U.S. Food Drug Administration

Center for **F**ood **S**afety **A**pplied **N**utrition

Cosmetics Compliance Program

IMPORTED COSMETICS PROGRAM

Issued December 8, 2000

7329.002

CHAPTER 29 - COSMETICS AND COLOR TECHNOLOGY

IMPORTED COSMETICS PROGRAM (FY 00/01/02)

IMPLEMENTATION DATE: UPON RECEIPT

COMPLETION DATE: 9/30/02

PRODUCT CODES: Industry Code 53

PRODUCT ASSIGNMENT CODE: 29002

FIELD REPORTING REQUIREMENTS

Refer to Part III, "2. - General Sampling Guidance, item A" for guidance on findings during sampling operations that may require contacting and possible hardcopy reporting to the CFSAN/Division of Enforcement (HFS-605).

* **NOTE:** The work to be accomplished under this compliance program has been identified as high priority by CFSAN. Label reviews for declaration of ingredients, warning statements and directions for use as required by 21 CFR Part 700 will be performed. The products to be collected are considered high risk because of the susceptible population for which the products are intended. Districts are requested to complete 100% of the operations planned in the ORA Field Workplan for this program. *

OASIS Reporting

Use the following Problem Area Flags (PAFs) when completing the collection report.

Microbiological Analysis

- * Use PAFs "MIC" for all microbiological examinations (positive and negative results) and identify the microorganism(s) and level if found. *
- Color Analysis
  Use PAFs "COL".

- Label Review
  Use PAFs "LBL".

FACTS Reporting

Use the following Problem Area Flags (PAFs) when reporting analytical results into FACTS.

Microbiological Analysis

- * Use PAFs "MIC" for all microbiological examinations (positive and negative results) and identify the microorganism(s) and level if found. *
- Color Analysis
  Use PAFs "COL".
- Label Review
  Use PAFs "FDF" and screen flag "FDL".

PART I - BACKGROUND

Cosmetics are defined in the Food, Drug, and Cosmetic Act as articles intended to be applied to, or introduced into, the human body for cleansing, beautifying, promoting attractiveness or altering the appearance without affecting the body's structure or function. Articles intended for use as components of cosmetic products are also considered cosmetics. Soap meeting the parameter of 21 CFR 701.20(a)(1) and (a)(2), is excluded from the term "cosmetic".

Some products perceived by consumers to be cosmetics may also be drugs if they are intended to cure, mitigate, treat or prevent disease, or to affect the structure or any function of the human body. These products usually make drug as well as cosmetic claims. Typical examples are: antiperspirant/deodorant products, sunscreen/suntan products, toothpaste/fluoridated toothpastes, and medicated cosmetics. Except for sunscreen/suntan products containing octyl dimethyl PABA and a nitrostating agent such as 2-bromo-2-nitro-1, 3-propanediol (Bronopol™), sunscreen/suntan products are not covered under this program.

It has been estimated that consumer expenditures for cosmetics exceed *35 billion* dollars annually in the United States. The estimated import share of this cosmetic market is 1 to 2%. These imported cosmetics come from a worldwide cosmetics industry.

PART II - IMPLEMENTATION

OBJECTIVES

- To determine if imported cosmetic products comply with the regulations enforced by the Food and Drug Administration.
- To initiate corrective actions when violations of the FD&C Act are identified.

PROGRAM MANAGEMENT INSTRUCTIONS

Any sampling accomplished under this Compliance Program must:

- Cover cosmetics only. To determine if a product is a cosmetic, refer to its list of ingredients. If an "active ingredient" is declared before a listing of the cosmetic ingredients, consider the product a drug (see 21 CFR 701.3(d)). If questions regarding applicability arise, contact your supervisor or CDER for guidance. If no "active ingredient" is declared, or the label bears no ingredient statement, cover the product as a cosmetic. Refer to applicable imported drug compliance program (s) for drug products.
- Include coverage of bovine-derived tissues and their ingredients.
- OASIS screening criteria have been adjusted to allow the entry reviewer to visually examine more entries of high-risk products for import field exams, sample collections and analyses.

  This will enable the field offices to complete their FY 01 ORA Workplan obligation by collecting or examining those products that CFSAN considers as high risk.

  These products are considered to be high-risk products by CFSAN because of a potential health hazard to consumers. These products have a high priority for sample collection and import field examinations.

  > **NOTE:** A list of the high priority products is provided in Part III of this program.

  <u>Coverage of Bovine-Derived Ingredients for Bovine Spongiform Encephalopathy (BSE)</u>

  By letter dated May 9, 1996 (ATTACHMENT C), FDA recommended that firms that manufacture or import cosmetic products and their ingredients containing specific bovine tissues, including extracts or substances derived from such tissues, take whatever steps necessary to assure themselves that such ingredients do not come from cattle born, raised, or slaughtered in countries where bovine spongiform encephalopathy (BSE) exists. BSE is a fatal transmissible spongiform encephalopathy similar to Creutzfeldt-Jakob disease in humans.

  BSE continues to be prevalent in Great Britain (including Northern Ireland and the Falklands), Belgium, Luxenbourg, the Netherlands, France,

Switzerland, Republic of Ireland, Oman, and Portugal. This list of BSE countries is subject to change. Refer to I.A. #17-04 for the most up-to-date list.

Manufacturers and importers of cosmetic products and their ingredients should have planned, systematic Procedures in place to provide assurances to themselves and to consumers that bovine-derived tissues do not come from cattle in countries where BSE occurs.

> **NOTE:** The list of tissues contained in the Agency's 5/9/96 letter has been expanded (ATTACHMENT B) to include additional bovine tissue or tissue-derived ingredients with a suspected risk of infectivity. The tissues and tissue derived-ingredients marked with asterisks are considered to present the highest risk of infectivity (hereinafter referred to as high-risk tissues).

PART III - INVESTIGATIONS

1. **Import Field Examinations**

NOTE: The only valid import field examination that can be performed for imported cosmetics are label examination for the mandatory labeling requirements.

International Harmonization of Cosmetics Nomenclature/Compliance with 21 CFR 701.3

To adequately evaluate compliance with the requirements of 21 CFR 701.3 (c) and the appropriateness of nomenclature currently being used in the ingredient declarations for imported cosmetics, the Districts should focus primarily on the declaration of botanical ingredients (e.g., plant extracts), colors and use of the term "+/-". Original labels declaring botanical ingredients in whole or in part with Latin designations, color additives being declared by Color Index (C.I.) numbers, and/or ingredient declarations using the term "+/-" alone or in conjunction with the term "may contain" should be forwarded to CFSAN, the Division of Enforcement and Programs, Imports Branch, HFS-606.

A. To determine whether proper labeling practices are followed. Check for:

*

1. Declaration of ingredients as required by 21 CFR 701.3 on all cosmetic products intended for sale to consumers. (Cosmetics

labeled "For Professional Use Only" are not exempt from ingredient labeling requirements if customarily sold to consumers for their personal use.)

2. Declaration of warning statements on cosmetics as required by 21 CFR 740. *On May 22, 2000, a new requirement for a warning statement for suntanning cosmetic products containing no sunscreen ingredients was added to 21 CFR 740.19.* The warning statement should read as follows:

   "Warning--This product does not contain a sunscreen and does not protect against sunburn. Repeated exposure of unprotected skin while tanning may increase the risk of skin aging, skin cancer, and other harmful effects to the skin, even if you do not burn."

3. Statement of appropriate warnings and directions for safe use on hair straighteners, depilatories, hair waving products, hair colors, hair bleaches, nail hardeners and suntan products. These statements differ from those in item e (2) in that the wording is not prescribed by regulation. However, the ability of the named products to cause skin irritation warrants these statements (see the February 1995 inspection guide).
4. Statement alerting consumers to tamper-resistant feature on liquid oral hygienic products and all cosmetic vaginal products as required by 21 CFR 700.25. *
5. Whether prohibited ingredients (21 CFR 250.250 and 21 CFR Part 700) or nonpermitted color additives (21 CFR 73, 74,81,82) are being used. Refer to IOM (2000) Appendix A, Color Additives Status List, for additional guidance.

B. Emphasize products more likely than others to be hazardous to human health because of their customary composition or conditions of use.
   - Aerosol cosmetic products. The uses of either fully halogenated chloroflurocarbon propellants or methylene chloride in aerosol cosmetic products are prohibited. Furthermore pursuant to 21 CFR 700.19 (FR Vol. 54, No. 124, June 29, 1989, pg. 27328-27342), any cosmetic products that contains methylene chloride as an ingredient are deemed adulterated and subject to regulatory action.
   - Liquid oral hygienic products. Check to determine that liquid oral hygenic products and all cosmetic vaginal products intended for retail sale comply with tamper-resistant packaging requirements (21 CFR 700.25).

C. Investigators should contact CFSAN, Office of Enforcement and Programs, Imports Branch (HFS-606) when the following types of products are encountered:

- Nail hardeners and nail builders. Hardeners may contain an excessive concentration of formaldehyde or inadequate instructions for use. Some builders contain methylmethacrylate or other methacrylates that may cause allergic or irritant reactions.
- Cosmetics containing triethanolamine, diethanolamine, or other alkanolamines and nitrosating agents, e.g., 2-bromo-2-nitro-1,3-propanediol (Bronopol™ or Onyxide 500™), tris (hydroxymethyl) nitromethane (Tris Nitro), or 5-bromo-5-nitro-1, 3-dioxane (Bronidox L™). These combinations of ingredients may form nitrosamines, e.g., N-nitrosodiethanolamine (NDELA), a reported animal carcinogen.
- Cosmetic suntanning preparations that contain octyl dimethyl PABA. Products containing this ingredient and a nitrosating agent such as 2-bromo-2-nitro-3-propanediol (Bronopol™) have been found to contain as a contaminant the nitrosamine, N-nitroso-N-methyl-p-aminobenzoic acid octyl ester (NMPABAO). Several nitrosamines other than NMPABAO have been identified as animal carcinogens.
- Cosmetics containing diethanolamine (DEA). This does not include DEA derivatives such as cocamide DEA.

  NOTE: Suntanning products labeled with specific SPF ratings are drugs and should be covered under CDER compliance programs.

2. **Product Priority List**

   The product priority list below should be used to determine which entries to examine first.

   A. Suntan preparations (lacking sunscreen) for the presence of the newly required 740.19 warning statement, "Warning - This product does not contain a sunscreen and does not protect against sun burn…". (Product Code: 53M...). There should be no overlap with products declaring the presence of a sunscreen or a SPF number. Such products should be coded as OTC drugs.
   B. Suntan Preparations (same product and code as above) for the ingredient DEA. Suntan preparations are the most likely cosmetic to contain DEA, a compound that is currently the subject of ongoing OCAC studies covering skin absorption, product concentrations, and risk assessment.
   C. Cosmetics with bovine by-products lacking certification that the tissue came from a country with no BSE problem (Product Code: 53R...).

3. **General Sampling Guidance**
    A. The following instructions apply to sampling operations performed under this program:
        0. Refer to the Field Import Alert Retrieval System (FIARS) for current import alerts covering cosmetics.
        1. Refer to FDA's Guide to Inspections of Cosmetic Product Manufacturers dated February 1995 for guidance regarding sample size.
        2. Collect import samples of cosmetics that are suspected of presenting a health hazard. Refer to FDA's Guide to Inspections of Cosmetic Product Manufacturers dated February 1995 for health hazard issues and labeling requirements.
        3. Collect make-up products, particularly those intended for use around the eye. Inadequately preserved products may become contaminated with microorganisms and cause eye injury.

            NOTE: Updated guidance for this program regarding direct reference authority for Pseudomonas contamination of cosmetics used in the eye area may be found in the March 1995 Compliance Policy Guides. Additional guidance for this program is also contained in a separate inspectional guide entitled "Guide to Inspections of Cosmetic Product Manufactures" (February 1995). If further guidance is needed contact CFSAN, Office of Enforcement and Programs, Imports Branch (HFS-606).

        4. Do not collect for microbiological examination samples of products in aerosol form or those that are self-preserving because they contain more than 10% ethanol, propylene glycol, glycerol, etc.
        5. Sample and analyze cosmetics with added "ingredients stickers" signifying possible relabeling of brand name (so called gray-market) cosmetics produced for markets outside of the U.S. to determine if the colors are permitted and declared correctly.

            NOTE: Cosmetics formulated for uses in other countries are <u>unlikely</u> to contain certifiable color additives or colors that originated from U.S. certified lots. Since it cannot be determined by analysis if a cosmetic contains colors subject to certification that in fact originated from certified lots, inspectors should request information (i.e., FDA certification lot numbers) indicating that certified lots of color additives were used when products were obviously relabeled, for

example, to include FD&C/D&C nomenclature rather than C.I. or E numbers.

4. **Sample Collection**
    - All samples are to be collected for compliance only. Do not collect surveillance samples.

      NOTE: All lots sampled for compliance must be held pending analysis.

    - When obvious violations are noted or suspected which require laboratory analysis/verification, collect a sample. If the violations pertain to label/labeling only, and laboratory analysis is not necessary, perform a label exam in OASIS under the work type "LEX" and PAF "LBL". Classify the label exam as a "3" and forward the entry paperwork to your compliance branch.
    - For color analysis, prohibited ingredients or label reviews only.
    - For microbiological analysis, from cosmetic products not in aerosol form and not self-preserving (i.e., containing less than 10% ethanol, propylene glycol, glycerol, etc.). When possible, collect samples from eye area cosmetics first before selecting body/face creams or cream lotions.
5. **Sample Shipment**

   Submit samples to the collecting District's servicing laboratory or specialized Headquarters laboratory as appropriate to conduct the intended analysis as indicated in PART IV, A, Analyzing Laboratories.

6. **Reporting**

   Report collection results into OASIS using the following Problem Area Flags (PAF):

    - Use PAF "COL" for non-permitted color additives
    - Use PAF "MIC" for microbiological examinations
    - Use PAF "LBL" for label reviews

PART IV - ANALYTICAL

1. **Analyzing Laboratories**
    A. Field Analyzing Labs

See Appendix III of the current ORA Workplan for a listing of servicing laboratories

Microbiological

General microbiological analysis and speciation of gram negative bacteria will be performed by the District's customary microbiological servicing laboratory. (See Appendix III of the current ORA Workplan for a listing of servicing laboratories.)

> **NOTE:** Identification of yeast and mold isolates will be done by the CFSAN, Division of Natural Products, Microanalytical Branch (HFS-315).

Colors

Servicing laboratories as listed in Appendix III of the current ORA Workplan.

> **NOTE:** Initial analysis may be accomplished by the servicing District laboratory. Either the original or check analysis for any potentially violative sample must be done by an experienced color analyst. Contact ORA/Division of Field Science (HFC-141) at (301) 827-7605 with questions regarding servicing laboratories and analyses.
>
> CFSAN's Color Technology Branch (HFS-126) (202) 205-0291 is available to advise the district servicing laboratory on analyses involving difficult color samples.

Label Review

All servicing District laboratories will conduct label reviews for declaration of ingredients, warning statements, and directions for use as required by 21 CFR Part 700.

B. **CFSAN Analyzing Labs**
   1. Yeast and Molds
      - The Office of Plant and Dairy Foods and Beverages, Division of Natural Products, Microanalytical Branch (HFS-315) will perform identification.
   2. The Office of Cosmetics and Colors, Division of Science and Applied Technology, (HFS-125), will perform the following analyses and/or review:
      - Confirmation of Color

NOTE: The Division of Science and Applied Technology, Color Technology Branch (HFS-126) will advise on color additive analyses for samples of cosmetic products not amenable to the typical analytical methods.

- Chemical Analysis
- Determination of Toxicity
- Consumer Complaint Sample Analysis

2. **Analysis**

A. **Microbiological Examination**

Refer to Bacteriological Analytical Manual, *8A Edition 1998*, Chapter 23 or later edition for methods to determine microbial contamination of cosmetics.

All Gram-positive microorganisms present in cosmetic products at levels greater than 500 colony forming units (CFU) per gram for eye area cosmetics or 1000 CFU per gram for non-eye area cosmetics are to be identified according to the methods in the Bacteriological Analytical Manual, *8A Edition 1998*, Chapter 23 or later edition.

All Gram-negative isolates from cosmetic products are to be identified at any level as to genus and species.

Identification of yeast and mold isolates will be conducted by the Division of Microanalytical Evaluations/CFSAN (HFS-315).

Prepare cultures for forwarding and further classification as follows:

1. Streak yeast and molds which grow at 37° C on Potato Dextrose Agar slants (screw cap tubes) and incubate at 37° C to ensure growth before shipping.
2. Incubate at 25° C isolates that grow at 25° C for a few days until growth is obvious.
3. Pack, label and ship isolates in accordance with Federal Standards for etiological agents.

B. **Color Analysis**

All determinations of color additives in cosmetic products will be performed in accordance with the instructions contained in Newburger's Manual of Cosmetic Analysis, 2nd Edition, Chapter 19; Determination of Color in Cosmetics, published by AOAC 1977. For additional color additive analytical instructions refer to the AOAC 15th

or 16th Editions, Chapter 46. See also compliance program 7309.006 (Imported Foods - Food and Color Additives; Part IV).

C. **Label Review**

Determine whether proper labeling practices are followed. See 21 CFR 701 and 740.

D. **Reporting**

Report analytical results into FACTS using the following Problem Area Flags (PAF):

- Use PAF "COL," for non-permitted color additives and identify the non-permitted color(s) found.
- Use PAF "MIC," for microbiological examinations and identify the microorganisms(s) and level.
- Use PAF "FDL," Result Flag "FDL" for label reviews and identify specific violation(s) found.

PART V - REGULATORY/ADMINISTRATIVE STRATEGY

A. Encourage participation of foreign firms through their U.S. representatives, to voluntarily register their manufacturing establishment (21 CFR 710) and their cosmetic product formulations (21 CFR 720).
B. Contact CFSAN, Division of Enforcement and Programs (DOEP), Imports Branch, HFS-606, at (202) 205-4606 for guidance in the following situations:
    1. If there is a suspected health hazard, health hazard evaluations should be requested from DOEP. For general information regarding health hazard evaluations refer to the Regulatory Procedures Manual (RPM), August 1997, Chapter 7 and 21 CFR 7.41(a).
    2. If their are questions concerning labeling/ingredients and recommendations for detention action.
C. Inform CFSAN, Division of Enforcement and Programs (DOEP), Imports Branch, HFS-606, at (202) 205-4606 whenever BSE high-risk products are detained:
    1. When a shipment from a firm is using high-risk tissue or tissue derived ingredients from identified BSE-countries is detained in referenced to IA #17-04. Currently BSE continues to be prevalent in Great Britain (including Northern Ireland and the Falklands), Belgium, France, Switzerland, Republic of Ireland, Oman and Portugal. Further information on BSE countries can be obtained from Import Alert 17-04.

D. Illegal Colors

Imported products found to contain nonpermitted colors may be detained on the basis of district analysis.

> **NOTE:** See Attachment "A" for additions/removals of color additives permitted/not permitted in the manufacture of cosmetics.

E. Detention Without Physical Examination (DWPE) Guidance

Chapter 9 of the Regulatory Procedures Manual (RPM) August, 1997 provides guidance in Subchapter Detention Without Physical Examination, on how Districts may initiate recommendations for DWPE and other pertinent guidance on entry control Procedures.

Refer to RPM Subchapter Detention Without Physical Examination for guidance concerning recommendation of detention based on one violative sample found to contain illegal colors, unsafe or prohibited ingredients, or that present a health hazard for other reasons. Recommendation for DWPE should be referred to ORA/ORO Division of Import Operations and Policy, HFC-170.

PART VI - REFERENCES AND PROGRAM CONTACTS

REFERENCES

- Inspection Operations Manual (IOM):

  - * Year 2000, Subchapter 600 -- Imports *
  - * Year 2000, Appendix A -- Food Additive Status List *

- Guide to Inspections of Cosmetic Product Manufacturers:

  - FEBRUARY 1995, Section IV -- Sample sizes
  - FEBRUARY 1995, Section II -- Health hazard issues and regulatory requirements

- FDA Import Alert Retrieval System (FIARS)
- Regulatory Procedures Manual (RPM), Chapter 9 - Imports
- Compliance Policy Guides Manual (CPGM), Chapters 27,28 - Colors, Cosmetics.
- Title 21, Code of Federal Regulations (CFR):

- Part 700, Subchapter G -- Cosmetics
- Part 250, Subpart D -- Requirements for Drugs and Cosmetics
- Parts 73, 74, 81, 82 -- Color additives

PROGRAM CONTACTS

General Program Inquiries	-	* Patricia Sherrod *, CFSAN, Division of Enforcement and Programs, Imports Branch, HFS-606, (202) 205-4606, FAX 260-0208.
Cosmetic and/or Color Policy	-	Allen R. Halper, CFSAN, Division of Programs and Enforcement Policy, OCAC HFS-105, (202) 205-4061.
Regulatory Inquiries	-	* Patricia Sherrod *, CFSAN, Division of Enforcement and Programs, Imports Branch, HFS-606, (202) 205-4606, FAX 260-0208.
Color Additive Methodology	-	Sandra Bell, CFSAN, Division of Science and Applied Technology, Color Technology Branch, HFS-126, (202) 205-0291.
Microbiological Analytical Procedures	-	Stanley Cichowicz, CFSAN, Division of Natural Products, Microanalytical Branch, HFS-315, (202) 205-4480.
Consumer and Trade Inquiries	-	* Lark A. Lambert *, Complaint Coordinator, CFSAN, Division of Programs and Enforcement Policy, Cosmetics Programs and Regulations Branch, HFS-106, (202) 205-4095.
General Methods Contacts	-	* Marsha Hayden *, ORA, Division of Field Science, HFC-141, (301) 827-1039.
General Import Operations and Policy	-	* Ted Poplawski *, ORA, Division of Import Operations and Operations Policy, HFC-170, (301) 594-3849.

PART VII - CENTER PROGRAM RESPONSIBILITY

Program Evaluation

- The Director, CFSAN, Office of Cosmetics and Colors, HFS-100, is responsible for submitting an annual evaluation of this program. The evaluation should be submitted to the Director, Division of Field Program

Planning and Evaluation by April 1, for the program ending September 30 of the previous fiscal year. The Division of Field Program Planning and Evaluation will provide accomplishment data when requested.

- Samples submitted by the Field to CFSAN are analyzed selectively as follows:
    a. Species Confirmation

       CFSAN/Division of Division of Natural Products, Microanalytical Branch (HFS-315) will identify submitted yeast and mold isolates.

    b. Chemical Analysis

       CFSAN/Division of Science and Applied Technology, Cosmetics Technology Branch (HFS-127) will analyze cosmetic products for prohibited or other potentially harmful ingredients or contaminants.

    c. Confirmation of Color

       CFSAN/Division of Science and Applied Technology, Color Technology Branch (HFS-126) will advise on color additive analyses on samples of cosmetic products not amenable to the typical analytical methods.

    d. Determination of Toxicity

       CFSAN/Division of Science and Applied Technology, Cosmetics Toxicology Branch (HFS-128) will determine topical or systemic toxicity as requested by the Division of Programs and Enforcement Policy (HFS-105).

    e. Label Review

       CFSAN/Division of Enforcement and Programs, Imports Branch (HFS-606) will provide assistance for determining violations of cosmetic labeling requirements.

Attachment A

RECENT APPROVALS - CERTIFIED COLORS

Listed below are the new approvals of certified colors, which may be used as color additives in the manufacture of eye-area products.

COLOR	COLOR APPROVAL	21	FEDERAL

	EFFECTIVE DATE	CFR	REGISTER
FD&C Blue #1 & Aluminum Lake	3/19/94	74.2101	Vol. 59, #32, p7635
D&C Green #5	9/12/94	74.2205	Vol. 59, #153, p40802
FD&C Red #40 & Aluminum Lake	3/19/94	74.2340	Vol. 59, #32, p7635
FD&C Yellow #5 & Aluminum Lake	12/30/94	74.2705	Vol. 59, #228, p60893

TERMINATION - PROVISIONAL LISTING OF COLORS

Due to the termination of selected provisional listings, certain colors are not permitted in cosmetics manufactured on/or after January 29, 1990. Listed below are those colors, which fall in this category

COLOR	COLOR TERMINATION DATE
FD&C Red #3 and its Lakes	1/29/90

Attachment B

BOVINE TISSUE AND TISSUE-DERIVED INGREDIENTS

MATERIALS WITH SUSPECTED RISK OF INFECTIVITY

Adrenal gland**
Basal ganglia/basal ganglion
Bone marrow**
Brain**
Brain extract**
Ceramide B-lactoside
Ceramide dihexoside
Cerebellum**
Cerebroside (sulfate)

Cerebrospinal fluid**
Cranial nerves**
Collagen (soluble)
Colon (proximal and distal)**
Digalactosylceramide
Diglycosylceramides (cytosides)
Disialoganglioside
Dura mater**
Elastin (source: oxen neck ligaments)
Eye**
Galactoc Cerebroside
Galactosylcerebroside (sulfate ester)
Ganglioside
Glucosylcerebroside
Glycerophospholipid
Glycosaminoglycan
Glycosphingolipid
Glycosylceramide
Hypothalamus**
Ileum**
Intercellular Lipids (ICL's)
Lactoc Cerebroside
Lactosylceramide
Lipisomes
Liver
Lung
Lymph nodes**
Monoglycosylceramide (cerebroside)
Monosialoganglioside
N-Nervonoyl cerebroside
N-Oleoyl cerebroside
N-Palmitoyl cerebroside
Nasal mucosa**
Olfactory bulb or gland**
Pancreas (including pancreatin)
Phospholipids
Pineal gland**
Pituitary gland**
Placenta**
Rowamyelin
Sciatic nerve
Sphinogomyelin
Sphingolipid
Spinal cord**

Spleen**
Suprarenal gland**
Tetraglycosylceramide
Thymus gland (sweet-bread)
Tonsil**
Triglycosylceramide
Trinitrophenylaminolauroylglucocerebroside
Trinitrophenylaminolauroylgalactocerebroside
Trisialoganglioside

Considered high risk for infectivity. If any of these tissues are obtained from known BSE countries, refer to Part III, Page 2 of the compliance program for additional information to be obtained for possible regulatory follow-up.

Attachment C

May 9, 1996

TO MANUFACTURERS AND IMPORTERS OF COSMETICS:

As the media have widely reported, the British government announced on March 20, 1996, that new information had been gathered about bovine spongiform encephalopathy (BSE) in cattle that suggests a possible relationship between BSE and ten cases of a newly identified form of Creutzfeldt-Jakob disease (CJD), a similar fatal transmissible spongiform encephalopathy (TSE), in humans. To serve our mutual interest in protecting public health, the Food and Drug Administration (FDA) believes it is prudent to reiterate concerns we have previously expressed on this issue.

BSE is an infectious neurologic disorder of cattle and is prevalent in certain parts of the world. BSE has never been diagnosed in cattle in the United States. It is believed that the rapid spread of BSE in cattle in some countries, particularly Great Britain, was caused by the feeding of certain infected cattle and sheep tissues to cattle. While transmission of the causative agent of BSE to humans has not been definitively documented to date, inter-species transfer has been demonstrated (e.g., mice can be infected by exposure to infected bovine tissues). Recent developments in Great Britain raise serious questions regarding potential hazards of the use of animal tissues containing the causative agent of BSE.

We strongly recommend that firms manufacturing or importing cosmetic products which contain specific bovine tissues (see appendix A), including extracts or substances derived from such tissues, take whatever steps are necessary to assure themselves and the public that such ingredients do not come from cattle born, raised, or slaughtered in countries where BSE exists. FDA believes that immediate and

concrete steps should be taken by manufacturers to reduce the potential risk of human exposure to, or transmission of, the infectious agent, which causes BSE in cattle.

The list of countries where BSE is known to exist is maintained by the U.S. Department of Agriculture (USDA) and codified in Title 9, Code of Federal Regulations, Part 94.18. A current list of these countries follows:

USDA LIST OF COUNTRIES WHERE BSE EXISTS
(Current as of May 1996)

Great Britain (including Northern Ireland and the Falklands)
Switzerland
France
Republic of Ireland
Oman
Portugal

A range of research projects into the exact nature of both the BSE agent and other TSE agents is ongoing. Available scientific information indicates that these agents are extremely resistant to inactivation by normal disinfection or sterilization Procedures.

The cosmetic industry has historically been a user of bovine-derived raw materials. These materials include extracts of bovine organs, including brain, placenta, liver, thymus, heart, mammary gland, marrow, ovary and spleen, as well as ingredients derived from animal tissues such as glycosaminoglycans, bovine lipids, proteins, amino acids, and most recently, sphingolipids isolated from central nervous system tissue.

The information that is currently available suggests that exposure of healthy, intact skin with BSE infectious agent represents an unlikely route of infection. Nevertheless, some ingredients used in cosmetics are derived from tissues that are considered highly infectious, and, if obtained from infected animals, may contain the BSE infectious agent. The possibility of infection cannot be completely ruled out, especially if exposure occurs with abraded or damaged skin or from contact of the infectious agent with the eyes or through ingestion.

Although there is still no definitive evidence that the use of bovine tissues that contain the infectious agent for BSE causes CJD in humans, FDA is concerned that appropriate measures to eliminate the use of bovine tissues from BSE-countries be instituted industry-wide.

At a future date, we will contact you with guidance on how best to provide assurance that your products do not contain potentially BSE-infected materials.

We appreciate your attention to and cooperation in this matter. If you need more information, please contact Dr. Elisa Elliot by phone at (202) 205-5140.

Sincerely,

/s/

Michael A. Friedman, M.D.
Deputy Commissioner for Operations

Enclosure

Appendix A

List of Tissues With Suspected Infectivity

Category I (High infectivity)

- brain
- spinal cord

Category II (Medium infectivity)

- ileum
- lymph nodes
- proximal colon
- spleen
- tonsil
- dura mater
- pineal gland
- placenta
- cerebrospinal fluid
- pituitary gland
- adrenal gland

Category III (Low infectivity)

- distal colon
- nasal mucus
- sciatic nerve
- bone marrow
- liver
- lung

- pancreas
- thymus gland

List taken from Report of a WHO Consultation on Public Health Issues Related to Animal and Human Spongiform Encephalopathies, World Health Organization, Office of International Epizootics, Geneva, Switzerland, November 12-14, 1991.