DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

0374 5 SEP 30 A9:32

Jane Houlihan
Arianne Callender
Environmental Working Group
1436 U Street, N.W., Suite 100
Washington, DC 20009

SEP 29 2005

Re: Docket No. 2004P-0266/CP1

Dear Ms. Houlihan and Ms. Callender:

This letter is in response to your citizen petition dated June 14, 2004, and filed on June 17, 2004, under docket number 2004P-0266/CP1, requesting the Food and Drug Administration (FDA) to take immediate action to cease the unlawful distribution of misbranded, adulterated, and unlabeled cosmetics. The petition states that you have identified "serious probable safety violations" under the Federal Food, Drug, and Cosmetic Act, and asserts that various products may be misbranded or adulterated. Specifically, the petition requests that FDA take the following actions:

- Institute a voluntary recall or court-ordered injunction or seizure for cosmetics containing ingredients that have not been proven safe through scientific testing that do not bear appropriate warnings;

- Clarify the requirements for adequate substantiation of safety;

- Establish a requirement that manufacturers remove from cosmetic products any ingredient that contains any toxic impurity or that may combine with other ingredients to form harmful impurities;

- Initiate a voluntary recall or court-ordered injunction or seizure for cosmetics containing ingredients that may cause injury through ordinary use;

- Publicly command all Internet vendors to display a conspicuous list of ingredients of cosmetic products sold on their websites, subject to injunction or seizure; and

- Conduct an investigation of products containing chemical ingredients prioritized according to prevalence and toxicity.

In accordance with 21 CFR 10.30(e)(3), this letter is advising you that FDA is denying your petition without prejudice. FDA has reviewed the information in your petition, the supplements to your petition, and the comment that we received on your petition. With respect to your requests for enforcement action, 21 CFR 10.30(k) provides that the citizen

2004P-0266 PDN 1

petition process "does not apply to the referral of a matter to a United States attorney for the initiation of court enforcement action." Such matters are within the exclusive discretion of the Commissioner. A denial of a request to take enforcement action does not constitute final agency action. See 21 CFR 10.45. Therefore, your requests for enforcement action are requests that are not appropriate for a citizen petition. Furthermore, with respect to your requests for enforcement action, based on our review of the information submitted in the petition, the agency concludes that there is not sufficient information to support your requests. With respect to your other requests, we believe that the requested actions are not warranted at this point in time.

FDA may take enforcement action if the agency has information to support that a cosmetic is adulterated or misbranded. FDA takes enforcement action on a case-by case basis based upon agency priorities and available resources. We do not advise the public in advance of our intentions to take enforcement action against particular products.

The following summarizes FDA's authority for regulating cosmetics. Section 601 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 361) provides that a cosmetic is adulterated if it bears or contains any poisonous or deleterious substance that may render it injurious to users under the conditions of use prescribed in the labeling or under such conditions of use as are customary or usual; if it consists of a filthy, putrid, or decomposed substance; if it has been prepared, packed, or held under insanitary conditions; if its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health; or if it contains an unapproved color additive. Section 602 of the FD&C Act (21 U.S.C. 362) provides, in part, that a cosmetic is misbranded if its labeling is false or misleading in any particular; if certain information does not appear on the label; if required information does not appear in a readable fashion; or if the container is made, formed, or filled to be misleading. Section 201(n) (21 U.S.C. 321(n)) of the FD&C Act states that if an article is alleged to be misbranded because the labeling is misleading, then in determining whether the labeling is misleading, there shall be taken into account not only representations made or suggested, but also the extent to which the labeling fails to reveal material facts in the light of such representations, with respect to consequences which may result from the use of the article under the conditions of use as are customary or usual (see also 21 CFR 1.21). The FD&C Act contains no provision that requires demonstration to FDA of the safety of ingredients of cosmetic products, other than color additives that are not coal-tar hair dyes, prior to marketing the product. In addition to the requirements of the FD&C Act, cosmetics that are offered for sale as consumer commodities are subject to the requirements of the Fair Packaging and Labeling Act.

We received one comment on your petition requesting that the public be alerted to the potentially harmful effects associated with the inhalation of fragrances. The comment was also submitted on Citizen Petition 1999P-1340, on file at FDA. The comment did not provide any additional data and information related to the requests in your petition.

We address your requests in the same order as they appeared in the petition.

1. Your petition requests that FDA institute a voluntary recall or court-ordered injunction or seizure for cosmetics containing ingredients that have not been proven safe through scientific

testing that do not bear appropriate warnings, pursuant to 21 U.S.C. 362, 21 U.S.C. 332, 21 U.S.C. 334, 21 CFR 7.40, and 21 CFR 7.45.

In support of this request, the petition asserts that 356 cosmetic products have not been adequately substantiated for safety and do not bear the warning required by 21 CFR 740.10. The petition states that these products may be misbranded and requests voluntary recall of or enforcement action against these products. The petition provides as support for this request a list of products containing 32 ingredients reported in the 2003 Cosmetic Ingredient Review (CIR) Compendium to have insufficient testing data to support their safe use in cosmetics and the CIR Expert Panel conclusions for the 32 ingredients (Petition Exhibit A). For each of the ingredients, the CIR Expert Panel has concluded either that the available data are insufficient to support their safety or that their safety has not been documented and substantiated.

FDA denies your request for enforcement action because, as stated above, requests for enforcement action are requests that are not appropriate for a citizen petition. See 21 CFR 10.30(k). Furthermore, the FD&C Act does not authorize FDA to order a recall for a defective or possibly harmful cosmetic product. Under 21 CFR 7.45, FDA may request a recall if the agency has determined that a product presents a risk of illness or injury or gross consumer deception, that a firm has not initiated a recall of the product, and that agency action is necessary to protect the public health. Manufacturers or distributors of defective or possibly harmful cosmetic products carry out recalls voluntarily. The information provided in the petition does not establish that the products present a risk of illness, injury, or gross deception to consumers such that the agency would request a recall under 21 CFR 7.45.

In addition, your petition did not provide sufficient data and information for FDA to evaluate the safety of each of the 32 ingredients identified in your petition in connection with the petition's assertion that the safety of the products has not been adequately substantiated. The data and information provided, i.e., the list of products, ingredients, and CIR Expert Panel conclusions regarding the ingredients, do not establish that the safety of the ingredients has not been adequately substantiated prior to marketing. Additional data and information would be needed to support the petition's contention that the safety of the 356 cosmetic products identified has not been substantiated and to determine whether the products are in fact adulterated or misbranded within the meaning of sections 601 or 602 of the FD&C Act, respectively. We note that your petition only asserts that these products may be misbranded.

FDA evaluates the safety of cosmetic products using data and information from sources including, but not limited to, the CFSAN Adverse Event Reporting System (CAERS), published scientific literature, the CIR Expert Panel, data provided directly to FDA by other government agencies as well as the cosmetic industry, FDA research, and other information submitted to the agency for review. The CIR Expert Panel is a group of scientists that reviews the safety of cosmetic ingredients under the aegis of the Cosmetic, Toiletry, and Fragrance Association (CTFA), a trade association of the cosmetics industry, and the CIR Expert Panel is one source of information on the evaluation of the safety of cosmetic ingredients. FDA's regulation at 21 CFR 740.10 states that, if a cosmetic product contains an ingredient that has not been adequately substantiated for safety, and the product does not bear the specified warning statement on its label, the product is misbranded. FDA is looking into the possibility of issuing guidance on the implementation of 21 CFR 740.10 in the future. FDA also may

take enforcement action if the agency has information to support that a cosmetic is otherwise adulterated or misbranded. FDA takes enforcement action on a case-by case basis based upon agency priorities and available resources. We do not advise the public in advance of our intentions to take enforcement action against particular products.

2. Your petition requests that FDA engage in rulemaking to clarify the requirements for adequate substantiation of safety, pursuant to 21 U.S.C. 371(a) and 21 CFR 740.10(a). The petition proposes the following definition for "adequately substantiated for safety:"

> *Substantiation, through peer-reviewed scientific publications or publicly available industry studies, of a reasonable certainty of no harm from aggregate exposures to the product and its component ingredients including impurities, taking into account chemicals that may increase penetration of the product or its component chemicals through the skin, and including all anticipated cosmetic exposures and all other exposures for which there is reliable information, taking into consideration vulnerable populations such as infants and pregnant women.*
>
> *Any finding of safety for a cosmetic product must explicitly account for risks posed by impurities until such time as impurities are removed from the component ingredients or the product is reformulated in such a way as to preclude the formation of impurities by the component ingredients in the product.*

FDA denies this request. FDA discussed the phrase "adequately substantiated for safety" in the preamble to the final rule that established 21 CFR 740.10 (40 FR 8912 at 8916, March 3, 1975). This preamble states that safety of a cosmetic product can be adequately substantiated through (a) reliance on already available toxicological test data on individual ingredients and on product formulations that are similar in composition to the particular cosmetic, and (b) performance of any additional toxicological and other tests that are appropriate in the light of such existing data and information. In addition, FDA's general approach to investigations of the safety of cosmetic ingredients includes consideration of such factors as routes of exposure and vulnerable populations.

The March 3, 1975, preamble also states that the manufacturer of a cosmetic ingredient is responsible for the safety of the ingredient under the conditions of use recommended in its labeling, as well as reasonably expected related uses, and that the safety of the ingredient must be adequately substantiated for use under these conditions. The preamble also states that separate definitions of safety for ingredients and finished products are inappropriate. Although safety has the same meaning under both circumstances, FDA recognizes that what constitutes adequate testing will differ depending upon whether the product is intended as an ingredient or as a finished cosmetic item, since the conditions of expected use are different.

We do not believe that undertaking rulemaking to define "adequately substantiated for safety" is necessary at this time in light of the agency's discussion of this term in the preamble to the final rule establishing 21 CFR 740.10. Furthermore, FDA is looking into the possibility of issuing guidance on the implementation of 21 CFR 740.10 in the future. We, therefore, decline at this time to engage in rulemaking to define "adequately substantiated for safety" as proposed in the petition.

3. Your petition requests that FDA engage in rulemaking to establish a requirement that manufacturers remove from cosmetic products any ingredient that contains any toxic impurity or that may combine with other ingredients to form harmful impurities, pursuant to 21 U.S.C. 371(a). The petition states that FDA has not articulated any firm safety standards limiting impurities in cosmetics and that FDA's regulation of hazardous impurities will limit consumers' risk of cancer and other avoidable harm from cosmetics.

The petition notes FDA's recommendation to manufacturers to voluntarily remove nitrosamines from cosmetics as toxic impurities formed from the combination of other ingredients.

FDA denies this request. It is the responsibility of the manufacturer and/or distributor to ensure that all cosmetic products are produced and marketed in compliance with the law (e.g., safe for use in the manner directed in the labeling or under customary or usual conditions of use and labeled in accordance with all applicable statutes and regulations). To minimize the risk of adulteration or misbranding of cosmetics, FDA recommends that cosmetic manufacturers follow good manufacturing practices in the preparation of their products. Cosmetic good manufacturing practice guidelines are available on FDA's website at http://www.cfsan.fda.gov/~dms/cos-gmp.html. Under section 704(a)(1) of the FD&C Act, FDA has the authority to perform inspections of establishments where cosmetics are manufactured, processed, packed, or held for introduction in interstate commerce. Inspections provide information to help FDA ensure that the cosmetics produced in these establishments are not adulterated or misbranded.

FDA has articulated safety standards limiting impurities in color additives permitted for use as ingredients in cosmetics, as well as in foods, drugs, and medical devices. The color additive listing regulations include chemical impurity specifications that are determined by FDA as part of its safety evaluations.

FDA investigates potentially adulterated or misbranded cosmetics, including those containing potentially toxic impurities, on a case-by-case basis based on the agency's priorities and available resources. If FDA determines there is a safety concern with a cosmetic ingredient, we inform the public of our findings and conclusions.

As the petition points out, FDA identified to the cosmetics industry the agency's safety concern about contamination of cosmetic products with nitrosamines in a notice published in the Federal Register of April 10, 1979 (44 FR 21365). In the notice, we described the evidence used for concluding that some topically applied cosmetics are contaminated with nitrosamines and may be hazardous to human health. We stated that cosmetics containing nitrosamines may be considered adulterated and subject to regulatory action because many nitrosamines have been determined to cause cancer in laboratory animals and have been shown to penetrate human skin. We urged cosmetic manufacturers to voluntarily remove from cosmetics any ingredient that may combine with others to form the nitrosamine of primary concern, N-nitrosodiethanolamine (NDELA), and to conduct additional testing to determine why cosmetics become contaminated with NDELA. Afterwards, NDLEA levels declined in cosmetic products on the market. Information currently available to the agency (through

analysis of products on the market) does not indicate that NDELA, at the levels detected in cosmetics, is a health hazard. In addition, the agency continues to monitor nitrosamines levels in cosmetics. See FDA's Cosmetics Compliance Programs at these website addresses: http://www.cfsan.fda.gov/~comm/cp29001.html (Domestic Cosmetics Program) and http://www.cfsan.fda.gov/~comm/cp29002.html (Imported Cosmetics Program). If the agency determines that nitrosamine levels in a cosmetic cause it to be adulterated within the meaning of the FD&C Act, we would determine whether regulatory action is appropriate based on the agency's priorities and available resources.

4. Your petition requests that FDA initiate a voluntary recall or court-ordered injunction or seizure for cosmetics containing ingredients that may cause injury through ordinary use, pursuant to 21 U.S.C. 361, 21 U.S.C. 332, 21 U.S.C. 334, 21 CFR 7.40, and 21 CFR 7.45.

In support of this request, the petition lists 20 products containing 9 ingredients that the petition states may cause harm when used according to package directions. For each product, the petition describes the package directions and cites the 2003 CIR Compendium conclusions that the petition contends the package directions violate (Petition Exhibit B). The petition states that cosmetics with ingredients that are unsafe for the uses indicated in the package directions meet the prerequisites for a recall.

FDA denies the request for enforcement action because, as stated above, requests for enforcement action are requests that are not appropriate for a citizen petition. See 21 CFR 10.30(k). Furthermore, the FD&C Act does not authorize FDA to order a recall for a defective or possibly harmful cosmetic product. Under 21 CFR 7.45, FDA may request a recall if the agency has determined that a product presents a risk of illness or injury or gross consumer deception, that a firm has not initiated a recall of the product, and that agency action is necessary to protect the public health. Manufacturers or distributors of defective or possibly harmful cosmetic products carry out recalls voluntarily. The information provided in the petition does not establish that the products present a risk of illness, injury, or gross deception to consumers such that the agency would request a recall under 21 CFR 7.45.

The petition did not provide the documentation that the agency would need to determine that the 9 ingredients cause the 20 products to be products that bear or contain a poisonous or deleterious substance that may render them injurious through ordinary use and, therefore, adulterated under the FD&C Act. Documentation that could establish that the products may cause injury through ordinary use would include information such as scientific evidence that these ingredients are hazardous under the conditions of use given in the product package directions and any reports of adverse events from use of the product. In addition, for the investigation of specific products, we generally obtain complete product labeling, the names and complete addresses of the manufacturers, distributors, and/or importers of the products, and the dates and ports of entry for products imported into the United States.

FDA notes that some of the products identified in the petition (e.g., products labeled as diaper rash ointment, acne treatment, sunblock spray, and first aid cream) are regulated as drugs or drugs and cosmetics. Drug products are handled by the Center for Drug Evaluation and Research (CDER) within FDA and are reviewed under a different set of regulatory requirements. If your intent is to request FDA evaluation of the safety of these drug products,

you should submit a separate petition with supporting information that addresses drug safety requirements.

FDA evaluates the safety of cosmetic products using data and information from sources including, but not limited to, the CFSAN Adverse Event Reporting System (CAERS), published scientific literature, the CIR Expert Panel, data provided directly to FDA by other government agencies as well as the cosmetic industry, FDA research, and other information submitted to the agency for review. The agency has prohibited or restricted some cosmetic ingredients by regulation, such as hexachlorophene, mercury compounds, chloroform, zirconium-containing complexes, and methylene chloride. We have taken regulatory action against the use of methyl methacrylate monomer in nail products. We have informed the cosmetic industry and the public of agency concerns regarding nitrosamines and 1,4-dioxane as contaminants of cosmetic products. We also have informed the cosmetic industry and the public of recommendations by cosmetic and fragrance trade associations to eliminate or limit the use of cosmetic ingredients such as chloroacetamide, ethoxyethanol and ethoxyethanol acetate, HC Blue No. 1, pyrocatechol, musk ambrette, and 6-methylcoumarin.

FDA provides extensive information to the cosmetic industry and the public on safety issues related to the use of cosmetic products and ingredients. Much of this information is available on FDA's website at http://www.cfsan.fda.gov/~dms/cos-210.html. FDA also may take enforcement action if the agency has information to support that a cosmetic is adulterated or misbranded. FDA takes enforcement action on a case-by-case basis based on the agency's priorities and available resources. We do not advise the public in advance of our intention to take enforcement action against particular products.

5. Your petition requests that FDA publicly command all Internet vendors to display a conspicuous list of ingredients of cosmetic products sold on their websites, subject to injunction or seizure, pursuant to 21 CFR 701.3, 21 CFR 701.2, 21 U.S.C. 362 , 21 U.S.C. 375, and 21 U.S.C. 336.

In support of this request, the petition lists 41 websites that the petition asserts are currently selling cosmetic products without displaying the ingredients (Petition Exhibit C). The petition states that these websites may be selling misbranded products in violation of labeling requirements and should be publicly notified of the violation and warned of potential injunction or seizure in the event of continued noncompliance.

FDA denies your request for enforcement action because, as stated above, requests for enforcement action are requests that are not appropriate for a citizen petition. See 21 CFR 10.30(k). Furthermore, FDA denies your request to publicly command all Internet vendors to display a conspicuous list of ingredients of cosmetic products sold on their websites. There is currently no requirement that a manufacturer put an ingredient list on a website.

The cosmetic labeling regulations in 21 CFR part 701 describe the labeling requirements for products purchased by consumers. Section 701.3(a) states that a declaration of ingredients must be displayed on the label of the product. Section 701.3(r) states that in the case of cosmetics distributed to consumers by direct mail, the ingredients list may alternatively appear in labeling accompanying the product or in a catalog or brochure. There is no

requirement that a manufacturer put an ingredient list on a website. Your petition has not provided any evidence that, for the products sold over the Internet, their label, labeling, or a catalog or brochure does not include a declaration of ingredients as required under 21 CFR 701.3. Evidence that the agency would obtain to determine whether the products comply with 21 CFR 701.3 would include information such as complete product labeling as well as catalogs and brochures, the names and complete addresses of the manufacturers, distributors, and/or importers of the products, and the dates and ports of entry for products imported into the United States.

6. Your petition identifies nine ingredients (Petition Exhibit D) and requests that FDA conduct an investigation of the safety of their use in cosmetic products, pursuant to 21 U.S.C. 372 , 21 U.S.C. 361-362, and 21 U.S.C. 374. The petition also states that products containing these ingredients may be misbranded or adulterated and are subject to FDA inspection, safety review, and enforcement action when warranted.

In support of this request, the petition cites 18 websites and studies reported in the scientific literature that conclude that under certain conditions the nine ingredients may be carcinogens or endocrine disruptors or that they may accumulate in human tissue. The petition also asserts that seven of the ingredients have not been studied by the FDA or CIR.

FDA denies your request for enforcement action because, as stated above, requests for enforcement action are requests that are not appropriate for a citizen petition. See 21 CFR 10.30(k).

Furthermore, your petition did not provide sufficient evidence for FDA to evaluate the safety of each of the nine ingredients identified in your petition, when used in cosmetics, and did not specify the products containing such ingredients. The petition's cited references do not provide the evidence FDA would need for a risk assessment or safety assessment of any of the nine ingredients as human carcinogens or endocrine disruptors or accumulators in human tissue when used in cosmetics. FDA has investigated the safety of all nine ingredients identified in the petition for various uses in food, drugs, and cosmetics, summarized below. Therefore, we do not believe that further investigation of these ingredients for use in cosmetics is warranted at this time.

- *Progesterone:* FDA tentatively concluded that progesterone is safe for use in cosmetic products under limited conditions described in a proposed rule published on September 9, 1993 (58 FR 47611). (The proposed rule was subsequently withdrawn on November 26, 2004 (69 FR 68831) as part of an overall regulatory reform strategy.)
- *Coal tar:* FDA considers coal tar, as defined in 21 CFR 358.703, to be safe for use in dandruff/seborrheic dermatitis/psoriasis shampoo over-the-counter (OTC) drug products (see 21 CFR 358.710).
- *Lead acetate* is listed under 21 CFR 73.2396 as a color additive permitted for use in hair dyes.
- *Methyl-, propyl-, and heptylparabens* are permitted for use as preservatives and antimicrobial agents in food (e.g., see 21 CFR 150.141, 172.145, and 184.1490).

- *Resorcinol* is included as an active ingredient in FDA monographs for anorectal and acne OTC drug products (see 21 CFR 346.20 and 333.310) and is a starting material for the manufacture of fluorescein color additives (e.g., see 21 CFR 74.1707).
- *Talc* is listed under 21 CFR 73.1550 as a color additive permitted for use in drugs. Talc has been proposed by FDA as a generally recognized as safe and effective ingredient for the treatment of diaper rash (see 55 FR 25204, June 20, 1990).
- *Carrageenan, phenol, resorcinol, silica, and talc* are permitted for use in food or food contact materials (e.g., see 21 CFR 172.620, 175.300, 177.1210, 182.70, and 182.90).

For the reasons discussed above, FDA is denying your petition without prejudice.

Sincerely yours,

Margaret O'K. Glavin
Associate Commissioner for Regulatory Affairs

cc:
Olivia James
P-5 Quincy Circle
Dayton, New Jersey 08810