798 (1969) (applying "the well-accepted principle that remedial

[9] Fred R. Shank, Ph.D., "Label Declaration of Allergenic Substances in Foods," *FDA Notice to Manufacturers* (June 10, 1996) ("FDA Notice"), at 3.

legislation such as the [FFDCA] is to be given a liberal construction consistent with the Act's overriding purpose to protect the public health . . ."); *216 Cartoned Bottles*, 409 F.2d at 741 ("[T]he Act . . . must be given a liberal construction to effectuate [its] high purpose."). The FFDCA confers authority on FDA to enforce the provisions of the statute by regulation (21 U.S.C. § 371(a)), and this regulatory authority, too, is "broad." *Cosmetic, Toiletry and Fragrance Ass'n v. Schmidt*, 409 F.Supp. 57, 64 (D.D.C. 1976) (upholding FDA Commissioner's authority to require warning statements on aerosolized food, drug, and cosmetic products). Finally, in evaluating the exercise of FDA's regulatory authority, courts accord great deference to the Agency's decisions, especially where they implicate the evaluation of scientific data within the Agency's technical expertise. *International Fabricare Inst. v. U.S. EPA*, 972 F.2d 384, 389 (D.C. Cir. 1992). *See also Community Nutrition Institute v. Young*, 476 U.S. 974, 981-82 (1986) (noting that "the FDA has been delegated broad discretion by Congress in any number of areas" and deferring to Agency expertise).

B. The Agency May Require the Declaration of Allergenic Substances on Ingredient Labels.

Several provisions of the FFDCA provide FDA with authority to require the labeling of allergenic foods in order to effectuate the statute's goal of protecting the public health. These are discussed below.

1. FDA May Require Labeling Pursuant to its Authority to Enforce the Prohibition on Misbranded Foods in Section 403(a) of the FFDCA.

The FFDCA prohibits the introduction into interstate commerce of any food or drug that is misbranded (21 U.S.C. § 331(a)), and, as noted above, FDA has broad authority to issue regulations to enforce this prohibition. 21 U.S.C. § 371(a). This authority permits the Agency to require the declaration of allergenic substances -- including (as discussed below in section IV.B.3) spices, flavorings, colors and "incidental" additives -- on food labels.

Section 403 of the FFDCA (21 U.S.C. § 343) sets forth the different ways in which a food product may be misbranded. Under section 403(a), a food is deemed to be misbranded if "its labeling [is] false or misleading in any particular . . . ." 21 U.S.C. § 343(a)(1).[10] Under FFDCA section 201(n) (21 U.S.C. § 321(n)), labeling of an article (including a food product) is "false or misleading" if it "fails to reveal [material] facts . . . with respect to consequences which may result from the use of the article to which the labeling or advertising relates . . . under such conditions of use as are customary or usual." The statute could not be clearer: the failure of a food label to provide material information regarding the potential adverse consequences of eating a food, no less than affirmative misrepresentations, can cause a food to be falsely or misleadingly labeled, and therefore misbranded. *See United States v. 62 Packages of Marmola Prescription Tablets*, 48 F.Supp. 878, 884 (W.D. Wisc. 1948) ("There is nothing indefinite or ambiguous about [21 U.S.C. § 321(n)].") FDA has adhered to this unambiguous language, confirming that "a food label is misleading if it does not disclose consequences that may result from consumption of the food." 61 Fed. Reg. 48102, 48106 (September 12, 1996). *See also* Frederick H. Degnan, "The Food Label and the Right to Know," 52 *Food Drug L.J.* 49, 51 (1997) (noting that "[t]he clear import of [21 U.S.C. § 321(n)] . . . is that labeling may be misleading not only because of what it says but because of what it fails to say" and that FDA has consistently "required declarations identifying the presence of ingredients possessing the potential to cause adverse reactions in consumers with sensitivities to such ingredients.")

That a food label can be misbranded because of the absence of material information, just as if the label included incorrect information, is of course consistent with the FFDCA's general

[10] A parallel provision concerning the false or misleading labeling of drugs and medical devices appears at 21 U.S.C. § 352(a).

goal of protecting "unwary customers in vital matters of health . . .". *216 Cartoned Bottles*, 409 F.2d at 741 (2d Cir. 1969). More specifically, "[m]isbranding was one of the chief evils Congress sought to stop when it enacted [the FFDCA]." *United States v. 45/194 Kg. Drums of Pure Vegetable Oil,* 961 F.2d 808, 812 (9th Cir. 1992). FDA and the courts have recognized that these important policy goals require the *inclusion* of material information regarding the consequences of using a product no less than the *exclusion* of false information about the product, so that consumers have available all the information, both positive and negative, necessary to inform their purchasing decisions. *See Henley v. FDA*, 77 F.3d 616, 621 (2d Cir. 1996) (noting that FDA construes 21 U.S.C. § 321(n) to mean that if consumers of oral contraceptives are not fully informed of the benefits and risks in the use of such products, such oral contraceptives are misbranded under the FFDCA); *V.E. Irons v. United States*, 244 F.2d 34, 40 (1st Cir. 1957) (whether label is "false or misleading" depends on its effect on consumers).

In the area of food safety, FDA relies primarily on nutrition and ingredient labeling, rather than on warning labels, to alert "unwary customers" to the risks of particular foods. *See* 53 Fed. Reg. 51065, 51076-78 (December 19, 1988) (disclaiming need for warning labels on foods containing sulfites in light of ingredient-labeling requirement for sulfites). The Agency recognizes ingredient labeling to be a particularly appropriate response where, as in the case of foods containing allergenic substances, the use of certain ingredients is potentially harmful to only a subset of the entire population. *Id.* at 51077 ("The agency has traditionally relied on ingredient labeling of food as the best means of ensuring that a subpopulation of sensitive individuals will be able to avoid certain food ingredients that are of no safety concern to the general population.") FDA's reliance on ingredient labeling in the food-safety context makes it

imperative for a food label to list ingredients that are recognized to have adverse health effects on consumers of that product. Food allergens are such ingredients.

In sum, (1) the general purpose of the FFDCA; (2) the Act's definition of "false or misleading" to encompass the exclusion of material information; (3) FDA's reliance on ingredient labeling to inform consumers of potentially harmful effects of consuming certain foods; and (4) the broad factual record concerning the threat posed by food allergens to millions of Americans all lead to one conclusion. If allergenic ingredients are not declared on food labels, the label lacks material information regarding the consequences of eating that food. The label is therefore "false or misleading," and the food product "misbranded," under the FFDCA. It is clearly within the Agency's authority to issue regulations to enforce the FFDCA's misbranding prohibition (21 U.S.C. § 371(a)), and therefore clearly within its authority to require the declaration of food allergens on ingredient labels.

2. The Agency May Require the Declaration of Allergenic Substances Pursuant to its Authority to Regulate Food Additives Under Section 409 of the FFDCA.

Section 409 of the FFDCA governs the FDA's authority to regulate the use of food additives. This section provides an alternative basis for a requirement that allergenic foods – including (as discussed below) spices, flavorings, and incidental additives -- be declared on ingredient labels.

Subject to certain exceptions, food additives are defined in the FFDCA as any substance that is a component of or otherwise is expected to affect the characteristics of food. 21 U.S.C. § 321(s). The eight allergens that are the focus of this petition often take the form of relatively minor components of other foods and therefore qualify at the threshold as food additives. However, a food substance that otherwise meets the definition of "food additive" in 21 U.S.C. § 321(s) is only deemed to be an additive subject to FDA regulation if it is not "generally

recognized . . . to be safe under the conditions of its intended use . . . ." 21 U.S.C. § 321(s). This so-called GRAS exception was enacted as part of the 1958 Food Additives Amendment to the FFDCA. The exception was in part designed to exempt from the FDA regulatory regime applicable to food additives those natural ingredients -- for example, starch -- that are commonly used in foods, but that over the course of time have been perceived as having no adverse health effects on consumers. *See Fmali Herb, Inc. v. Heckler*, 715 F.2d 1385, 1388-89 (9th Cir. 1983) (discussing legislative history of GRAS provisions). It is critical, however, to recognize that the mere fact that a food has been in common use for a long period of time is not sufficient in and of itself to make that food GRAS. Rather, '"common use in food' merely describes one form of evidence that may be introduced by a proponent for the purpose of meeting the ultimate standard, which is whether the ingredient is safe for human consumption." *Id.* at 1389.

The eight principal food allergens, no matter how long they have been in use as components of food, cannot meet that ultimate standard. The evidence is unequivocal. 29,000 people per year are rushed to hospital emergency rooms because of allergic reactions to foods.[11] Studies place the number of "severe" reactions to these allergens at anywhere from 950 to 2,500 per year. *See* Attorneys General petition at 14 (citing studies). And, as noted earlier, 150 Americans per year are estimated to die as a result of these reactions. "It is generally recognized that GRAS requires a fairly high level of scientific consensus." Lars Noah and Richard Merrill, "Starting from Scratch?: Reinventing the Food Additive Approval Process", 78 *B.U. L. Rev.* 329, 352 (1998)) ("Noah & Merrill"). *See also Cutler v. Hayes*, 818 F.2d 879, 894 (D.C. Cir. 1987) ("For a drug to be generally recognized as effective, there must be expert consensus founded upon substantial evidence") (internal quotations, citations omitted). The only consensus that

[11] Bock, *supra* n. 6 at 193.

appears to exist with respect to food allergens is that they are generally recognized as *unsafe* for a significant sector of the population.

Sections 409(c) and (d) of the FFDCA authorize, and in the case of section 409(c) *requires*, FDA to issue regulations prescribing the conditions under which a food additive must be used if that additive is to be permitted to remain on the market.[12] 21 U.S.C. §§ 348(c), (d). Such regulations may include "any directions or other labeling or packaging requirements for such additive deemed necessary by [the Agency] to assure the safety of . . . use [of the additive]." 21 U.S.C. § 348(c)(1). Clearly, therefore, if food manufacturers -- both domestic and foreign selling in this country -- do not all voluntarily include allergen information on food labels, the Agency may (indeed, must) require the declaration of food allergens if those allergens are to be kept on the market.

Even if food allergens have been accorded GRAS status by FDA, and are therefore currently exempted from the food additive regulatory process, FDA may still require label information regarding these foods.

First, FDA has made clear that "[n]ew information may at any time require reconsideration of the GRAS status of a food ingredient." 21 C.F.R. § 170.30(l). And indeed, revocation of GRAS status is not extraordinary. *See, e.g., Saccharin and its Salts; Removal from Generally Recognized as Safe List; Provisional Regulation Prescribing Conditions of Safe Use*, 36 Fed. Reg. 12109 (June 25, 1971) (proposing to revoke saccharin's GRAS status and substitute a provisional food additive regulation); *Cyclamic Acid and Its Salts*, 34 Fed. Reg. 17063

[12] Section 409(c) governs the Secretary's authority to issue regulations in response to a food additive petition. 21 U.S.C. § 348(c). Section 409(d) governs the Secretary's authority to issue on his or her own initiative regulations governing the use of food additives. 21 U.S.C. § 348(d).

(October 21, 1969) (revoking cyclamate's GRAS status).[13] As the Attorneys General petition notes, at page 14, the studies revealing the risks of food allergens are of relatively recent vintage and furnish the Agency with ample authority to revisit its prior conclusion that a consensus existed as to the safety of these substances.[14]

Second, even if a food retains its GRAS status, FDA regulations permit the Agency to regulate uses of that food as a condition of continued GRAS status. *See* 21 C.F.R. § 170.30(j); Noah & Merrill at 358 ("GRAS substances are not exempt from all FDA controls. For instance, users must comply with any specific usage limitations in a GRAS affirmation regulation.") (Citing 21 C.F.R. § 170.30.) Thus, FDA could require a food allergen to be declared on food labels as a condition of that allergen's continued GRAS status.

In short, whether a particular food allergen is determined to be a food additive under FFDCA section 409, or is entitled to GRAS status, FDA has ample authority to regulate uses of that allergen through the imposition of labeling requirements.

It should also be noted that just as FFDCA sections 409(c) and (d), governing food additives, provide FDA with authority to regulate allergenic substances, so too does section 721(b) of the FFDCA, a parallel provision governing *color* additives (21 U.S.C. § 379e(b)). None of the eight allergenic substances that are the focus of this petition is a color additive, but to the extent that FDA identifies color additives that, by virtue of their allergenic qualities,

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[13] FDA need not issue a regulation to remove a food substance from the GRAS list, but need only publish notice in the Federal Register that a substance is not GRAS and is a food additive subject to regulation under FFDCA section 409. 21 U.S.C. § 348. *See* 21 C.F.R. § 170.38.

[14] *See also* Formanek *supra*. n. 4 ("'The prevalence of food allergy is growing and probably will continue along with all allergic diseases'")(quoting Dr. Robert A. Wood, director of pediatric allergy clinic at Johns Hopkins Medical Institutions).

endanger the public health,[15] section 721(b) provides the Agency with authority to require the declaration of such additives. *E.g.*, 21 C.F.R. § 74.705(d)(2) (requiring declaration of the color additive Yellow Dye No. 5).

3. Neither the Exemption for Spices, Flavorings, and Colors Contained in FFDCA Section 403(i) Nor the "Incidental Additive" Exception in FDA's Regulations Limits FDA's Ability to Require Declaration of Food Allergens.

a. Spices, Flavorings, and Colors Exemption

Allergenic substances may appear in foods as spices, flavorings, or colors. For example, "natural flavorings" that contain peanut flour may be used in packaged soup and partially hydrated casein may be found in hot dogs.[16] Although section 403(i) of the FFDCA generally requires that *all* ingredients in foods fabricated from two or more ingredients be declared on the food's label, that section exempts from these requirements spices, flavorings, and colorings, which may be collectively, rather than individually, designated. 21 U.S.C. § 343(i). Clearly, however, the exemption in section 403(i) does not preclude FDA from requiring the declaration under FFDCA section 403(a) of any spices, colors, or flavorings, such as those containing food allergens, that cause adverse health effects in consumers of foods containing those ingredients. Nor does section 403(i) preclude the Agency from requiring the declaration of allergens pursuant

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[15] For example, carmine or cochineal extract (natural colorings in popsicles), saffron, and annatto colorings have been found to trigger allergic reactions in some individuals. Baldwin JL, Chou AH, Solomon WR, "Popsicle-induced anaphylaxis due to carmine dye allergy." *Ann Allergy Asthma Immunol* 1997;79:415-9. Lucas CD, Hallagan JB, Taylor SL. "The role of natural color additives in food allergy." *Adv Food Nutr Res* 2001; 43:195-216. CSPI has petitioned FDA to require labeling of carmine and cochineal extract colorings. *See* CSPI Petition, August 24, 1998.

[16] McKenna C, Klontz KC, "Systemic allergic reaction following ingestion of undeclared peanut flour in a peanut-sensitive woman," *Ann Asthma Imunol.* 1997; 79:234-6; Gern JE, Yang E, Evrard HM, Sampson HA, "Allergic reaction to mil-contaminated 'non-dairy' products," *New Engl J Med* 1991; 324:976-9.

to its authority to regulate food and color additives. Such a reading of section 403(i) would be contrary to established Agency practice, to longstanding rules of statutory construction, and to the overall purpose of the FFDCA.

FDA has routinely required spices, flavorings, and colors to be declared on food labels where it determined that such requirements were necessary as a matter of public health. For example, Agency regulations require that:

- Any monosodium glutamate used as an ingredient in food be declared by its common or usual name, "monosodium glutamate." 21 C.F.R. § 101.22(h)(5).
- Any protein hydrolysate used in foods for its effect on flavor be declared by its specific or common name, not simply designated as "flavor" or "flavoring." 22 C.F.R.§ 101.22(h)(7).
- *All* ingredients, including spices, flavorings, and colorings, contained in foods that purport to be hypoallergenic be declared. 21 C.F.R. § 105.62
- *All* ingredients, including spices, flavorings, and colorings, contained in foods that purport to be for infant use be declared. 21 C.F.R. § 105.65.
- The coloring additive Yellow Dye No. 5 be declared. 21 C.F.R. § 74.705(d)(2).

In requiring ingredient labeling of certain spices, flavorings, and colorings, notwithstanding the section 403(i) labeling exemption, FDA has recognized that section 403(a), 409, and 721, on one hand, and 403(i), on the other, *complement* one another. It is precisely because the FFDCA permits FDA to require the declaration of potentially dangerous food and color additives that it is generally acceptable to exempt spices, flavorings, and colors from coverage under 403(i).

Thus, a food allergen *never* qualifies as an incidental additive under the Agency's regulations and is therefore not exempt from any labeling requirements the Agency may promulgate. *See* April 19 FDA Compliance Policy Guide ("FDA. . . has never considered food allergens eligible for [the incidental additive] exemption."). Moreover, an "incidental additive" must also have no technical or functional effect in the finished food. 21 C.F.R. § 101.100(a)(3). In many cases, a food allergen added as an ingredient *does* have such an effect, and therefore does not qualify for the exemption. *See* FDA Notice at 1 (noting that egg whites added as a binder in breading used on a breaded fish product is not an incidental additive for purposes of 21 C.F.R. § 101.100(a)(3)).[17]

C. FDA May Establish GMPs to Avoid Cross-Contamination of Non-Allergenic Foods Pursuant to its Authority to Enforce the Prohibition Against Adulterated Foods in Section 402 of the FFDCA.

Label declaration requirements for food allergens enable consumers to identify foods that are *intended* to contain allergenic substances. As discussed in the statement of factual grounds, however, the *inadvertent* inclusion of allergens in foods is also a serious problem, due to the potential for "cross-contamination."[18] Thus, the public health requires FDA to establish by

[17] While food allergens should presumptively be ineligible for the "incidental additive" exemption, it is possible that the amount of an allergen in a particular food may be so insignificant that that allergen will not cause any reaction in those circumstances. CSPI believes that if a manufacturer can prove that the amount of an allergen in its product is below any reasonable threshold for allergenicity, that allergen could be treated as an "incidental additive" that is entitled to a regulatory exemption from labeling requirements.

[18] Examples of reactions due to cross-contamination include two instances of children suffering anaphylaxis due to milk protein in sorbet, and a reaction to peanut antigen contained in gingersnap cookies. Laoprasert N, Wallen NF, Jones RT, Hefle SL, Taylor SL, "Anaphylaxis in milk-allergic children following ingestion of lemon sorbet containing trace quantities of milk," *J Food Prot* 1998;61;1522-4. Jones RT, Squillace DL, Yunginger JW, "Anaphylaxis in a milk-allergic child after ingestion of milk-contaminated kosher-pareve-labeled 'dairy-free' desert," *Ann Allergy* 1992;68:223-7. Kemp SF, Lockey RF, "Peanut anaphylaxis from food cross-contamination," *JAMA* 1996;275:1636-7.

regulation GMPs that will guide manufacturers in their efforts to prevent cross-contamination. Indeed, FDA has recognized that "adhering to GMPs is essential for effective reduction of adverse [allergic] reactions" and that advisory "may contain" labeling is not an appropriate substitute for such adherence. 66 Fed. Reg. 38591, 38592 (July 25, 2001).[19] The FFDCA provides FDA with ample authority to issue these GMPs, just as it provides the Agency with authority to require the label declaration of allergens.

In addition to banning the circulation in interstate commerce of "misbranded" foods, the FFDCA also prohibits the introduction into interstate commerce of foods that are "adulterated." 21 U.S.C. § 331(a). Section 402 (a) (4) of the FFDCA (21 U.S.C. § 342 (a) (4)) defines "adulterated foods" to include foods "prepared, packed, or held under insanitary conditions whereby [they] may have . . . been rendered injurious to health." FDA has recognized that foods containing allergens inadvertently introduced through cross-contamination may be considered "adulterated" under section 402. 66 Fed. Reg. 398591, 38592-93 (July 25, 2001); April 19 FDA Compliance Policy Guide. Moreover, the FFDCA clearly permits the use by FDA of GMPs as a benchmark for determining whether a food product was manufactured in "insanitary" conditions, and FDA has routinely exercised this authority. *See, e.g.,* 21 C.F.R. § 110.5 (criteria for good manufacturing practices "shall apply in determining whether a food . . . has been prepared, packed, or held under insanitary conditions . . . whereby it may have been rendered injurious to health"). The current GMPs do not address the problem of food allergens. However, it is clear that FDA has the authority to adopt GMPs to prevent cross-contamination of non-allergenic foods and thereby to enforce the prohibition of adulterated foods found in the FFDCA.

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[19] As noted below, however, "may contain" labeling may be appropriate where GMPs alone cannot ensure lack of cross-contamination.

Moreover, as discussed above, to the extent that a food allergen is determined to be a "food additive" under section 409 of the FFDCA or "color additive" under FFDCA section 721, FDA must prescribe regulations for its safe use. 21 U.S.C. 348(c)(1)(A); 21 U.S.C. 379(e). And to the extent that a food retains its GRAS status, FDA may impose use limitations as a condition of continued GRAS status. 21 C.F.R. § 370.130(j). Just as such regulations could include labeling requirements, they may also set forth GMPs to prevent the inadvertent introduction of allergenic foods into non-allergenic foods.

Of course, reliance on GMPs presumes that a manufacturer, through the use of the prescribed practices, can prevent the inadvertent introduction of allergens into foods. CSPI recognizes, however, that under some circumstances it may be impossible for a manufacturer to ensure lack of cross-contamination. Under those circumstances, advisory or "may contain" labeling serves to warn consumers of the possibility that an allergen may have been introduced inadvertently into a food. "May contain" labeling, however, should not serve as a substitute for GMPs when the latter may safely guarantee no cross-contamination. Rather, it is only when GMPs are unable to prevent cross-contamination that these "may contain" labeling requirements are appropriate, indeed essential.

V. Conclusions and Recommendations

In light of the overwhelming evidence that food allergens pose substantial health risks to millions of Americans, CSPI urges FDA to establish at the earliest possible date requirements for the label declaration of the eight principal food allergens. CSPI also urges the Agency to establish GMPs and "may contain" labeling to address the problem of inadvertent cross-contamination by allergens of non-allergenic foods.

VI. Environmental Impact

CSPI believes that the action requested in this petition has no significant environmental impact.

VII. Economic Impact

No statement of the economic impact of the requested revisions to the rules is presented because none has been requested by the Commissioner.[20]

VIII. Certification

The undersigned certify that, to their best knowledge and belief, this petition includes all information and views on which the petitioner relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

William B. Schultz

William B. Schultz
Carlos T. Angulo
Zuckerman Spaeder LLP
1201 Connecticut Avenue, N.W.
Washington, D.C. 20036

Attorneys for Center for Science in the Public Interest

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[20] 21 C.F.R. § 10.30(b).