CSPI CENTER FOR SCIENCE IN THE PUBLIC INTEREST
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August 24. 1998

U.S. Food and Drug Administration
Dockets Management Branch
12420 Parklawn Drive
Room 123
Rockville, MD 20857

Dear Sir or Madam,

Please file the following Petition for Proposed Rulemaking and Regulatory Action to Provide Ingredient and Source Labeling, Scientific Review of Allergenicity, and Possible Prohibition of Cochineal Extract and Carmine Color Additives.

Thank you for your attention to this matter.

Sincerely,

Deborah Reichmann
Staff Attorney

98P-0724

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Executive Director: *Michael Jacobson, Ph.D.*

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Petition for Proposed Rulemaking and Regulatory Action to Provide Ingredient and Source Labeling, Scientific Review of Allergericity, and Possibble Prohibition of Cochineal Extract and Carmine Color Additives	)	Docket No._____

Submitted by the

Center for Science in the Public Interest

August 24, 1998

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August 24, 1998

U.S. Food and Drug Administration
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CITIZEN'S PETITION

The Center for Science in the Public Interest (CSPI) submits this petition pursuant to § 4(d) of the Administrative Procedures Act, 5 U.S.C. § 553(e), and §§ 201(n), 403(a), 701(a) and 721(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. §§ 321(n), 343(a), 371(a) and 379e(d), respectively, and 21 C.F.R. §§ 10.30, 70.25 and 71.30. We request that the Food and Drug Administration (FDA) (a) require that cochineal extract and carmine[1] color additives be listed specifically by name and origin in ingredient lists of foods, drugs and cosmetics; (b) initiate scientific reviews or require scientific studies to assess the safety of cochineal extract and carmine; and (c) if necessary to protect sensitive consumers, prohibit the use of the additives.

I. REQUESTED ACTION

We request that the FDA take the following actions:

- Immediately require that cochineal extract and/or carmine be listed by name in the ingredient lists of all foods, drugs, and cosmetics to help protect individuals who know they are sensitive to the colorings;
- Immediately require labeling of animal (insect) origin of cochineal extract and carmine;
- Undertake or require scientific reviews or studies to determine the specific allergenic component of cochineal extract and carmine and whether it could be

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[1] ... listed in 21 C.F.R. 73.100 (foods), 21 C.F.R. 73.1100 (drugs),

eliminated from the coloring, as well as to determine the prevalence and maximum severity of allergic reactions;

eliminated from the coloring, as well as to determine the prevalence and maximum severity of allergic reactions;

- If necessary, prohibit the use of cochineal extract and carmine entirely.

II. STATEMENT OF FACTUAL GROUNDS

Cochineal extract and carmine are natural color additives that have been widely used in food, cosmetics, drugs, and other products for many years. Recent medical research has demonstrated that cochineal extract and carmine can cause severe allergic reactions, including hives, sneezing, rhinitis, and life-threatening anaphylactic reactions.

In 1994, the first reported allergic reaction to carmine in food was in a woman who experienced a severe anaphylactic reaction to Campari-Orange alcoholic beverage.[2] The reaction proved to be IgE-mediated (positive skin prick test and RAST) to carmine.

A year later an allergic reaction was found to have been caused by artificially colored yogurt.[3] That case was also shown to be IgE-mediated and due to carmine (skin prick test and leukocyte histamine-release test). The researchers estimated that 1 mg of carmine triggered the patient's reaction.

European researchers have reported five cases of anaphylactic reaction to carmine after patients drank Campari aperitifs containing that ingredient. Subsequent skin prick tests demonstrated sensitivity to the carmine/cochineal extract used by the manufacturer of the

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[2] Martin Kägi, Brunello Wüthrich, & SGO Johansson. *Campari-Orange anaphylaxis due to carmine allergy*. 344 LANCET 60, 1994. *See* Exhibit 1.

[3] Etienne Beaudouin, Gisele Kanny, Henri Lambert, et al. *Food anaphylaxis following ingestion of carmine*. 74 ANN ALLERGY ASTHMA IMMUNOL 427,1995. *See* Exhibit 2.

beverage.[4]

In 1997 University of Michigan researchers published a report about a woman who suffered a severe anaphylactic reaction and required emergency medical treatment. Her reaction was traced to carmine and confirmed by a skin prick test and the Prausnitz-Kustner test. The paper notes that the researchers identified two additional patients who had anaphylaxis following the ingestion of carmine-containing foods; positive skin prick tests demonstrated sensitivity to carmine.[5] Since publication of their study, the researchers have identified two additional cases.[6]

Other cases of carmine sensitivity were linked to the use of makeup and to industrial exposure by inhalation.[7] In those cases, carmine acted as a potent contact and inhalant allergen.[8]

III. STATEMENT OF LEGAL GROUNDS

A. Cochineal Extract and Carmine Should be Listed by Name and Origin on Ingredient Lists of Foods, Drugs, and Cosmetics

FDA has the authority, under section 701 (a) of the FFDCA, to require the disclosure of

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[4] Brunello Wüthrich, Martin Kägi, W. Stucker. *Anaphylactic reactions to ingested carmine (E120).* 52 ALLERGY 1133, 1997. *See* Exhibit 3.

[5] James L. Baldwin, Alice H. Chou, William R. Solomon. *Popsicle-induced anaphylaxis due to carmine dye allergy.* 79 ANN ALLERGY ASTHMA IMMUNOL 415, 1997. *See* Exhibit 4.

[6] Personal communication, Dr. James Baldwin, August 12, 1998.

[7] S. Quirce, M. Cuevas, J.M. Olaguibel, A.I.Tabar. *Occupational asthma and immunologic responses induced by inhaled carmine among employees at a factory making natural dyes.* 93 J. ALLERGY CLIN IMMUNOL 44, 1994. *See* Exhibit 5 (abstract only).
P.S. Burge, I.M. O'Brien, M.G. Harries, J. Pepys. *Occupational asthma due to inhaled carmine.* 9 CLIN ALLERGY 185, 1979. *See* Exhibit 6 (abstract only).

[8] *See* Wüthrich et al. *supra* note 4.

cochineal extract and carmine in the ingredient lists of products that contain the color additives. Section 701(a) authorizes the agency to adopt regulations for the "efficient enforcement of this Act."[9] General labeling requirements for color additives are found in 21 C.F.R. 70.25(a), which states that "[a]ll color additives shall be labeled with sufficient information to assure their safe use. . ."

FDA was confronted with an analogous situation concerning the regulation of FD&C Yellow No. 5.[10] Yellow 5 was found to cause moderate allergic reactions in a small subset of people. Subsequently the FDA required specific labeling of the dye in foods, drugs, and cosmetics to protect sensitive individuals, even though there was no risk to the general population. The factors that the agency considered included the potential impact upon the general public, the severity of the reactions experienced by people sensitive to the color, the protection afforded the sensitive population by a label declaration or warning, the number of sensitive persons, and the availability of alternative products free of the color.[11] In the instant situation, the relationship between cochineal extract or carmine and severe allergic reactions should be sufficient, at the very least, for the FDA immediately to require the colorings to be listed on ingredient labels. That is particularly so because reactions appear to be more severe than with Yellow No. 5.

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[9] 21 U.S.C. § 371(a)

[10] Proposed and final rule on FD&C Yellow No. 5, 42 F.R. 6835, (1977) and 44 F.R. 37212 (1979), Published regulation, 21 C.F.R. §74.705(d)

[11] "[E]vidence of a causal relationship between FD&C Yellow No. 5 and serious allergic-type responses in certain susceptible individuals is sufficient to warrant label declaration." 44 F.R. 37212, at 37213.

We also urge the agency immediately to require labeling that indicates clearly the color additive's animal (insect) origin so as not to mislead vegetarians or consumers who follow religious dietary restrictions.[12] Precedent for this type of labeling is found in the regulation of labeling for wax coating on fresh fruits and vegetables. As a response to a citizen's petition asking for identification for preservative coatings on fresh fruits and vegetables, the agency revised its labeling provisions to require a declaration of organic origin of the coating material.[13]

We recommend that the labels should state: "artificial coloring (cochineal extract [carmine], animal- *[or insect-]* based)," "artificial coloring (carmine [cochineal extract], animal- *[or insect-]* based)" -- with the first form of the coloring listed being the one that is actually in the product to ensure that sensitive people who know only one of the two names are not misled if a food contained the other coloring.

B. The FDA Should Conduct Scientific Reviews or Require Studies to Assess the Safety of Cochineal Extract and Carmine and Determine Whether Approval Should Be Revoked

We question whether an additive that can cause severe allergic reactions, but provides no nutritive or safety function, should be permitted in the food supply, even if it is identified in ingredient lists. Thus, we request that the agency undertake scientific reviews or studies, possibly in conjunction with the Centers for Disease Control and professional associations of allergists, to

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[12] 21 U.S.C. §§ 321(n) and 343(a).

[13] 56 F.R. 28592, at 28614 (1991). "Wax and resin ingredients on fresh produce when such produce is held for retail sale . . . shall be declared collectively by the phrase 'coated with food-grade animal-based wax, to maintain freshness' or the phrase 'coated with food-grade vegetable-, petroleum-, beeswax-, and/or shellac-based wax or resin, to maintain freshness' as appropriate." 21 C.F.R. 101.4 (b)(22)

estimate the prevalence and potential severity of allergic reactions to cochineal extract and carmine.

The agency also should condition continued approval of the colorings upon the manufacturers and distributors determining within a specified period (e.g., 180 days) the exact allergenic substance in these colorings.[14] If, for instance, the studies determined that the allergenic component could be removed or neutralized, then the FDA should require that the use of the colorings only be permitted if they were so processed.

Should labeling be deemed ineffective in providing adequate consumer protection from potentially life-threatening reactions[15] and should scientific studies not find means to eliminate the allergen, the FDA should revoke the approval of cochineal extract and carmine. Such action would be appropriate considering that carmine is a completely unnecessary coloring that could be replaced by other approved natural or synthetic colorings.[16]

Some of the comments to the proposed rule mandating labeling for Yellow 5 urged the agency to prohibit the use of the color additive. The agency's response, at that time, was that if labeling proved insufficient for informing persons of the presence of Yellow 5, the possibility of a

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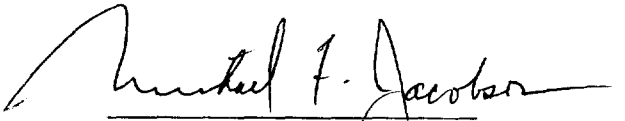
[14] 21 C.F.R. § 70.55.

[15] Ingredient labels may not offer sufficient protection because consumers would likely need to suffer numerous potentially life-threatening reactions before they identified the cause of those reactions. That is different from the case of Yellow 5, which generally causes mild or moderate reactions.

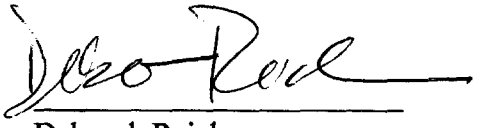
[16] Manufacturers told CSPI that FD&C Red No. 40 (possibly mixed with FD&C Yellow No. 6), anthocyanins, and betanins are possible alternatives.

ban would be considered.[17] In the instant case, if labeling is insufficient, and the additives cannot be considered to be generally regarded as safe, then a prohibition of their use may be the only effective means of protecting the public's health.[18]

Respectfully submitted,



Michael F. Jacobson, Ph.D.
Executive Director



Deborah Reichmann
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[17] 44 F.R. 37212, at 37214. In addition, legislative history points to Congress placing a lesser value upon color additives and, as such, raising the safety standards required for their approval. HR Rep No. 1761, at 15, 86th Cong. 2d Sess. 9 (1960).

[18] If a color additive is deemed unsafe under 21 U.S.C. § 721 (a), then food containing said additive is adulterated under 21 U.S.C. § 402 (c).