CHAPTER 29 – COLORS AND COSMETICS TECHNOLOGY

SUBJECT:	**IMPLEMENTATION DATE**
COSMETICS PROGRAM; IMPORT AND DOMESTIC (FY 07/08) This program has completed a Good Guidance Practices clearance by CFSAN's ORP and OC/DFP/CPB in December 2006.	2/20/07
	COMPLETION DATE 9/30/08

DATA REPORTING	
PRODUCT CODES	PRODUCT/ASSIGNMENT CODES
INDUSTRY CODE : 53 USE APPROPRIATE PRODUCT CODES	29001 (for both domestic and import work)

Note: Material that is not releasable under the Freedom of Information Act (FOIA) has been redacted/deleted from this electronic version of the program. Deletions are marked as follows: (#) denotes one or more words were deleted; (&) denotes one or more paragraphs were deleted; and (%) denotes an entire attachment was deleted.

FIELD REPORTING REQUIREMENTS

1. Investigations Branches

   a) Consumer and Trade Complaints--Selective hardcopy reporting for adverse reaction/injuries may be required. Adverse events/injuries should be recorded in FACTS, or contact CFSAN CAERS. Cosmetic inquiries can be forwarded to Lark Lambert, Office of Cosmetics and Colors (OCAC), HFS-125. Refer to Part III of this program and Subchapter 8.4 of the Investigations Operations Manual (IOM) for additional instructions. The e-IOM can be accessed on line at http://www.fda.gov/ora/inspect_ref/iom/iomtc.html.

   b) Certain findings require immediate telephone contact and possible hardcopy reporting to the Center for Food Safety and Applied Nutrition (CFSAN), Division of Enforcement (DE). Refer to Part III, Section 6.

   c) Coverage of Ruminant Tissue and Tissue-Derived Ingredients. Completion of the questionnaire at ATTACHMENT B is required during each inspection under this program.

Refer to Part III, Section 3. Completed questionnaire should be mailed or faxed to:

Cosmetics Program Monitor
Food and Drug Administration
Center for Food Safety and Applied Nutrition (HFS-636)
5100 Paint Branch Parkway, Rm. 3C087
College Park, MD 20740
Phone (301) 436-1616
Fax (301) 436-2657

2. Laboratory Branches

Report all analyses into the Field Accomplishment and Compliance Tracking System (FACTS) using the following Problem Area Flags (PAF) for the various types of analyses.

Microbiological Analyses - MIC
Color Additive Analyses - COL
Label Reviews - FDF (Result Flag = FDL)

SPECIAL INSTRUCTIONS

1. General

Collect samples for color analysis, prohibited ingredients, or label reviews on a compliance basis only.

Do not report import label exams, inspections, sample collections or analyses of drug products under this program.

2. Domestic

Conduct routine surveillance inspections only at firms manufacturing or repacking eye area cosmetics or skin care preparations and lotions. These products present the greatest potential health hazard if they become contaminated with bacteria. However, once in the firm, all cosmetics produced by the firm must be covered using the instructions provided in Part III of this program. Note: The questionnaire on ruminant-derived tissue (ATTACHMENT B) applies to all cosmetic products being manufactured or imported by the firm being inspected and is not limited solely to eye area cosmetics and skin care preparations and lotions.

3. Imports

In accordance with applicable instructions provided in Part III of this program, import label examinations should include review for compliance with mandatory labeling requirements, including, but not limited to, required warning statements; prohibited ingredients and non-permitted color additives; and cosmetics containing ruminant-derived tissues imported from BSE affected or at-risk countries.

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 intending to affect the body's structure or function [201(i)]. Articles intended for use as components of cosmetic products are also considered cosmetics. Soap meeting the criteria of 21 CFR 701.20(a)(1) and (a)(2)is excluded from the term "cosmetic" and is not subject to regulation under the FD&C Act.

Some products perceived by consumers to be cosmetics may also be drugs if, in addition to their cosmetic function, 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, antidandruff shampoos and other medicated cosmetics.

U. S. consumers purchase cosmetics manufactured and marketed by a worldwide cosmetics industry. It has been estimated that consumer expenditures for cosmetics exceed 35 billion dollars annually. The estimated import share of this cosmetic market is 1 to 2%. It is further estimated that the marketed cosmetics are being produced in more than 1400 domestic manufacturing and repacking establishments and represent more than 25,000 product formulations. About 12,500 different cosmetic ingredients and a similar number of fragrance ingredients are being used by the cosmetic industry.

In recent years, there have been several recalls of cosmetic products contaminated with pathogenic microorganisms or containing non-permitted color additives.

Refer to the Division of Field Investigations (DFI) Guide to Inspections of Cosmetic Product Manufacturers (hereinafter referred to as the DFI inspection guide) for discussions of problems of current interest. This guide is available at http://www.fda.gov/ora/inspect_ref/igs/cosmet.html.

PART II - IMPLEMENTATION

1. Objectives

To provide coverage of import and domestic cosmetics through inspection and sample analysis.

2. Program Management Instructions

Interaction with other compliance programs

Additional instructions on color additives may be found in the Imported Food and Color Additives Compliance Program (7309.006) and the Domestic Food Safety Compliance Program (7303.803).

Criteria for selecting firms to inspect are listed below in order of relative priority.

a) Manufacturers who have recalled cosmetics because of microbial contamination during the previous 3-year period;

b) Manufacturers of the types of products discussed below, i.e., eye area cosmetics, etc., that have had an OAI or VAI inspection within the previous 3-year period; or

c) Any firm that manufactures the types of products discussed below. To aid the districts in selecting firms to cover, CFSAN/Division of Field Programs (DFP) can provide an inventory of firms that have been determined to be producing these types of products based on previous inspectional observations.

Any routine surveillance inspection under this Compliance Program should:

a) be made only at firms manufacturing or repacking cosmetic products intended for use in the area of the eye or skin care preparations and lotions (this includes firms that produce eye area cosmetics and other products, however, if the firm does not produce eye area cosmetics, then they are not a high priority);

b) cover only cosmetics (see Part III, Section 1., for instructions in determining whether a product is a cosmetic, a drug, or a drug as well as a cosmetic); and

c) include coverage of ruminant-derived tissues and their ingredients.

3. Coverage of Ruminant Tissue and Tissue Derived Ingredients for Bovine Spongiform Encephalopathy (BSE)

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. Investigators must refer to USDA APHIS website at http://www.aphis.usda.gov/NCIE/country.html for an up-to-date list of countries. The list contains both countries and other regions in which BSE is known to exist, as well as countries and other regions which, because of import requirements that are less restrictive than those that would be acceptable for import into the United States and/or because of inadequate surveillance, present a significant risk of introducing BSE.

On February 9, 2001, USDA's Animal and Plant Health Inspection Service (APHIS) further prohibited the importation into the United States of certain edible ruminant products from BSE affected or at-risk countries. FDA supported the APHIS prohibition by issuing revised I.A. #17-04 to require that FDA entry review be done to determine whether cosmetic products offered for entry contain ingredients subject to APHIS prohibition.

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

Manufacturers and importers of cosmetic products and their ingredients should have steps in place to provide assurances to themselves and to consumers that ruminant-derived tissues do not come from cattle in countries where BSE occurs. Inspections under this compliance program will include completion of the questionnaire (ATTACHMENT B) to determine whether the firm being inspected is aware of our concerns about the transmission of BSE as outlined in the May 9, 1996 letter, and whether the firm has procedures in place to provide assurance that ruminant-derived tissues do not come from BSE affected or at-risk countries.

NOTE: The list of tissues contained in the Agency's 5/9/96 letter has been expanded (ATTACHMENT A) to include additional ruminant tissue or tissue-derived ingredients with a suspected risk of infectivity. NOTE: Although ATTACHMENTS A and C contain a list of tissues to assist investigators in identifying potential ruminant-derived ingredients, the lists are not intended to identify all ruminant-derived ingredients about which the Agency has concerns. Unless otherwise explicitly stated, any ruminant tissue or tissue-derived ingredient from a BSE affected or at-risk country should be considered a possible risk.

PART III – INSPECTIONAL

1. General

General guidelines for the areas to be covered during inspections and label examinations conducted under this program can be found in the document entitled “Cosmetic Good Manufacturing Practice Guidelines” which is located on CFSAN’s website at: http://www.cfsan.fda.gov/~dms/cos-gmp.html.

Note: Additional background information concerning topics related to cosmetics may also be found at: http://www.fda.gov/ora/inspect_ref/igs/cosmetic.html; however, investigators must use the CGMP guideline document referenced above and this compliance program to guide their inspections.

All work done under this program must cover cosmetics only. To determine if a product should be covered under this program, refer to its list of ingredients. The product should be covered as a cosmetic if no "active ingredient" is declared and there are no indications of intended drug use (i.e., labeling claims, promotional statements, etc.). If the product is declared a drug, it should not be covered under this program.

An Intercenter Agreement between CDER and CFSAN is in effect which is intended to assist FDA in implementing the cosmetic and drug provisions of the Federal Food, Drug, and Cosmetic Act (the Act) by clarifying program responsibilities in light of overlapping jurisdiction between CDER and CFSAN. Under this agreement, CDER and CFSAN shall have concurrent jurisdiction over a product which purports to be a cosmetic but meets the definition of drug. **Both CDER** and **CFSAN** may bring regulatory action relating to such product. CFSAN will not include drug charges in any such action without first notifying CDER of the charges that will be included. CDER will not include cosmetic charges in such an action without first obtaining CFSAN’s concurrence. A complete copy of this agreement can be seen at: http://www.cfsan.fda.gov/~dms/cos-mou.html.

2. Inspections

In addition to the instructions provided in the CGMP guidelines for cosmetics referenced above and in items 3 through 6. Below, the following additional items should be covered during inspections of cosmetic manufacturers.

a) Adequacy of Preservation

Determine whether each batch of cosmetic that is not self-preserving, i.e., contains less than 10% ethanol, propylene glycol, glycerol, etc., or is not in a self-pressurized container, is tested for microbial contamination before the batch is released for interstate shipment.

Determine whether each cosmetic, particularly each eye area cosmetic, has been tested during product development for adequacy of preservation against microbial contamination that may occur under reasonably foreseeable conditions of consumer use.

Review the qualitative and quantitative composition of the preservative system of each eye area cosmetic.

b) Voluntary Registration

Determine whether the firm has voluntarily registered its manufacturing establishment (21 CFR 710) and its cosmetic product formulations (21 CFR 720). If not, encourage participation in these voluntary programs.

c) Small Business Assistance

At the conclusion of each inspection, make the firm's management aware of FDA's Small Business Assistance Program. Provide the address of the Regional Small Business Representative (SBR).

d) Cosmetics Making Drug Claims

CFSAN and CDER have an intercenter agreement on this issue and investigators should refer to the agreement posted at http://www.cfsan.fda.gov/~dms/cos-mou.html for additional instructions on reviewing product labels for drug claims.

e) Alpha Hydroxy Acids (AHAs) “Sun Alert” Labeling Statement

On December 2, 2002, FDA published for comment draft guidance concerning a “Sun Alert” labeling statement on the labels of cosmetics containing alpha hydroxy acids (AHAs)(e.g., glycolic acid, lactic acid). Investigators are requested to notify firms manufacturing cosmetics containing AHAs of the Agency’s draft guidance on AHAs. The draft guidance is available online at http://www.cfsan.fda.gov/~dms/ahaguide.html.

f) Warning Statements and Directions for Safe Use

Products described below are known to produce adverse reactions in individuals when not properly formulated or when improperly used by the consumer. The hazards posed by improperly formulated products are described at: http://www.fda.gov.ora/inspec_ref/igs/cosmet.html. The firms’ manufacturing processes and labeling of these products bears careful attention during cosmetic inspections.

- Depilatories and hair straighteners;
- Permanent wave neutralizers;
- Nail builders, hardeners, and enamels;
- Artificial or sculptured fingernail glue; and
- Coal tar hair dyes (cautionary statement and adequate directions for use).

g) In the past, formation of nitrosamines in cosmetic products containing the preservative Bronopol™ (2-bromo-2-nitro 1,3-propanetiol) has been an issue. Bronopol ™ is no longer widely used, and as a result of product reformulation the occurrence of nitrosamines has been significantly reduced. It is necessary, however, to monitor the use of Bronopol ™ in cosmetic products to assure that a nitrosamine issue does not reoccur. If the ingredient Bronopol ™ is encountered in a cosmetic product, include a complete list of the product ingredients in the EIR for submission to CFSAN so the potential for nitrosamine formulation can be evaluated.

3. Coverage of Ruminant Tissue and Tissue-Derived Ingredients

The questionnaire at ATTACHMENT B was developed to determine the following in each domestic firm inspected.

a) Whether the firm manufactures or imports products containing ruminant tissue or tissue-derived ingredients.

b) Whether the firm has procedures in place to ensure that it does not receive ruminant tissue or tissue-derived ingredients from BSE affected or at-risk countries. Recordkeeping Requirements for Human Food and Cosmetics Manufactured From, Processed With, or Otherwise Containing Material Cattle can be found at http://www.cfsan.fda.gov/~lrd/fr061011.html.

c) The origin of all ruminant tissue or tissue-derived ingredients used and the products containing them.

Upon completion, the questionnaire (ATTACHMENT B) must be mailed or faxed to the CFSAN contact listed in the beginning of this compliance program.

The current list of BSE affected or at-risk countries can be found at: http://www.aphis.usda.gov/NCIE/country.html. The list is subject to change, and investigators must refer to it for the up-to-date list.

As indicated in item c) above, information concerning the origin of all ruminant tissue and tissue-derived ingredients used by the firm and the products containing them will be obtained and noted on ATTACHMENT B.

Additional documentation in the EIR as outlined below is required only when a firm is manufacturing or importing cosmetic products or their ingredients using any ruminant tissue or tissue-derived ingredients from any country listed at the above USDA website. The district must document the following items in the EIR and forward to CFSAN/DE/Domestic Branch (HFS-607) for regulatory consideration:

a) the tissue or tissue-derived ingredients being used;

b) the finished products containing them;

c) the specific country of origin of the tissue; and

d) the name and address of the importer or other responsible party.

4. Prohibited/Restricted Ingredients

Determine whether any of the following prohibited ingredients are being used by the firm in the production of cosmetic products.

a) Hexachlorophene (21 CFR 250.250)—Because of its neurotoxic effect and ability to penetrate human skin, the use of hexachlorophene (HCP) as a cosmetic ingredient is restricted to use as a preservative where an alternative preservative has not been shown to be as effective. Refer to the regulation for permitted concentration of HCP in cosmetics.

   Check for use of HCP in the manufacture of cosmetics and report in the EIR the name of each HCP containing product, the HCP concentration, and the reasons given for not using another preservative in its place.

b) Mercury Compounds(21 CFR 700.13)—The use of mercury compounds as cosmetic ingredients is limited to use as preservatives in eye area cosmetics at concentrations not exceeding 65 ppm (0.0065%) of mercury calculated as the metal (about 100 ppm or 0.01% of phenylmercuric acetate or nitrate) and provided no other effective and safe preservative is available for use.

   Check for use of mercury compounds in the manufacture of cosmetics and determine the kinds and concentrations of compounds used as well as the products in which they are used.

c) Chlorofluorocarbon Propellants (21 CFR 700.23 and 2.125)—The use of chlorofluorocarbon propellants (fully halogenated chlorofluoroalkanes) in cosmetics aerosol products intended for domestic consumption is prohibited. The following are fully halogenated chlorofluorocarbons: chlorofluorocarbon 11 (trichlorofluoromethane), chlorofluorocarbon 12 (dichloro-difluoromethane), chlorofluorocarbon 113 (trichlorotri-fluoroethane), chlorofluorocarbon 114 (dichlorotetra-fluoroethane) and fluorocyclobutane C318 (octofluoro-cyclobutane).

   Chlorofluorocarbon-containing cosmetic aerosol products may continue to be manufactured for export provided they are not in conflict with 801 (e) for circumstances under which they are to be exported, and a control system is being followed by the firm which ensures that there is no likelihood, by mistake or otherwise, of diversion of products into domestic commerce.

d) The following substances are prohibited as cosmetic ingredients.

   - Bithionol (21 CFR 700.11)
   - Halogenated Salicylanilides (21 CFR 700.15)
   - Chloroform (21 CFR 700.18)
   - Vinyl Chloride as an ingredient of aerosol products (21 CFR 700.14)
   - Zirconium containing complexes in aerosol cosmetic products (21 CFR 700.16); and
   - Methylene chloride (21 CFR 700.19).

5. Ingredients of Concern When Used in Cosmetics

The presence of the following ingredients, while not prohibited, warrant investigation and documentation in the EIR for Center review.

a) Acetyl ethyl tetramethyl tetralin (AETT)—Found to cause serious neurotoxic disorders and discoloration of internal organs.

b) 6-Methylcoumarin (6-MC)—potent photocontact sensitizer.

c) Musk Ambrette—may cause photocontact sensitization.

6. Non-certified or Non-Permitted Color Additives

Investigators should refer to the Domestic Food Safety Compliance Program (7303.803) and the Import Food and Color Additives Compliance Program (7309.006) for additional information at it applies to color additives.

Except for coal-tar hair dyes used to dye hair, only color additives specifically permitted by regulation for use in cosmetics may be legally used, and then only in accordance with the provisions of the specific color additive regulation. See 21 CFR Parts 73, 74, 81, 82 for a complete listing of permitted color additives. Refer to CFSAN's website at: http://www.cfsan.fda.gov/~dms/opa-col2.html for a complete listing and permitted uses of each color additive approved for use in cosmetics.

a) In determining whether non-certified color additives are present in the product, it is important to note that a label declaration of, for example, "C.I. 45410" or Phloxine B (common designations for a color additive which is certifiable as D&C Red No. 28), is NOT synonymous with a certified lot of the color additive. Furthermore, laboratory analysis of a cosmetic cannot be used to determine whether a lot of color additive used was certified.

   With respect to individual color additives subject to certification, during inspections, investigators should document instances where bulk color additive ingredients used in cosmetics (other than those used in hair dye products) are not labeled with the appropriate color additive nomenclature found at 21 CFR Parts 74 and 82 and/or do not contain appropriate FDA certification lot numbers on the labels of the bulk color additive. In the case of color additive mixtures, investigators should document if the label declares a control number that can be traced to the FDA certification lot numbers of the color additive present in the mixture. This control number should be documented for verification.

   Since it can not be determined by analysis if a cosmetic contains colors subject to certification that in fact originated from certified lots, investigators 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. For color additives, FDA currently does not object to C.I. numbers being used in a dual declaration with the C.I. numbers parenthetical to the official sanctioned FDA name as in the listed regulation, provided the color additive regulation requirements are met (e.g., colors subject to certification have in fact been certified).

b) During domestic inspections, if bulk non-permitted color additives (e.g., those labeled solely by a trade or common name, "E" numbers of C.I. numbers) are encountered at a firm, investigators should not only determine all facts regarding their use in cosmetics but use of all permitted color additives as well (e.g., those that have been by certified by FDA).

   When investigating use of non-permitted color additives, investigators should pay particular attention to color additives used in cosmetics intended for the area of the eye (see 21 CFR 70.3(s) for a definition of "area of the eye") as there are only a limited number that are specifically permitted by regulation for use in eye area cosmetics. Refer to CFSAN's website at http://www.cfsan.fda.gov/~dms/opa-col2.html.

7. Mandatory Labeling and Packaging Requirements

Determine labeling and packaging practices for the following:

a) 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.)

To adequately evaluate compliance with the requirements of 21 CFR 701.3(c) and the appropriateness of nomenclature currently being used in the ingredient declaration of cosmetics, districts should focus primarily on the declaration of botanical ingredients (e.g., plant extracts) and color additives.

In 1995/1996 correspondence between the Office of Cosmetics and Colors (OCAC)and the Cosmetic, Toiletry and Fragrance Association (CTFA), the use of Latinized taxonomy with respect to botanical ingredients and the use of Color Index (C.I.) numbers for color additives were addressed. These letters may be viewed online at http://www.cfsan.fda.gov/~dms/cos-intl.html (Requests Regarding the Harmonization of Ingredient Nomenclature).

Currently, the Agency does not object to a dual (parenthetical) declaration for botanical ingredients where both a Latinized (LINNE) taxonomic (genus/species) name and English “common or usual name” are listed, provided that the English “common or usual name” is listed first. If there is no English “common or usual name”, the Agency has not objected to the LINNE name being used alone, per 21 CFR 701.3(c)(4). For color additives, the Agency currently does not object to C.I. numbers being used in a dual declaration with the C.I. numbers parenthetical to the official sanctioned FDA name as in the listed regulation, provided the color additive regulation requirements are met (e.g., colors subject to certification have in fact been certified).

Investigators should refer to ATTACHMENT D of this compliance program for examples of nomenclature that may appear on the labels of cosmetic products marketed for domestic and/or international marketplaces, respectively.

NOTE: Abbreviated names for color additives specified in the 1996 Federal Register proposed rule Permanent Listing of Color Additive Lakes (March 4, 1996, 61 FR 8372, at page 8417) have been used in the examples provided.

b) Required warning statement for suntanning cosmetic products containing no sunscreen ingredients (21 CFR 740.19). The warning statement must 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."

c) Required warning statements on cosmetics packaged in self-pressurized containers (21 CFR 740.11). The wording for this statements is prescribed by regulation and must be correctly stated as follows:

> "Warning—Avoid spraying in eyes. Contents under pressure. Do not puncture or incinerate. Do not store at temperature above 120°F. Keep out of reach of children."

In addition to the above warning statement, if the propellant used consists in whole or in part of a halocarbon or a hydrocarbon the following additional warning statement must be used:

> "Warning—Use only as directed. Intentional misuse by deliberately concentrating and inhaling the contents can be harmful or fatal."

d) Statement of appropriate warnings and directions for safe use of children's foaming detergent bath products, i.e., children's bubble bath products and all foaming detergent batch products not labeled as intended for use exclusively by adults (21 CFR 740.17). The product label must bear adequate directions for safe use and the following caution:

> "Caution—Use only as directed. Excessive use or prolonged exposure may cause irritation to skin and urinary tract. Discontinue if rash, redness, or itching occur. Consult your physician if irritation persists. Keep out of reach of children."

e) Determine whether cosmetic liquid oral hygienic products and all cosmetic vaginal products intended for retail sale comply with tamper-resistant packaging requirements and assure that the product label bears the statement alerting consumers to the tamper-resistant features(21 CFR 700.25).

f) Cautionary statement and adequate directions for use required on coal-tar hair dyes (i.e., materials derived from petroleum) 21 U.S.C. 601(a).

8. Import Label Examinations

ORA's Field Workplan includes resources for conducting label examinations of import entries to be conducted under this program. Each label examination must:

a) Cover cosmetics only. (See Part III, Section 1., for instructions in determining whether a product is a cosmetic, a drug, or drug as well as cosmetic and the listing of cosmetic product categories at 21 CFR 720.4(c));

b) Include a review for compliance with mandatory labeling and packaging requirements, including required warning statements; prohibited/restricted ingredients; and non-certified or non-permitted color additives utilizing the instructions provided above under Inspections;

c) Include a review of cosmetic labels with added "ingredients stickers" signifying possible re-labeling of brand name (so called gray market) cosmetics produced for markets outside of the U.S. to determine if the color additives are permitted and declared correctly. Cosmetics formulated for use in other countries may contain color additives not permitted in the U.S.

Imported cosmetics may bear ingredient labels identifying color additives with their European name or ("E") color designation with a corresponding number (e.g., E104, E122, E123, and E124), by using a color index number (e.g., C.I. 15985) or using the trade or common name of the color additive (e.g., Sunset Yellow FCF). This suggests that the color additive used may not be certified. When a cosmetic bears only the aforementioned designations; districts should consider detaining without sampling based on the appearance of adulteration (e.g., the product appears to contain an uncertified color additive).

For products that are detained, if the importer provides valid documentation that the color was from an FDA certified list, the district should consider release.

d) Include adequate coverage of ruminant-derived tissues and their ingredients as directed in Import Alert #17-04 "Detention Without Physical Examination of Bulk Shipments of High Risk Bovine Tissue From BSE Countries" http://www.fda.gov/ora/fiars/ora_import_ia1704.html. Recordkeeping Requirements for Human Food and Cosmetics Manufactured From, Processed With, or Otherwise Containing Material Cattle can be found at http://www.cfsan.fda.gov/~lrd/fr061011.html.

Import entry reviewers must refer to I.A. #17-04 for instructions. OASIS screening criteria have been modified to allow 100% entry review for any import entry of finished cosmetic products that may contain ruminant tissue or tissue-derived ingredients. Districts should be alert to entries of finished products from BSE affected and at-risk countries which contain high-risk bovine tissues or tissue derived ingredients listed in the product ingredient declaration. All entries containing high-risk bovine tissues or ingredients as listed in Attachment A of I.A. #17-04, originating from countries listed in the Import Alert, should be detained until such time as the importer can provide certification that the tissues are not from a BSE affected or at-risk country or that the animal from which the tissue was rendered was from a BSE free herd.

9. Plano (non-corrective) Contact Lenses

An amendment to the FD&C Act on November 9, 2005 made all contact lenses devices. Reference to this amendment has been incorporated into the FD&C Act at Section 520(n)(1) All contact lenses shall be deemed to be devices under section 201(h).(2) Paragraph (1) shall not be construed as bearing on or being relevant to the question of whether any product other than a contact lens is a device as defined by section 201(h) or a drug as defined by section 201(g).

10. Consumer and Trade Complaints

Prior to conducting follow-up on any cosmetic complaint, including sampling, the district should contact Lark Lambert (Lark.Lambert@FDA.HHS.GOV), OCAC, HFS-125. Many types of cosmetic products are known to cause adverse reactions under certain conditions, therefore automatic follow-up and sampling for adverse reaction reports on cosmetics may not be necessary. OCAC can advise the investigating district of appropriate follow-up. If unable to contact that office, the district should proceed to investigate reports initiated on those complaints involving serious or unusual adverse reactions, e.g., multiple complaints, and contact OCAC as soon as possible afterwards.

The FACTS Consumer Complaint Cosmetic Report should be used for adverse events related to cosmetics (See Subchapter 8.4.5 of the IOM). If collection of cosmetic consumer complaint samples is necessary, follow the instructions provided in Subchapter 8.4.7 of the IOM. These samples will be analyzed by the appropriate district servicing laboratory or Center laboratory as discussed in Part IV of this compliance program.

11. Sample Collections

a) Collect domestic samples of eye area cosmetics or skin care preparations and lotions that are not self-preserving, i.e., contain less than 10% ethanol, propylene glycol, glycerol, etc., or are not in a self-pressurized container for microbiological analysis. All samples collected under this program must be collected when inspectional evidence or product packaging and labeling indicates that a violation of the FD&C Act may exist. To determine if sampling is warranted, refer to the instructions contained above and in the Cosmetic CGMP Guidelines at http://www.cfsan.fda.gov/~dms/cos-gmp.html. If uncertain whether to collect a sample, contact the appropriate CFSAN regulatory contact listed in Part VI of this program for additional instructions.

b) Collect import samples of eye area cosmetics or skin care preparations and lotions that are not self-preserving i.e., contain less than 10% ethanol, propylene glycol, glycerol, etc., or are not in a self-pressurized container for microbiological analysis.. All imported samples collected under this program must be compliance samples collected when product packaging and labeling indicates that a violation of the FD&C Act may exist.

c) Collect the following quantities as determined by the type of analyses required.

Chemical Analysis—Collect in duplicate

Aerosol products—680 gm (24 oz)
Bath Salts—680 gm (24 oz)
Bubble Baths--680 gm (24 oz)
Eye Make-up – 56 gm (2 oz)
Facial Make-up—225 gm (8 oz)
Mouthwashes—680 gm (24 oz)
Nail preparations—160 gm (6 oz)
Perfumes—160 gm (6 oz)
Pressed Powders—160 gm (6 oz)

Microbiological analysis and filth examination—Collect in duplicate

Collect at least ten individual retail units [20 units if less than 14 gm (½ oz) each] or 1-100 gm (4 oz) subsample from each of ten containers of bulk material.

d) All import lots sampled under this program must be held pending analysis.

12. Sample Shipment

Submit samples to your district's servicing laboratory or specialized CFSAN laboratory as appropriate to conduct the intended analysis as indicated in PART IV, Section A.

Important Note: For samples collected for field lab analysis, refer to Appendix 3 of the ORA Field Workplan. For this reason, for each type of analysis to be performed by CFSAN, a contact person is provided in Part IV, Section B. Collecting districts should contact that person by e-mail to confirm the shipping address prior to shipping any samples to CFSAN. For CFSAN, refer to CFSAN contact list.

PART IV – ANALYTICAL

Implementation

a) To analyze samples of eye area cosmetics and skin care preparations and lotions that could become contaminated with bacteria and other pathogenic microorganisms, i.e., fungi, yeasts and molds, due to the lack of a preservative system or due to the presence of an inadequate preservative system.

b) To analyze cosmetics for color additives and prohibited ingredients and to conduct label reviews when suspected violations of the FD&C Act and the FPLA are encountered during inspections and import label examinations.

c) To cover ruminant tissue and tissue-derived ingredient use in all cosmetics manufactured or imported by domestic firms and in all entries of imported cosmetic raw material or finished products.

A. ANALYZING LABORATORIES

1. Field

a) Microbiological

General microbiological analysis will be performed by the district's customary microbiological servicing laboratory. (See Appendix III of the current ORA Field Workplan for a listing of servicing laboratories.)

NOTE: Identification of mold isolates will be done by CFSAN/Division of Natural Products/Mycology Laboratory (HFS-315).

b) Color Additives

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

NOTE: Initial analysis may be accomplished by the servicing district laboratory; however, either the original or check analysis for any potentially violative sample must be done by an analyst trained in certified color additive determination. 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) is available to advise the district servicing laboratory on analyses involving difficult color samples.

c) 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 Parts 700, 701 and 740. CFSAN's website at http://www.cfsan.fda.gov/~dms/cos-lbl.html has comprehensive material on cosmetic labeling requirements that should be used in conducting label review.

2. Center

Identification of Molds – Bioanalytical Branch/Mycology Laboratory (HFS-315) will conduct analyses. Servicing laboratories must use the instructions below under B.1. for preparing isolates for shipment to HFS-315.

The following will be performed by CFSAN/Division of Science and Applied Technology, Office of Cosmetics and Colors (HFS-125). Investigations branches should e-mail the Center contact listed below in B. 2. before shipping any samples to the Center for analyses.

Chemical Analysis

Determination of Toxicity

B. ANALYSIS

1. Field

a) Microbiological

All method references to the e-BAM refer to the Bacteriological Analytical Manual current edition available online on CFSAN's website http://www.cfsan.fda.gov/~ebam/bam-toc.html.

Refer to the e-BAM, Chapter 23 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 e-BAM, Chapter 23.

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

Identification of mold isolates will be conducted by the CFSAN/Division of Natural Products/Bioanalytical Branch/Mycology Laboratory (HFS-315).

Prepare cultures for forwarding and further classification as follows:

- Re-culture mold isolates which grow at 37°C on Potato Dextrose Agar slants (screw cap tubes) and incubate at 37°C to ensure growth before shipping.
- Incubate at 25°C isolates that grow at 25°C for a few days until growth is obvious.
- Pack, label and ship isolates in accordance with Federal Standards for Etiological Agents.

b) Color Additive 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 7303.803 (Domestic Food Safety; Attachment C, Analytical Instructions); or 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 and the instructions provided at: http://www.cfsan.fda.gov/~dms/cos-lbl.html.

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

2. Center

Samples submitted by the Field to specialized laboratories are analyzed as follows:

a) Species Identification

The Division of Natural Products/Mycology Laboratory(HFS-315) will identify submitted mold isolates. Contact Dr. Douglas Park at 301-436-2401 or via e-mail at DPark@FDA.HHS.GOV prior to shipping isolates.

b) Chemical Analysis

The Division of Science and Applied Technology, Cosmetics Technology Branch (HFS-127) will analyze cosmetic products for prohibited or other potentially harmful ingredients or contaminants. Contact Donald Havery via e-mail at Donald.Havery@FDA.HHS.GOV prior to shipping samples.

c) Confirmation of Color Additives

The Division Science and Applied Technology, Color Technology Branch (HFS-126) will conduct color additive analyses on samples of cosmetic products not amenable to the typical analytical methods. Contact Lark Lambert via e-mail at Lark.Lambert@FDA.HHS.GOV prior to shipping samples.

d) Determination of Toxicity

The Division of Science and Applied Technology, Cosmetics Toxicology Branch (HFS-128) will evaluate topical toxicity or the potential for systemic toxicity as requested by the Division of Programs and Enforcement Policy (HFS-105). Contact Lark Lambert or Dr. Robert Bronaugh for sampling instructions on potentially toxic cosmetic samples.

e) Label Review

The Division of Programs and Enforcement and Policy (HFS-105) will provide assistance for determining violations of cosmetic labeling requirements. Contact Lark Lambert with questions relating to cosmetic labeling.

PART V - REGULATORY/ADMINISTRATIVE STRATEGY

1. Situations Warranting CFSAN Contact

Contact CFSAN, Office of Compliance (OC), Division of Enforcement (DE), Domestic Branch (HFS-607), at (301)436-2040 or (301)436-2094; or Import Branch (HFS-606) for imports at (301) 436-2413 for instructions in the following situations:

a) If there is a suspected health hazard (see Part III for situations that may constitute a health hazard). In such cases, a health hazard evaluation should be requested from CFSAN/OC/DE, and the CFSAN Office of Cosmetics and Colors (OCAC), Division of Programs and Enforcement Policy (HFS-105) should also be notified. Refer to the Regulatory Procedures Manual (RPM), August 1997, Chapter 7 and 21 CFR 7.41(a) for information regarding health hazard evaluations. The RPM is available online at http://www.fda.gov/ora/compliance_ref/rpm_new2/.

   The receipt of a large number of adverse event reports for a particular product and/or adverse events involving severe chemical burns or severe eye injuries may also be indicative of a potential health hazard situation.

b) If a product presenting a potential health hazard has been distributed.

c) If a cosmetic is found to contain microorganisms at concentrations greater than 500 CFU/gram for eye area cosmetics or 1000 CFU/gram for non-eye area cosmetics.

d) If a domestic firm is using ruminant tissue or tissue-derived ingredients from BSE affected or at-risk countries. Updated information on BSE affected or BSE at-risk countries must be obtained from I.A. #17-04 and USDA regulation 9 CFR 94.18—Restrictions on importation of meat and edible products from ruminants due to bovine spongiform encephalopathy. An updated list of countries may also be obtained from USDA/APHIS website at: http://www.aphis.usda.gov/NCIE/country.html

   NOTE: The absence of procedures to preclude use of ruminant tissue or tissue-derived ingredients from BSE affected or at-risk countries is not, by itself, a sufficient basis for a regulatory recommendation.

e) If a cosmetic is making a drug claim(s). CFSAN and CDER recently renewed their intercenter agreement which provides for concurrent jurisdiction over products that purport to be cosmetics but meet the statutory definition of a drug. The agreement is on the FDA website at http://www.cfsan.fda.gov/~dms/cos-mou.html. Districts may submit recommendations for enforcement action to CFSAN, and CFSAN will coordinate the action with CDER.

f) Contact CFSAN/OC/DE/Imports Branch (HFS-606) at (301)436-2413 if necessary for assistance when an import shipment is detained in accordance with I.A. #17-04.

2. Direct Reference Seizure Authority

Updated instructions regarding direct reference seizure authority for *Pseudomonas* contamination of cosmetics used in the eye area may be found at Section 590.300 of the Compliance Policy Guide Manual (CPG). This CPG Manual is available online at http://www.fda.gov/ora/compliance_ref/cpg/cpgfod/cpg590-300.htm. The specimen charge is stated in the CPG.

Complete labeling and worksheets must accompany direct seizure recommendations when forwarded to the Office of Chief Counsel through the Division of Compliance Management and Operations (HFC-210).

3. Direct to Seizure with Center Review

If any of the situations below are encountered for domestic products, districts should submit a recommendation for seizure (including sample analyses), electronic copy (e.g., .doc, .pdf files, etc) through the Case Information Submission link on the Office of Compliance's intranet home page at #. CFSAN will review to determine Center support for the recommended action. Districts should submit legible digital copies of the labels be submitted via the intranet site as well.

a) Prohibited/ Restricted Ingredients. Determine whether prohibited or restricted ingredients (21 CFR 2.125, 21 CFR 250.250 and part 700) are being used.

- Prohibited as cosmetic ingredients:

i. bithionol (21 CFR 700.11);
ii. halogenated salicylanilides (di-, tri-, metabrom-salan and tetrachlorosalicylanilide) (21 CFR 700.15);
iii. chloroform (21 CFR 700.18); and
iv. methylene chloride (21 CFR 700.19).

- Prohibited as ingredients of cosmetic aerosol products:

i. vinyl chloride (21 CFR 700.14); and
ii. zirconium (21 CFR 700.16).

- Restricted ingredients of cosmetic products unless used as specified in the regulations:

  i. hexachlorophene (HCP) (21 CFR 250.250);
  ii. mercury compounds (21 CFR 700.13); and
  iii. chlorofluorocarbon propellants (21 CFR 700.23 and 2.125).

SPECIMEN CHARGE:
The article is adulterated within the meaning of Section 601(a) of the Act in that it bears or contains a poisonous or deleterious substance, namely [name of substance], which may render it injurious to users under the conditions of use prescribed in the labeling thereof or under such conditions of use as are customary and usual.

b) Non-Certified or Non-Permitted Color Additives. Determine whether non-certified or non-permitted color additives (21 CFR 73, 74, 81, 82) are being used. Refer to CFSAN's website at http://www.cfsan.fda.gov/~dms/opa-col2.html for additional instructions. See also the February 1995 inspection guide.

For cosmetics containing non-permitted color additives (for products other than hair dyes), if seizable size lots are not found, the district should consider a Warning Letter recommendation using the sample warning letter language found at Exhibit 4-14 of the Regulatory Procedures Manual, August 1997.

SPECIMEN CHARGE:
The article is adulterated within the meaning of Section 601(e) of the Act in that it bears or contains a color additive, namely [color], which is unsafe within the meaning of Section 721(a).

When a certifiable color additive is not declared on the label, FDA may or may not have certified it for use in cosmetic products. Without evidence that the color came from a batch that has been certified (e.g., FDA certification lot number, or other inspectional evidence), the appropriate charge would be a 602(e) adulteration charge.

c) Tamper-Resistant Packaging. Cosmetic liquid oral hygiene products, e.g., mouthwashes and breath fresheners, and any kind of cosmetic vaginal product introduced into interstate commerce must be packaged in tamper-resistant packages if intended to be accessible to the public while held for retail sale under 21 CFR 700.25. If not in tamper-resistant packaging, the product is adulterated under Section 601 of the Federal Food, Drug and Cosmetic Act (the Act). (See Section 4b Mandatory Labeling and Packaging Requirements for misbranding charges regarding tamper-resistant packaging and labeling requirements.)

SPECIMEN CHARGE: The article is adulterated within the meaning of Sections 601(a) and/or 601(c) of the Act in that it is not packaged in a tamper-resistant package as required in 21 CFR 700.25.

4. Other Findings

If the situations described in this section are found, enforcement action may be warranted. This is not an all-inclusive list of potential deviations. Districts should use their best judgment to determine the appropriate action (i.e., warning letter, seizure, etc.) and submit a recommendation to CFSAN. If additional assistance is needed, districts should contact the regulatory contacts listed in Part VI.

a) Adequacy of Preservation. Cosmetics need not be sterile, however, they must not be contaminated with microorganisms which may be pathogenic, and the density of non-pathogenic microorganisms should be low. Enforcement action against contaminated products (i.e., products without adequate preservation) may be considered if there are FDA analytical data to show the presence of microorganisms. Such products may be deemed adulterated under Section 601(c) of the Act.

b) Mandatory Labeling and Packaging Requirements. Cosmetics must bear labeling as specified in the FD&C Act, the FPLA, and the cosmetic regulations (21 CFR Part 701). Failure to include necessary labeling elements may cause a product to be misbranded under the FD&C Act and/or FPLA (Sections 602(b)(1) and (2) of the Act, Section 1456(a) of the FPLA). (See Part III—Inspectional for additional information on ingredient declaration)

Some cosmetic products are also subject to the packaging provisions of the Poison Prevention Packaging Act of 1970 and the implementing regulations (16 CFR Part 1700 et. seq.). Products which do not comply with the regulations promulgated under this law are misbranded within the meaning of Section 602(f) of the FD&C Act.

- Appropriate Cautionary Statements and Directions for Safe Use.

The following products may be deemed adulterated or misbranded if the labeling does not contain an appropriate warning statement(s) and/or directions for safe use (see the appropriate section of the Act in parentheses):

i. Depilatories and hair straighteners (Section 602(a) of the Act);

ii. Cosmetic hair dye products containing lead acetate (21 CFR 73.2396), bismuth citrate (21 CFR 73.2110), and/ or henna (21 CFR 73.2190) (Sections 601(e) and 602(a) of the FD&C Act);

iii. Coal-tar hair dyes (Section 601(a) of the Act); and

iv. Nail builders, hardeners, and enamels (may require immediate CFSAN review depending on the facts involved (Section 602(a) of the Act).

- Child Resistant Packaging

  The following products must be packaged in child resistant packaging:

  i. Home permanent wave neutralizers containing sodium bromate or potassium bromate [16 CFR 1700.14(a)(19), Section 602(f) of the Act]; and

  ii. Artificial or sculptured fingernail glue removers containing acetonitrile [16 CFR 1700.14(a)(18), Section 602(f) of the Act].

- Suntanning Products

  These products may be drugs and/or cosmetics, depending on the claims. If the product labeling includes any of the following claims, the product will be regulated as a drug:

  i. The labeling bears any direct or implied statement that the product screens out ultraviolet sunlight, prevents or treats sunburn, helps prevent wrinkles, or prevents premature aging of the skin;

  ii. The label bears a number representing the sun protection factor (SPF) value; or

  iii. The sunscreen ingredient is declared as an active drug ingredient and is listed before the listing of the cosmetic ingredients - Section 502(e)(1) of the Act and 21 CFR 701.3(d).

  Suntan cosmetic products that do not contain a sunscreen must bear adequate directions for safe use and the warning statement required under 21 CFR 740.19. If the products do not comply with the regulation, they are misbranded under Section 602(a) of the Act.

  There are "tanning pills" manufactured as capsules intended for ingestion. These products usually contain beta carotene and/or canthaxanthin. They act by entering the blood stream and are partially deposited in skin tissue, giving the skin a tan-like color. Neither beta carotene nor canthaxanthin is approved for this use, and tanning pill products containing these color additives are considered adulterated under Section 601(e). (NOTE: "Suntan accelerators" are new drugs within the meaning of Section 201(p) of the Act).

- Cosmetics Containing Sunscreen Ingredients

  These products may contain a sunscreen ingredient for purposes other than sun protection (e.g., as a color additive or to protect the color of the product). Such products are required to be labeled with qualifying information in conjunction with the term "sunscreen" or other similar protection terminology used in the labeling as required in 21 CFR 700.35. If the products do not comply with the regulation, they are misbranded under Section 602(a) of the Act.

- Cosmetics packaged in self-pressurized containers

  Cosmetic aerosol products are misbranded unless the labeling bears the label statements required for cosmetics in self-pressurized containers (21 CFR 740.11, Sections 602(a) and 201(n) of the Act).

- Children's foaming detergent bath products

  Such products (e.g., bubble bath products) are misbranded unless the labeling bears adequate directions for safe use and precautionary statement (21 CFR 740.17, Sections 602(a) and 201(n) of the Act).

- Feminine deodorant sprays

  Such products are misbranded unless the labeling bears explicit warnings and directions for safe use (when applicable) (21 CFR 740.12, Section 602(a) of the Act). Additionally, these products may be considered misbranded under Sections 602(a) and 201(n) if the labeling contains the word "hygiene" or a similar word. If the product is represented to have a medical usefulness, it may be considered a drug and would be misbranded under Section 502(a) (21 CFR 740.12).

- Tamper-resistant packaging

  Cosmetic liquid oral hygiene products and vaginal products are required to include a statement regarding the tamper-resistant features of the packages [21 CFR 700.25(c)]. If a product does not contain such statement, or if the labeling contains a statement that the package is tamper-proof, the product may be misbranded under Sections 602(a) and 201(n) of the Act. (See Section 3c Direct to Seizure with Center Review for an adulteration charge regarding tamper-resistant packaging requirements.)

c) Ingredients of Concern When Used in Cosmetics. The presence of the following ingredients, while not prohibited, may be of public health concern. CFSAN should be contacted to review such products on a case-by-case basis.

- Products containing the following fragrance ingredient(s):

  i. acetyl ethyl tetramethyl tetralin (AETT)
  ii. 6-methylcoumarin (6-MC)
  iii. musk ambrette

- Nitrosamines may be formed in cosmetics containing amines and amino derivative ingredients (e.g., diethanolamine (DEA) combined with a nitrosating agent (e.g., 2-bromo-2-nitropropane-1,3-diol (Bronopol™, Onyxide 500), 5-bromo-5-nitro-1,3-dioxane (Bronidox C) or tris(hydroxymethyl)nitromethane (Tris Nitro)); or they may become contaminated with a nitrosating agent (e.g., sodium nitrite).

d) Insanitary conditions. If the inspection finds there to be gross GMP deficiencies, such that the product may become contaminated with filth or may be rendered injurious to health , refer the case to CFSAN for consideration.

5. Plano (non-corrective) Contact Lenses

An amendment to the FD&C Act on November 9, 2005 made all contact lenses devices. Reference to this amendment has been incorporated into the FD&C Act at Section 520(n)(1) All contact lenses shall be deemed to be devices under section 201(h).(2) Paragraph (1) shall not be construed as bearing on or being relevant to the question of whether any product other than a contact lens is a device as defined by section 201(h) or a drug as defined by section 201(g).

6. Imports

Refer to the Regulatory Procedures Manual (RPM) Chapter 9—Automatic Detentions for instructions concerning recommendation for detention based on one violative sample found to contain illegal color additives, unsafe or prohibited ingredients, or that present a health hazard for other reasons as outlined in Part III of this program. Recommendations for Detention Without Physical Examination (DWPE) must be referred to ORA/ORO Division of Import Operations and Policy (HFC-170). Recommendations must be accompanied by a complete regulatory package consisting of all analytical worksheets for original and check analyses (if required—see note below), and other appropriate documentation (e.g., entry paperwork, collection reports, original labels, etc.).

Note: In the case of cosmetic products bearing ingredient labels identifying colors with **ONLY** their European "E" color designation (e.g., E110), color index number (e.g., C.I. 15985), or a trade or common name of the color additive (e.g., Sunset Yellow FCF), FDA laboratory analysis to confirm the presence of the color is not necessary for Detention/DWPE Actions.

PART VI - ATTACHMENTS REFERENCES AND CONTACTS

1. ATTACHMENTS

Attachment A--Ruminant Tissue and Tissue-Derived Ingredients
Attachment B--Questionnaire on Ruminant Tissue and Tissue-Derived Ingredients
Attachment C--May 6, 1996 Letter to Manufacturers and Importers of Cosmetics
Attachment D—Examples of Cosmetic Ingredient Label Declarations for Domestic and International Markets

2. REFERENCES

Online IOM--http://www.fda.gov/ora/inspect_ref/iom/iomtc.html
DFI Inspection Guide--
http://www.fda.gov/ora/inspect_ref/igs/cosmet.html
Compliance Policy Guide--
http://www.fda.gov/ora/compliance_ref/cpg/default.htm
Regulatory Procedures Manual--
http://www.fda.gov/ora/compliance_ref/rpm_new2/

3. CONTACTS

Direct compliance program inquiries to Brenda K. Aloi, Compliance Programs Branch (HFS-636)(301) 436-2065, Fax (301)436-2657.

Direct all regulatory action inquiries and compliance sampling questions to CFSAN's Division of Enforcement. Domestic questions to Lynn Szybist at 301-436-2040 or Jennifer Thomas at 301-436-2094; import questions to Patricia Stephenson, Rosemary Gary, Standra Purnell, or Doriliz Mestey at (301) 436-2413.

Direct questions related to BAM Chapter 23 to: Anthony Hitchins, Ph.D., CFSAN/OPDFB/DMS at 301-436-1649. Direct questions related to chemical analyses to: Helen Jones, ORA/Division of Field Science at 301-827-1233. Direct questions related to microbiological analyses to: Marsha Hayden, ORA/Division of Field Science at 301-827-1039.

Use e-mail to contact CFSAN/OCAC personnel until upcoming office moves and phone number changes are completed.

Direct all policy inquiries except those related to BSE to Lark Lambert CFSAN/OCAC/Division of Cosmetics and Compliance.

Direct questions concerning BSE policy to Stanley R. Milstein, Ph.D., CFSAN/OCAC.

Direct all questions related to color additive methodology to Julie Barrows, CFSAN/OCAC/Color Technology Branch, HFS-125.

Direct all questions from consumers and consumer or trade complaints to Lark A. Lambert, CFSAN/OCAC/Division of Programs and Enforcement Policy.

Direct all questions related to inspectional procedures to Barbara Marcelletti, ORA/Division of Field Investigations (HFC-132), (301) 827-5635.

Direct all questions related to import matters to Denise Jones, ORA/Division of Import Operations (HFC-170), at 301-443-6553.

PART VII - CENTER RESPONSIBILITY

PROGRAM EVALUATIONS

The Director, Office of Plant and Dairy Foods (OPDF) has the responsibility to prepare periodic formal evaluations of this compliance program. When completed and cleared, the evaluation will be available for Agency personnel on CFSAN's OC Intranet site #. Additionally, the evaluation should appear on CFSAN's Internet website.

RUMINANT 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)
Deer Fat
Deer Antler Velvet
Digalactosylceramide
Diglycosylceramides (cytosides)
Disialoganglioside
Dura mater
Elastin (source: oxen neck ligaments)
Eye
Galactocerebroside
Galactosylcerebroside (sulfate ester)
Ganglioside
Glucosylcerebroside
Glycerophospholipid
Glycosaminoglycan
Glycosphingolipid
Glycosylceramide
Hypothalamus
Ileum
Intercellular Lipids (ICL's)
Lactocerebroside
Lactosylceramide
Liposomes
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
Sphingosine phosphatide
Sphinogomyelin
Sphingolipid
Spinal cord
Spleen
Suprarenal gland
Tetraglycosylceramide
Thymus gland (sweet-bread)
Tonsil
Triglycosylceramide
Trinitrophenylaminolauroylglucocerebroside
Trinitrophenylaminolauroylgalactocerebroside
Trisialoganglioside

NOTE: Although the May 9, 1996 letter and this attachment contain a list of tissues to assist investigators in identifying potential ruminant-derived ingredients, the list are not intended to identify all ruminant-derived ingredients about which the Agency has concerns. If any ruminant tissues or tissue derived ingredients are offered for import or being used as an ingredient in cosmetics, if the ingredient is from a BSE affected or at-risk country, refer to Part III of this program for additional instructions.

QUESTIONNAIRE ON RUMINANT TISSUE AND TISSUE-DERIVED INGREDIENTS

PART A--To be Completed in Each Firm Inspected

Inspecting District:	Date of Inspection:
Firm Name and Address	FEI:

Does the firm manufacture or import products containing ruminant tissue or tissue-derived ingredients?
Yes ___ No

If the answer is no, do not complete the remainder of questionnaire. Give firm management a copy of the Agency's 5/6/96 letter (ATTACHMENT C) for future reference and mail or fax the questionnaire to CFSAN as instructed on page 2.

PART B--To be Completed in Firms Using Ruminant-Derived Material

	YES	NO
1. Is the firm aware of the Agency's 5/6/96 letter to cosmetic firms? If the answer is no provide firm management with a copy of the Agency's 5/6/96 letter (Attachment C).		
2. Has the firm put in place procedures to ensure that it does not receive tissues from animals born, raised or slaughtered in any of the countries listed below?		
3. Do procedures include a mechanism to identify all countries where the animals used were born, raised or slaughtered?		
4. Does the firm have a means of identifying the origin of each lot of ruminant-derived material and further identifying products made with these materials?		
5. Does the firm have a means of tracing the disposition of imported products which contain ruminant-derived material?		

Indicate the origin(s) of the ruminant tissue or tissue-derived ingredients used by the firm.

Domestic ___ Import _____

If import origin, list below the country(ies) of origin.

_____ _____

_____ _____

Note: Investigators must refer to I.A. #17-04 or USDA 9 CFR 94.18 for an up-to-date list of BSE-countries. If one of the countries listed is the country of origin, refer to Part III of the compliance program (7329.001) for instructions on documentation for possible regulatory follow-up.

QUESTIONNAIRE ON RUMINANT TISSUE AND TISSUE-DERIVED INGREDIENTS

PART C--To be Completed in Firms Using Ruminant-Derived Material

List in the space below all products manufactured or imported by the firm that contain a ruminant-derived ingredient (see ATTACHMENT A). **ATTACHMENT A is not intended to be an all inclusive list of ruminant-derived ingredients**. If a ruminant-derived ingredient is listed on the finished product label, the label may be submitted to CFSAN as instructed below along with Parts A and B of this questionnaire in lieu of completing Part C.

Product Name (Including Any Brand Name(s) Used)	Specific Ruminant-Derived Material in Product

Send this completed questionnaire along with any product labels collected under Part C to: Brenda Aloi, HFS-636, Rm. 3C007, 5100 Paint Branch Parkway, College Park, MD 20840, Phone (301) 436-2065 or FAX (301) 436-2657.

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

NOTE: The BSE contact for cosmetics related questions has been changed to Dr. Stanley Milstein who can be reached via e-mail at Stanley.Milstein@FDA.HHS.GOV.

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 mucosa
- sciatic nerve
- bone marrow
- liver
- lung
- pancreas
- thymus gland