CHAPTER 29 – COLORS AND COSMETICS TECHNOLOGY

SUBJECT:	**IMPLEMENTATION DATE**
COSMETICS PROGRAM; IMPORT AND DOMESTIC	03/15/2010
	COMPLETION DATE
	Continuing

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

Note: To assist the reader in locating various topics in this document, please see Attachment A "Index".

1. Investigations Branches

a) Consumer adverse events or complaints, and trade complaints should be entered in FACTS. FDA Field Offices should handle cosmetic problems and emergencies on a case by case basis as the severity of the situation requires. However, since FACTS entries must be closed out before they can be downloaded into CFSAN's adverse event database, CAERS, there can be a significant length of time before FDA headquarters or the Office of Cosmetics and Colors might be informed of an unusual event. Therefore, in case of an unusual or high priority situation involving a cosmetic product, please contact the Office of Emergency Operations (OEO) at 301-443-1240 (24 hours) or email emergency.operations@fda.hhs.gov to report these situations (in addition to data entry into FACTS).

b) Within 30 days after completion of each inspection, forward the following items to Denise Beuttenmuller via hard copy at fax# 301-436-2975 or submit electronically to denise.beuttenmuller@fda.hhs.gov:

1) a copy of the "Summary of Findings" for each inspection
2) a copy of the vendor/supplier list collected for each inspection.

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

Do not collect surveillance samples. Collect product samples for color analysis and prohibited ingredients on a compliance basis only. Collect samples of labeling to document potential findings.

Report only COSMETIC import label exams, inspections, sample collections under this program.

2. Domestic

Conduct routine surveillance inspections only at firms manufacturing or repacking eye area cosmetics, skin care preparations and lotions, no-alcohol oral care products, and products intended for use by and on infants and children. 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.

3. Imports

In accordance with 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 bovine-derived tissues imported from BSE affected or at-risk countries.

PART I - BACKGROUND

Cosmetics are defined in section 201(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) as "(1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (2) articles intended for use as a component of any such articles; except that such term shall not include soap." 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 (see the definition of a "drug" in section 201(g)of the FD&C Act). Examples of such products include anti-dandruff shampoos, toothpastes that contain fluoride, deodorants that are also antiperspirants, and moisturizers and makeup marketed with sun-protection claims (including SPF values). Such products must comply with the requirements for both cosmetics and drugs.

The overwhelming majority of the American population – males and females of all ages – applies a variety of cosmetics every day. Over the past 5-10 years there has been an explosion in the numbers and types of cosmetic products sold annually, and a concomitant explosion in the variety of new ingredients. The numbers of products targeting the men's market has increased significantly. Likewise, the numbers of products marketed specifically for use by infants or children has grown dramatically and is still following an upward trend.

The cosmetic industry is rapidly undergoing other significant changes as the technologies underlying these products are becoming increasingly sophisticated, the manufacturing base becoming more global, and the ingredients ever more diverse. For some of these ingredients, there is little information available to substantiate safety. In recent years, FDA has seen an increase in the number and variety of botanical extracts in cosmetic formulations and the use of so-called "active" ingredients. Significantly, there has been a dramatic increase in the number of products marketed as cosmetics that contain "active" ingredients and also have drug claims in their labeling.

Adverse events associated with the use of cosmetic products are not uncommon. There have been several recalls of cosmetic products contaminated with pathogenic microorganisms. Several of the more well-publicized examples include a contaminated non-alcohol mouthwash associated with an outbreak of illness in hospitalized patients and contaminated face paints associated with clusters of cases of severe rashes and lesions in children. Eye-area products contaminated with pathogenic microorganisms, which pose a significant risk of partial or total loss of vision, surface periodically. Microbiological contamination has also been detected in a variety of skin care products.

PART II - IMPLEMENTATION

1. Objectives

To help ensure that import and domestic cosmetics meet regulatory requirements through inspection, sample collection and analysis.

2. Program Management Instructions

Interaction with other compliance programs

Include coverage of this program during inspections conducted under CDER's Drug Process Inspection Compliance Program when it is determined that the firm manufacturers both cosmetics and drugs. Use the appropriate CFSAN and CDER Program Assignment Codes (PACS) when reporting time for these inspections.

Planning Instructions

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).

Select firms for inspection in the following order of priority:

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

b) Manufacturers of high-risk products that have had an OAI or VAI inspection within the previous 3-year period. High-risk products include:

1. eye area cosmetics
2. skin care preparations and lotions
3. cosmetic non-alcohol oral care products
4. wet wipes used by infants or children

c) Refer to your district's cosmetic Official Establishment Inventory (OEI) to select firms that manufacture/repack high-risk products. To aid the districts in selecting firms, CFSAN will provide an inventory of firms that have been determined to be producing high-risk products. Use the firms provided on CFSAN's list to supplement OEI inspections.

d) Any routine surveillance inspection under this Compliance Program should be made only at firms manufacturing or repacking cosmetic products.

Note: CFSAN's OCAC or OC may be contacting selected districts during the year to arrange for OCAC personnel to accompany field investigators during routine inspections conducted under this program. A first-hand knowledge of the firms comprising this industry and the manufacturing practices employed by these firms will be invaluable to OCAC headquarters personnel in development of regulations and guidance regarding cosmetic products.

PART III - INSPECTIONAL

A. General

The instructions in the program apply to ***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 determined to be a drug, it should not be covered under this program.

An Inter-Center Agreement between CDER and CFSAN is in effect, which is intended to assist FDA in implementing the cosmetic and drug provisions of the FD&C 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.

B. Inspections

General guidelines for the areas to be covered during activities conducted under this program can be found in the document entitled "Cosmetic Good Manufacturing Practice Guidelines." Items covered under this program include building and facilities, equipment, personnel, raw materials, production, laboratory controls, records labeling and complaints.

Additional details are provided in the "Guide to Inspections of Cosmetic Product Manufacturers."

Note: Additional background information concerning topics related to cosmetics may also be found on the FDA Cosmetic website.

The following additional items should be covered during inspections of cosmetic manufacturers under this compliance program:

1. Cosmetics Making Drug Claims (DOMESTICS AND IMPORTS)

Labels, packaging and inserts for products making drug claims should be collected and submitted to Kathleen Lewis, Team Leader, Labeling Compliance Team at CFSAN/OC/DE (HFS-608). For general information on the differences between cosmetics and drug products, see "Is It a Cosmetic, a Drug, or Both? (Or Is It Soap?)."

For general information on reviewing product labels for cosmetic products see Cosmetic Labeling: Overview.

2. Prohibited/Restricted Ingredients (DOMESTICS AND IMPORTS)

   By examination of labels for finished products and raw materials, determine whether any of the following ***prohibited*** ingredients are being used by the firm in the production of cosmetic products. Examination of batch records (for domestics) if provided, and other documents (e.g.

product formulations, certificates of analysis), may also provide useful information. If these ingredients do not appear in any of the documents, query the firm directly.

- 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).
- Prohibited cattle material (21 CFR 700.27). See below for additional information.

Similarly, determine whether any of the following ***restricted*** 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. Hexachlorophene may be used as a preservative in cosmetic products other than those which in normal use may be applied to mucous membranes or which are intended to be used on mucous membranes, at a level that is no higher than necessary to achieve the intended preservative function, and in no event higher than 0.1 percent.

   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)
   - fluorocyclobutane C318 (octofluoro-cyclobutane).

Prohibited Cattle Material (Coverage of Bovine Tissue and Tissue-Derived Ingredients for Bovine Spongiform Encephalopathy (BSE))
(DOMESTICS AND IMPORTS)

BSE, commonly known as mad-cow disease, is a fatal disease in cattle similar to Creutzfeldt-Jakob disease, a degenerative neurological disorder in humans. The BSE infectious agent has been found in different bovine tissues which range in their suspected infectivity.

The cosmetic industry has historically been a user of bovine-derived raw materials. While currently available information suggests that exposure of healthy, intact skin to the BSE infectious agent represents an unlikely route of infection, the possibility of infection cannot be completely ruled out. This is especially true if exposure occurs on abraded or damaged skin or from contact with the infectious agent with the eyes or through ingestion. Cosmetics such as lipstick, dentifrices, mouthwash, and breath fresheners, could have an oral route of infection. Cosmetics that have a high likelihood of being applied to cut or abraded skin include shaving creams, gels, and lotions. Products applied to the eye area such as mascara, eye brow pencils, eyeliners, eye lotions, and eye makeup removers as well as other cosmetics that can get into the eye such as shampoo are also possible vehicles for infection.

The agency has determined that certain raw materials from cattle ("bovine-derived" raw materials) are potentially highly infectious, and, if obtained from infected animals, may contain the BSE infectious agent. Cattle materials prohibited from use in cosmetics are listed in 21 CFR 700.27 and include:

- The small intestine of all cattle except as provided in paragraph (b)(2) of 21 CFR 700.27
- material from non-ambulatory disabled cattle
- material from cattle not inspected and passed
- mechanically separated (MS) (Beef)
- "specified risk materials" identified in paragraph (a)(5) of 21 CFR 700.27:
    - brain
    - skull
    - eyes
    - trigeminal ganglia
    - spinal cord
    - vertebral column (excluding the vertebrae of the tail, the transverse processes of the thoracic and lumbar vertebrae, and the wings of the sacrum)
    - dorsal root ganglia of cattle 30 months and older
    - tonsils and distal ileum of the small intestine of all cattle

Refer to 21 CFR 700.27 for more information, particularly for more information on the definition for cattle "inspected and passed" and the process for foreign countries to be designated for exemption from provisions regarding prohibited cattle material. A current listing of countries designated for exemption under paragraph (e) of 21 CFR 700.27 may be obtained from CFSAN OFS (Amber McCoig - 301-436-2131).

BSE Record Keeping Requirements:

In accordance with 21 CFR 700.27(c), manufacturers and processors of a cosmetic that is manufactured from, processed with, or otherwise contains, material from cattle must establish and maintain records sufficient to demonstrate that the cosmetic is not manufactured from, processed with, or does not otherwise contain, prohibited cattle materials.

These records must be retained for 2 years after the date they were created and must be retained at the manufacturing or processing establishment or at a reasonably accessible location. Electronic records are acceptable and are considered to be reasonably accessible if they are accessible from an onsite location.

These records must be available to FDA for inspection and copying.

Product labels and of cosmetic raw materials, bulk cosmetic formulations, and finished cosmetic products and relevant records should be reviewed to determine if any of the products or ingredients contain prohibited cattle material.

If a firm manufacturing or importing cosmetic products or their ingredients uses any prohibited cattle material, document the following:

- The finished products containing the prohibited tissue
- The specific country of origin of the tissue
- The name and address of the importer or other responsible party.

Forward the EIR to CFSAN/OC/DE/Manufacturing and Storage Adulteration Branch (HFS-607) for regulatory consideration:

FDA has also provided recommendations to manufacturers and importers of cosmetics that they have procedures in place to ensure that other bovine tissues are not infected with the agent that causes BSE.

Attachment B "Bovine Tissue and Tissue-Derived Ingredients, Materials with Suspected Risk of Infectivity" contains a list of tissues to assist investigators in identifying tissues and tissue-derived ingredients at high risk for infection with the agent that causes BSE. This list includes the "specified risk materials" specifically identified in 21 CFR 700.27 as well as additional bovine tissues with suspected infectivity. If a firm manufacturing or importing cosmetic products or their ingredients uses a tissue or tissue-derived ingredient listed in Attachment B but not otherwise listed as prohibited cattle material in 21 CFR 700.27, the FDA investigator should determine whether it has been exported from and/or originated from a BSE affected or at-risk country. If so, the investigator should contact CFSAN for further guidance.

A current list of BSE affected or at-risk countries can be found at: USDA's Animal and Plant Health Inspection Service (APHIS) Web site and typing in the search term "countries/regions affected by BSE" for an up-to-date list of countries.

Note: FDA labs do not conduct BSE analysis and thus no sampling guidance is issued for BSE. The basis for any regulatory action on a cosmetic product with respect to prohibited cattle material relies on review of records as described above, labeling and other documents.

3. Adequacy of Preservation (DOMESTICS)

Numerous factors can influence the ability of a product to resist microbial contamination. Proper sanitation practices and adherence to the "Guide to Inspections of Cosmetic Product Manufacturers" are critical. The choice of preservative system is also important, along with other factors. In some instances, such as products dispensed from pressurized containers, there may be no need for added preservatives.

As appropriate, review the manufacturer's records and determine the identity and level of preservatives intended for each formulation. (See Attachment C "Preservation Systems for Cosmetics" for a list of common cosmetic preservatives and other considerations in evaluating a preservative system.) Verify that batch records indicate the addition of these preservatives to each formulation.

The ability of a product to resist microbial contamination is often determined through a microbial challenge test. This test involves inoculating the product with bacteria, molds, and yeast and determining the ability of the formulation to inhibit microbial growth. Ascertain if the manufacturer has conducted a challenge test on its formulations and obtain this documentation. Ensure that the product challenged in this test actually reflects the ingredient composition of the formulation being produced at the facility. Note any inconsistencies between the product being manufactured and the product that was subjected to challenge testing. Since resistance to microbial contamination is especially important in the case of eye area products (especially those that are water-based), skin lotions and no-alcohol mouthwash, collect samples of recently produced and retained products when the manufacturer is unable to produce adequate challenge test documentation or the adequacy of preservation is otherwise in doubt*[see Section III on Import and Domestic sample collection].*

4. Color Additives (DOMESTICS AND IMPORTS)

For an overview, see "Color Additives and Cosmetics."

Color additives are subject to a strict system of approval under U.S. law [FD&C Act, sec. 721; 21 U.S.C. 379e]. Except in the case of coal-tar hair dyes, failure to meet U.S. color additive requirements causes a cosmetic to be adulterated [FD&C Act, sec. 601(e); 21 U.S. Code 361(e)]. Color additives used in cosmetics include both color additives exempt from certification (21 CFR Part 73) and color additives subject to certification (21 CFR Part 74 and Part 82 [Lakes]). Only color additives specifically permitted by regulation may be legally used in cosmetics, and then only in accordance with the provisions of the specific color additive regulation.

For a complete listing and permitted uses of each color additive approved for use in cosmetics, refer to "Color Additives Permitted for Use in Cosmetics."

Click on the "CFR Section Number" on the right-hand side to view the actual regulation, including uses, specifications, and restrictions for each color additive.

Investigators should perform a label review of finished cosmetic products. Ensure that all color additives in the product are permitted for use in that product type and that they are otherwise being used in conformance with the specifications in the listing regulations. 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.

Special Considerations for Color Additives Subject to Certification: (DOMESTICS AND IMPORTS)

Certifiable color additives, sometimes referred to as "synthetic-organic colors" must undergo batch testing by FDA. This process, known as color additive certification, assures the safety, quality, consistency and strength of the color additive prior to its use in cosmetics. Part 74, Subpart C, details color additives subject to batch certification. When FDA certifies a batch of bulk color additive, the color additive manufacturer is assigned a unique, six-digit lot number, beginning with two alpha characters followed by four number characters (e.g. XX1234). Finished-product manufacturers must ensure they purchase certified color additives labeled with the batch certification lot number from color additive manufacturers.

Investigators may encounter certified color additives as raw material or as an ingredient listed on a product label. Each color additive included in a cosmetic product must be identified on the product declaration of ingredients (using either it's listed or abbreviated name e.g., Ext. D&C Yellow No. 7 or Ext. Yellow 7). Laboratory analysis of a cosmetic cannot be used to determine whether a lot of color additive used was certified, therefore, investigators should ask manufacturers to provide FDA Certification Lot Number(s) for color additives used in cosmetic products. Check the authenticity of each lot number by accessing FDA's Color Certification database and keying in the six digit code.

The information returned from the site includes:

- the name of the certified color additive
- the batch certification number of the original color additive that was manufactured
- the name of the company associated with the certified color additive
- the certification date

(Note: First time database users will be directed to click on the "Request Access" box for verification; permission is granted via email.)

In the case of color additive mixtures, the label should declare a control number that can be traced to the FDA certification lot number of the color additives present in the mixture.

5. Cosmetic Product Labeling Requirements– Ingredients (DOMESTIC AND IMPORTS)

Examine the declaration of ingredients on all cosmetic products intended for sale to consumers to determine compliance with 21 CFR 701.3. Note that products that are used *only* in salons and not sold to consumers (usually labeled "For Professional Use Only") or free samples where another purchase is not required to receive the free sample, are not required to bear an

ingredient declaration under the FPLA (Section 1459). If however, these products are customarily sold to consumers for their personal use, they are not exempt from ingredient labeling requirements and must bear an ingredient statement.

As the cosmetic marketplace has become more global, certain situations now arise with greater frequency and should receive special attention:

Use of a language other than English – All words, statements, and other information required by or under authority of the FD&C Act to appear on the label or labeling shall appear in the English language (except in the case of products distributed solely in Puerto Rico or in a U.S. Territory where the predominant language is other than English). If the label or labeling also contains any representation in a foreign language, then all words, statements, and representations must be made in that language.

"Dual declaration" of certain ingredients – In the mid-1990's correspondence between the Office of Cosmetics and Colors (OCAC)and the Cosmetic, Toiletry and Fragrance Association (CTFA) addressed several issues related to international harmonization of cosmetic labeling requirements and the use of "dual declaration" for certain types of cosmetic ingredients. These letters may be viewed online under Cosmetic Ingredient Nomenclature: Industry Requests & FDA Responses.

For color additives, FDA does not object to C.I. numbers being used in a dual declaration with the official FDA-sanctioned name, provided all of the requirements of the relevant color additive regulations have been met and the FDA-sanctioned name is listed first. An acceptable dual declaration will list the FDA-sanctioned name first followed by the C.I. number in parentheses.

Example: FD&C Blue No. 1 (C.I. 42090)

The Agency also does not object to a similar type of dual declaration for botanical ingredients where both the Linnaean taxonomic (genus/species) name and English "common or usual name" are listed, ***provided*** that the English "common or usual name" is listed first.

Example: Dandelion Leaf Extract (Taraxacum officinale Leaf Extract)

If there is no English "common or usual name" for a botanical ingredient, FDA does not object to the Linnaean name being used alone, per 21 CFR 701.3(c)(4).

Investigators should refer to Attachment D "Examples of Hypothetical Cosmetic Ingredient Label Declarations for Domestic and International Markets" 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.

6. Cosmetic Product Labeling Requirements– Warning Statements(DOMESTIC AND IMPORTS)

a) 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."

b) Required warning statement for "feminine deodorant spray" (any spray deodorant product whose labeling represents or suggest that the product is for use in the female genital area or for use all over the body):

"Caution – For external use only. Spray at least 8 inches from skin. Do not apply to broken, irritated or itching skin. Persistent, unusual odor or discharge may indicate conditions for which a physician should be consulted. Discontinue use immediately if rash, irritation, or discomfort develops."

Use of the word "hygiene" or "hygienic" or a similar word or words renders any such product misbranded under section 602(a) of the FD&C Act. The use of any word or words which represent or suggest that such products have a medical usefulness renders the products misbranded under section 502(a) of the Act and renders them illegal new drugs marketed in violation of section 505 of the Act.

c) 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."

d) Required warning statement for sun tanning 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."

e) Cautionary statement and adequate directions for use needed for the exception from adulteration on coal-tar hair dyes (i.e., hair dye color additives derived from coal tar or petroleum) as provided under section 601(a) of the FD&C Act. The labeling should also include adequate directions for such preliminary testing and use of the product. Note: these dyes cannot be used for dyeing the eyebrows or eyelashes.

''Caution—This product contains ingredients which may cause skin irritation on certain individuals and a preliminary test according to accompanying directions should first be made. This product must not be used for dyeing the eyelashes or eyebrows; to do so may cause blindness,''

7. Directions for Safe Use (DOMESTICS AND IMPORTS)

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 in "Guide to Inspections of Cosmetic Product Manufacturers."

The firms' labeling of the products below warrants close attention during cosmetic inspections. Adequate instructions for use must be provided, including, but not limited to, any necessary time limits on application, instructions for washing off, or patch tests on small areas of the body, as appropriate. Questions about the adequacy of use instructions should be referred to CFSAN's Office of Cosmetics and Colors at 301-436-1130.

- Depilatories and hair straighteners;
- Permanent wave neutralizers;
- Nail builders, hardeners, and enamels;
- Artificial or sculptured fingernail glue; and
- Coal tar hair dyes (Under section 601 (a) the label *must* bear instructions for preliminary patch testing for possible skin irritation)

8. Cosmetic Product Packaging Requirements (DOMESTIC AND IMPORTS)

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).

9. Field Exam and/or Document Review (IMPORTS)

Note: Districts must refer to the FDA Import Alert Retrieval System (FIARS) for an up-to-date index of applicable import alerts and bulletins.

ORA includes resources for conducting label examinations of import entries under this program. Each label examination must:

- Cover cosmetics only. (See Part I "Background," and Part III "Inspectional", Section 1. "General" in this Cosmetic Program Guidance Manual, for instructions in determining whether a product is a cosmetic, a drug, or drug as well as cosmetic. A listing of cosmetic product categories can be found at 21 CFR 720.4(c));
- Include a review to ensure the product complies 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 Part III, "Inspections";
- Include a review of cosmetic labels with added "ingredient stickers" signifying possible re-labeling of a brand name (so called "gray market cosmetics" produced for markets outside of the U.S.) Cosmetics formulated for use in other

countries may contain color additives not permitted in the U.S.

- Color additive violations are a common reason for detaining imported cosmetic products offered for entry into this country.

Include coverage of imported cosmetics containing color additives. See IA#53-06 "Detention Without Physical Examination of Cosmetics Containing Illegal Colors."

When performing a field exam, please review Part III, Section 4, "Color Additives" for instructions in determining whether a product may contain non-certified or non-permitted color additives.

In addition, if the label of an imported cosmetics identifies color additives with their European name or ("E") color designation with a corresponding number (e.g., E104, E122, E123, and E124), a color index number (e.g., C.I. 15985) or the trade name of the color additive (e.g., Sunset Yellow FCF) alone without the U.S. approved designation, this suggests that the color additive used may not be certified or permitted. In these situations, districts should consider detaining without sampling based on the appearance of adulteration (i.e., the product appears to contain an uncertified color additive). These situations can be processed in OASIS using a violative label exam (Work Type LEX).

If the imported product appears to contain undeclared color additives, the entry should be processed for detention.

To confirm that a product contains certified color additives, request that the filer/importer provide a valid FDA certified Lot number for the color additive(s) used. Using the Color Additive Certification Database "Color Additives Permitted for Use in Cosmetics." confirm that the lot number provided can be validated. Then, the product can be released, provided the label declares the color additive(s) by the certified name, such as FD&C Yellow No. 6 or Yellow 6. If the product contains certified color additive(s), and the certified color additive(s) is not correctly declared on the label, process the entry for detention. If the firm intends to relabel, they must submit an FDA-766 Application to Relabel.

- Include a review for prohibited cattle material. Please review Part III, Section 2 "Coverage of Bovine Tissue and Tissue-Derived Ingredients for Bovine Spongiform Encephalopathy (BSE" for additional information.

OASIS screening criteria allow 100% entry review for any import entry of finished cosmetic products that may contain bovine tissue or tissue-derived ingredients. These include all products with industry code 53R[][][].

Product labels and entry documentation of finished cosmetics should be reviewed to determine if the products contain any of the prohibited cattle

material listed in 21 CFR 700.27. See above discussion under "Special Considerations Regarding Prohibited Cattle Material" for more information.

If a cosmetic product contains or is suspected to contain prohibited cattle material, it should be detained and the importer of record requested to provide, within 5 days, records sufficient to demonstrate that the cosmetic is not manufactured from, processed with, or does not otherwise contain, prohibited cattle material. Examples of documents that may be useful to the reviewer in making a determination include, but are not limited to:

- a relevant USDA/APHIS veterinary certificate
- a country of origin certificate
- relevant manufacturing records

In addition, bulk shipments of bovine tissue and tissue-derived ingredients are flagged for review under Import Alert 17-04 "Detention without Physical Examination of Bulk Shipments of High Risk Bovine Tissue from BSE Countries." Bulk shipments of bovine material intended for use in cosmetic products are product coded as 53P[][]01 and 53P[][]02. The specific bovine tissues and tissue derived ingredients of concern are listed in IA 17-04.

If a bulk shipment of a bovine tissue or tissue-derived cosmetic ingredient is detained under Import Alert 17-04 "Detention Without Physical Examination of Bulk Shipments of High Risk Bovine Tissue From BSE Countries" the reviewer should request the importer or manufacturer provide documentation that establishes the bovine tissue or tissue-derived ingredient is from BSE-free cattle or from a non-BSE affected country. See Import Alert 17-04 for more information.

Attachment B Bovines Tissue and Tissue-Derived Ingredients, Materials with Suspected Risk of Infectivity" contains a list of tissues to further assist investigators in identifying tissues and tissue-derived ingredients at high risk for infection with the agent that causes BSE. This list includes the "specified risk materials" specifically identified in 21 CFR 700.27 as well as additional bovine tissues with suspected infectivity. If a firm manufacturing or importing cosmetic products or their ingredients uses a tissue or tissue-derived ingredient listed in Attachment B but not otherwise listed as prohibited cattle material in 21 CFR 700.27, the FDA investigator should determine whether it has been exported from and/or originated from a BSE affected or at-risk country. If so, the investigator should contact CFSAN for further guidance.

A current list of BSE affected or at-risk countries can be found at: USDA's Animal and Plant Health Inspection Service (APHIS) Web site and then typing in the search term "countries/regions affected by BSE" for an up-to-date list of countries.

10. Alpha Hydroxy Acids (AHAs) "Sunburn Alert" AHA Labeling Statement (DOMESTICS AND IMPORTS)

Because of the potential for increased sensitivity to the sun, FDA encourages manufacturers to use the following guidance labeling statement for topically applied cosmetic products containing AHAs (e.g., glycolic acid, lactic acid) as ingredients -

Sunburn Alert: This product contains an alpha hydroxy acid (AHA) that may increase your skin's sensitivity to the sun and particularly the possibility

of sunburn. Use a sunscreen, wear protective clothing, and limit sun exposure while using this product and for a week afterwards.

Investigators are requested to notify firms manufacturing cosmetics containing AHAs of "Guidance for Industry: Labeling for Topically Applied Cosmetic Products Containing Alpha Hydroxy Acids as Ingredients."

11. Consumer and Trade Complaints (DOMESTICS)

The District Offices should use their own discretion concerning immediate follow-up on more serious or unusual consumer adverse reactions for cosmetic products, e.g., multiple or serious complaints for the same product. Prior to conducting follow-up on a cosmetic adverse event, including sampling, the district may wish to contact Lark Lambert (Lark.Lambert@FDA.HHS.GOV)at 301-436-1143, Office of Cosmetics and Colors (OCAC), Cosmetics Staff(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 staff can advise the investigating district of appropriate follow-up. As stated on page 1 of this document, for serious incidences, Emergency Operations (301-443-1240) should also be notified.

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.

12. Close-out of Domestic Inspection (DOMESTICS):

a) Voluntary Registration (DOMESTICS)

At the conclusion of each inspection, determine whether the firm has registered its manufacturing establishment (21 CFR 710) and/or its cosmetic product formulations (21 CFR 720) under the Voluntary Cosmetic Registration Program (VCRP).
. If not, encourage participation in these voluntary programs.

b) Small Business Assistance (DOMESTICS)

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).

c) Fact Sheet for Cosmetic Manufacturers, Packers and Distributors

During an inspection, questions frequently arise as to products regulated by FDA and questions concerning cosmetics, such as labeling, BSE, color additives, voluntary registration, importing and exporting products and small business assistance. A fact sheet has been designed to answer some of these questions and provide the firm with helpful FDA links. At the closeout of each inspection, disseminate Attachment D "Food and Drug Administration, Office of Cosmetics and Colors Fact Sheet

for Cosmetic Manufacturers, Packers and Distributors" to firm management.

C. Sample Collections

For cosmetic color additive samples consult Chapter 4 of the current edition of the IOM (Chart 9), "Sample Schedule for Color Containing Product, Color Additive".

Note: Bulk color additives that are used as cosmetic ingredients should be collected under Industry Code 50. For straight colors, collect 28 gm (1 oz.) of powder. For color mixtures, collect 100 gm (4oz.) of liquid, paste or powder. If the color mixture contains over 50% pure dye, collect 55 gm (2oz.).

Color additive samples of finished cosmetics should be collected under Industry Code 53. If the product is strongly colored (e.g., lipsticks, hair coloring, products, eye mascara, eye liner, make-up, pencils of all types) collect four retail packages of the same lot code for each shade (color) in the product line. If the product is lightly colored (e.g., creams, lotions, shampoos, bath products, shaving preparations and perfumes), collect a sufficient number of retail packages to equal 1 lb (dry) or 1 pt (liquid) of sample. Always collect a minimum of two retail units of each product.

For bulk cosmetic products, collect samples for color additive analysis in the following quantities:

- dry 454 gm (1 lb.);
- Liquids – Minimum of 36 fl. Oz.

DOMESTICS:

Collect, for microbiological analysis, samples of eye area cosmetics or skin care preparations and lotions that are not in self-pressurized containers, where adequate challenge test documentation cannot be produced or the adequacy of preservation is otherwise in doubt. 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 GMP Guidelines.

If uncertain whether to collect a sample, contact the appropriate CFSAN regulatory contact listed in Part VI of this program for additional instructions.

IMPORTS:

All import samples collected under this program must be compliance sample when product packaging and labeling indicates that a violation of the FD&C Act may exist.

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

DOMESTIC AND IMPORTS:

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)
Skin Lotion – 680 gm (24 oz)
Shampoos and conditioners – 680 gm (24 oz)

Microbiological analysis and filth examination— Collect in duplicate

Collect at least **ten (10)** individual retail units [20 units if less than 14 gm (½ oz) each]
OR
one (1) 100 gm (4 oz) subsample from each of ten containers of bulk material.

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

SAMPLE SHIPMENT

Submit samples to your district's analytical 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 the Servicing Laboratories section 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.

A. ANALYZING LABORATORIES

1. Field

a) Microbiological

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

NOTE: Identification of mold isolates will be done by CFSAN/ORS/Division of Microbiology (HFS-712).

b) Color Additives

FACTS automatically assigns a servicing laboratory through the automatic National Sample Distributor (NSD) system when a sample collection report (C/R) is prepared. If a specific laboratory has been indicated in a sampling assignment then the NSD can be overridden during the C/R preparation process.

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 (contact Julie Barrows, 301-436-1119).

c) Label Review

All servicing analytical laboratories will conduct review of the labeling (21 CFR Parts 700 and 701) for declaration of ingredients (21 CFR 701.3), and warning statements (21 CFR 740), and directions for use as necessary (see Part III 2. f. of this guidance document). For comprehensive material on cosmetic labeling requirements that should be used in conducting label review, refer to the resources listed at Cosmetic Labeling and Label Claims.

2. Center

The following may be performed by CFSAN. Investigations branches should e-mail the Center contact listed below before shipping any samples to the Center for analyses.

a) Species Identification

CFSAN/ORS/Division of Microbiology (HFS-712) will identify submitted mold isolates. Servicing laboratories must use the instructions below under B.1. for preparing isolates for shipment to HFS-712. Contact Valerie Tournas at 301-436-1963 or via e-mail at valerie.tournas@fda.hhs.gov prior to shipping isolates.

b) Chemical Analysis

CFSAN/ORS(HFS-700) will provide support for analysis of cosmetic products for prohibited or other potentially harmful ingredients or contaminants. Contact Jeanne Rader at CFSAN/ORS/DBC (HFS-715) at 301-436-1786 or via e-mail at jeanne.rader@fda.hhs.gov prior to shipping samples.

c) Confirmation of Color Additives

The Division Color Certification and Technology, Color Technology Team (HFS-106) will provide color additive support for samples of cosmetic products not amenable to the typical analytical methods. Contact Dr. Julie Barrows via e-mail at Julie.Barrows@FDA.HHS.GOV (301-436-1119) for information prior to shipping samples.

d) Determination of Toxicity

The Office of Cosmetics and Colors, Cosmetics Staff (HFS-125) will provide support for evaluating topical toxicity or the potential for systemic toxicity as requested. Contact Dr. Robert Bronaugh (301-436-1124)or Donald Havery (301-436-1257) for sampling instructions on potentially toxic cosmetic samples.

e) Label Review

CFSAN/OC/Division of Enforcement (HFS-608) will provide assistance for determining violations of cosmetic labeling requirements. Contact Kathleen Lewis, Team Leader, Labeling Compliance Team (HFS-608) at via email at Kathleen.lewis@fda.hhs.gov Tel. No. 301-436-2148 with questions relating to cosmetic labeling.

B. ANALYSIS

a) Microbiological

All method references to the e-BAM refer to the current edition of the Bacteriological Analytical Manual.

Refer to the e-BAM, Chapter 23 for methods to determine microbial contamination of cosmetics.

All Gram-positive and Gram-negative microbial isolates from aerobic count plates or enrichments are to be identified to genus and species level using e-BAM, chapter 23 methods and commercial identification systems such as Vitek.

Prepare mold/yeast 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, Official Methods of Analysis, 15th through 18th editions, Chapter 46, or most current edition.. 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 resources provided at Cosmetic Labeling and Label Claims.

Suspected labeling violations should be forwarded to Kathleen Lewis, Team Leader of the Labeling Compliance Team at CFSAN/OC/Division of Enforcement (HFS-608).

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 "FDL" for label reviews and identify specific violation(s) found.

PART V - REGULATORY/ADMINISTRATIVE STRATEGY

1. Situations Warranting CFSAN Contact

Contact CFSAN, Office of Compliance (OC), Division of Enforcement (DE), (HFS-608), at (301)436-2148 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), The Cosmetics Staff (HFS-125)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 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) (#)

d) If there are questions regarding the adequacy of the preservation system of the product.

If a cosmetic appears to be making drug claims:

An Inter-Center Agreement between CDER and CFSAN is in effect, which is intended to assist FDA in implementing the cosmetic and drug provisions of the FD&C 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.

Districts may submit recommendations for enforcement action to CFSAN, and CFSAN will coordinate the action with CDER.

e) Contact CFSAN/OC/DE/ (HFS-608) at 301-436-2148 if necessary for assistance when an import shipment is detained in accordance with I.A. #17-04 for bulk shipments of high-risk bovine tissues and tissue-derived ingredients.

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). The specimen charge is stated in the CPG.

SPECIMEN CHARGE:

The article (was adulterated while introduced into and while in interstate commerce) or (is adulterated while held for sale after shipment in interstate commerce) within the meaning of the Act, 21 U.S.C. 361(a) in that it contains a poisonous or deleterious substance , ***Pseudomonas aeruginosa,*** which may render it injurious to users under such conditions of use as are customary or usual.

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. Seizure with Center Review

All other cases must be submitted to the Center for Food Safety an Applied Nutrition (CFSAN) through the electronic MARCS-CMS system. MARCS-CMS is a collection of modules supporting Agency compliance management and work flow for compliance-related activities. MARCS-CMS provides the mechanism to electronically send this information to the appropriate organizational unit based on individual organizations' business practices. It also provides the means to associate all evidence needed to support the Compliance Action. This evidence may contain enforcement, precedent scientific, or interpretive information relating to the Compliance Action.

Users can access the system by navigating through INSIDE.FDA.GOV. From this screen select MARCS-CMS link. A user's Guide is available within the application under the User's Guide link located at the top of the MARCS-CMS Main Screen.

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 MARCS-CMS system. CFSAN will review to determine Center support for the recommended action. Districts should submit legible digital copies of the labels via the intranet site as well to Kathleen Lewis, Team Leader, Labeling Compliance Team (HFS-608).

a) Prohibited/ Restricted Ingredients. Determine whether prohibited or restricted ingredients (21 CFR 2.125, 21 CFR 250.250 and part 700) are being used. (Confirm status of ingredients at all 3 "bullets" below)

- 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 Color Additives Permitted for Use in Cosmetics for more information.

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 in Chapter 4 of the Regulatory Procedures Manual, 2009.

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), the appropriate charge would be a 601(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 charged as follows:

- This article is misbranded within the meaning of section 602(a) of the F, D & C Act in that it appears that it's labeling is false or misleading in any particular. (IMPORTS only)
- This article is misbranded within the meaning of section 1454(c)(3)(B) of the Fair Packaging and Labeling Act in that it appears that the label fails to bear an ingredient declaration in accordance with 21 CFR 701.3 (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].

- Sun-tanning 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, prevents 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) Insanitary conditions. Enforcement action may be warranted if the inspection finds there to be gross deviations from the "Guide to Inspections of Cosmetic Product Manufacturers", such that the product may become contaminated with filth or may be rendered injurious to health (Section 601(c) of the Act).

6. Imports

Refer to the Regulatory Procedures Manual (RPM) Chapter 9 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) through the Case Management System (CMS). 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--Index
Attachment B— Bovine Tissue and Tissue-Derived Materials with Suspected Risk of Infectivity
Attachment C— Preservation Systems for Cosmetics
Attachment D- Examples of Hypothetical Cosmetic Ingredient Label Declarations for Domestic and International Markets
Attachment E- FDA OCAC Fact Sheet for Cosmetic Manufacturers, Packers, and Distributors

2) REFERENCES

Online IOM—
http://www.fda.gov/ICECI/Inspections/IOM/default.htm
DFI Inspection Guide--
http://www.fda.gov/ICECI/Inspections/InspectionGuides/ucm074952.htm
Compliance Policy Guide--
http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm119194.htm
Regulatory Procedures Manual--
http://www.fda.gov/ICECI/ComplianceManuals/RegulatoryProceduresManual/default.htm

3) CONTACTS

Compliance Program Inquiries:
Melinda E. Chen, Field Programs Branch (HFS-615)(301) 436-1471, Fax (301)436-2657.

Regulatory Action Inquiries (both domestic and import):
Kathleen Lewis at 301-436-2148 or Felicia Binion Williams at 301-436-2566

Consumers Question, Complaints or Adverse Events:
CFSAN/OCAC: Denise Beuttenmuller at 301-436-1344 or Main Office Number 301-436-1130.

Inspectional procedures Inquiries :
Norman Fogg, ORA/Division of Field Investigations (HFC-132), (301) 827-5645.

Import Inquiries:
John Verbeten, ORA/Division of Import Operations and Policy (HFC-170), at 301-796-3698

4) ANALYTICAL CONTACTS:

BAM Chapter 23 Inquiries:
Anthony Hitchins, Ph.D., CFSAN/OCD/ORS/ at 301-436-1649.

Chemical Analyses Inquiries:
Ann Westerman, ORA/Division of Field Science at 301-827-1482.

Microbiological Analyses Inquiries:
Ann Westerman, ORA/Division of Field Science at 301-827-1482.

Color Additive Methodology Inquiries:
Julie Barrows,Ph.D. CFSAN/OCAC/Color Technology Team (HFS-106) at 301-1119

Mold Species Identification Inquiries:
Valerie Tournas, CFSAN/ORS/DM/MMSB at 301-436-1963

PART VII - CENTER RESPONSIBILITY

Program Evaluation

During the course of this program, the Office of Cosmetics and Colors will monitor and evaluate the progress and results of the field operations conducted under this program.

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Sun-tanning products (not sunscreens) – V
Toxicity determination – IV
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Voluntary Cosmetic Registration Program (VCRP) – III
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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)
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: If any bovine 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.

Preservation Systems for Cosmetics

Preservative Compounds Commonly Used in Cosmetics:

1. Parabens (methyl, ethyl, propyl, and butyl)
2. Quaternium 15 (aka "Dowicil")
3. Diazolidinyl urea
4. Imidazolidinyl urea
5. DMDM Hydantoin
6. 2-bromo-2-nitropropane-1,3-diol (aka "Bronopol")
7. Sodium hydroxyglycinate
8. Phenoxyethanol
9. Sorbic acid / Potassium sorbate
10. Methylisothiazolinone (aka "MI")
11. Methylchloroisothiazoline (aka "CMI" often in combination with MI as Kathon CG)
12. Sodium benzoate
13. Caprylyl glycol
14. Sodium dehydroacetate
15. Formaldehyde

Other Important Factors in Evaluating a Preservation System:

1. Appropriate packaging - Is product packaging and closure consistent with the preservative system of the product? For example, a product dispensed with a pump, a container with a flip cap, or a single use container would require a much less vigorous preservative system than a product in a wide mouth jar or mascara that the consumer can contaminate with every use.
3. Water activity - Products such as powders with little or no water do not require as strong a preservative system as aqueous emulsions.
4. pH control - Microorganisms grow best between pH 6.5 to 7.5. Products with pH in this range require more microbial control than products outside this range.

Often described as "self-preserving":

Ethanol – when present at >15%
Butylene glycol – when present at >10%
Propylene glycol – when present at >20%

Other Substances Used as Preservatives in Cosmetics:

MDM Hydantoin
Sodium hydroxymethylglycinate
Benzisothiazolinone
Phenoxyethanol
Benzyl Alcohol
Dehydroacetic acid
Benzoic acid
Salicylic Acid
Iodopropynyl Butylcarbamate
Chloroxylenol
Methyldibromo Glutaronitrile
Chlorphenesin
Triclosan
Benzalkonium Chloride
Chlorhexidine
Polyaminopropyl Biguanide
5-Bromo-5-Nitro-1,3-Dioxane (Bronidox)
Hexamidine Diisethionate
Pentylene Glycol
1,2-Hexanediol
1,2-Octanediol
Ethylhexylglycerin
Triclocarban
Glyceryl Caprylate
o-Cymen-5-ol
Chlorphenesin
Glyceryl Monolaurate

Examples of Hypothetical Cosmetic Ingredient Label Declarations For Domestic and International Markets

Examples of hypothetical cosmetic ingredient label declarations are provided, as they might appear under current regulations codified at 21 CFR 701.3 and in conjunction with correspondence between OCAC and the Personal Care Products Council (PCP; formerly the CTFA) on international harmonization of ingredient nomenclature.

a) **Cocoa Butter and Coconut Oil Lotion for Extra Dry Skin**

Caveat: It has been proposed (and we currently allow) that FDA listed color additives be permitted to be declared in cosmetic ingredient labels by abbreviated names (c.f., 61 FR 8372 @ 8417, March 4, 1996)

Current Cosmetic Ingredient Label Declaration:

INGREDIENTS: Water, Cocoa Butter, Coconut Oil, Glyceryl Stearate, Mineral Oil, Propylene Glycol, Glycerin, Petrolatum, Cetyl Alcohol, PEG-8 Stearate, Tocopheryl Acetate, Methylparaben, Propylparaben, FD&C Yellow No. 5, D&C Orange No. 4.

Proposed Interim Harmonization Cosmetic Ingredient Label Declaration:

INGREDIENTS: Water (Aqua), Cocoa (Theobroma cacao) Butter, Coconut (Cocos nucifera) Oil, Glyceryl Stearate, Mineral Oil (Paraffinum liquidum), Propylene Glycol, Glycerin, Petrolatum, Cetyl Alcohol, PEG-8 Stearate, Tocopheryl Acetate, Stapyrium Chloride, Methylparaben, Propylparaben, Yellow 5 (CI 19140), Orange 4 (CI 15510).

b) **Moisturizing Herbal Shampoo**

Caveat: Certain botanical (plant) ingredients may have Linne System (Latin genus/species) names that have no English language 'common or usual name' equivalents (e.g., "Sambucus nigra Extract"). Semi-synthetic derivatives of botanical (plant) ingredients are not subject to the Interim Harmonization Proposals (e.g., "PEG-40 Hydrogenated Castor Oil").

Current Cosmetic Ingredient Label Declaration:

INGREDIENTS: Water, Sodium Laureth-7 Sulfate, Lauramide DEA, Cocamidopropyl Betaine, Disodium Laureth Sulfosuccinate, Fragrance, Panthenol, Quaternium-75, Sambucus Nigra Extract, Yarrow Extract, Comfrey Extract, Boysenberry Extract, Sweet Grass Extract, Sweet Cherry Pit Oil, Butylene Glycol, PEG-40 Hydrogenated Castor Oil, Benzophenone-4, Disodium EDTA, Citric Acid, Sodium Chloride, Methylchloroisothiazolinone, Methylisothiazolinone, Ext. D&C Violet No. 2.

Proposed Interim Harmonization Cosmetic Ingredient Label Declaration:

INGREDIENTS: Water (Aqua), Sodium Laureth-7 Sulfate, Lauramide DEA, Cocamidopropyl Betaine, Disodium Laureth Sulfosuccinate, Fragrance (Parfum),

Panthenol, Quaternium-75, Sambucus Nigra Extract, Yarrow (Achillea millefolium) Extract, Comfrey (Symphytum officinale) Extract, Boysenberry (Rubus deliciosus) Extract, Sweet Grass (Hierochloe odorata) Extract, Sweet Cherry (Prunus avium) Pit Oil, Butylene Glycol, PEG-40 Hydrogenated Castor Oil, Benzophenone-4, Disodium EDTA, Citric Acid, Sodium Chloride, Methylchloroisothiazolinone, Methylisothiazolinone, Ext. Violet 2 (CI 60730).

Abbreviated names for color additives (e.g., Ext. D&C Violet No. 2 can be stated as Violet 2, and the lake of FD&C Yellow No. 5 can be stated as Yellow 5 Lake) specified in the 1996 Federal Register proposed rule Permanent Listing of Color Additive Lakes (March 4, 1996, 61 FR 8372, at page 8417).

Food and Drug Administration, Office of Cosmetic and Colors
FACT SHEET FOR COSMETIC MANUFACTURERS, PACKERS AND DISTRIBUTORS

This fact sheet provides answers to some frequently asked questions and lists some useful Web resources.

For more information, please visit FDA's homepage at www.fda.gov. You can access Cosmetics from the list in the upper right-hand corner, or go directly to the Cosmetics home page (http://www.fda.gov/Cosmetics/default.htm). You can access Color Additives resources by going to the A-Z Subject Index, selecting "C," and scrolling down to Color Additives, or going directly to the Color Additives page (http://www.fda.gov/ForIndustry/ColorAdditives/default.htm).

Are cosmetics regulated by FDA?

Yes. For information on FDA's regulation of cosmetics, see
"FDA Authority Over Cosmetics"
http://www.fda.gov/Cosmetics/GuidanceComplianceRegulatoryInformation/ucm074162.htm

"Inspection of Cosmetics"
http://www.fda.gov/Cosmetics/GuidanceComplianceRegulatoryInformation/ComplianceEnforcement/ucm136455.htm

When is a cosmetic considered a drug?

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 (see the definition of a "drug" in section 201(g)of the FD&C Act). Some products can be both a drug and cosmetic, in which case, the product must comply with both the drug and cosmetic regulations. Typical examples of drug/cosmetic claims are: antiperspirant/deodorant products; sunscreen/suntan products; fluoridated toothpaste/toothpastes; antidandruff shampoos/cleansing beautifying shampoos; an SPF claim on a moisturizer or other cosmetics.

For more information, see "Is It a Cosmetic, a Drug, or Both? (or Is It Soap?)"
http://www.fda.gov/Cosmetics/GuidanceComplianceRegulatoryInformation/ucm074201.htm

For information regarding drug registration and listing, see "Drug Registration and Listing System:
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/DrugRegistrationandListing/default.htm.

Where can I find information related to cosmetics?

See FDA's Cosmetics home page: http://www.fda.gov/Cosmetics/default.htm

For a quick-reference list of resources often requested by industry, see Cosmetic Manufacturers, Packagers, and Distributors:
http://www.fda.gov/Cosmetics/ResourcesForYou/CosmeticsManufacturersPackagersDistributors/default.htm

Where can I find safety and regulatory information on Bovine Spongiform Encephalopathy (BSE)?

Resources are listed under Bovine Spongiform Encephalopathy (BSE)
http://www.fda.gov/Cosmetics/ProductandIngredientSafety/PotentialContaminants/ucm136786.htm.

Where can I find guidance documents?

See the resources listed at
http://www.fda.gov/Cosmetics/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/default.htm

Where can I find information related to color additives used in cosmetics?
Information on FDA's regulation of color additives for use in all FDA-products is listed at "Color Additives": http://www.fda.gov/ForIndustry/ColorAdditives/default.htm.

For information specifically on color additives for use in cosmetics, see "Color Additives in Cosmetics" http://www.fda.gov/ForIndustry/ColorAdditives/ColorAdditivesinSpecificProducts/InCosmetics/default.htm.

For a quick-reference list with links to the regulations, see "Color Additives Permitted for Use in Cosmetics"
http://www.fda.gov/Cosmetics/GuidanceComplianceRegulatoryInformation/VoluntaryCosmeticsRegistrationProgramVCRP/OnlineRegistration/ucm109084.htm.

What is the Voluntary Cosmetic Regulation (VCRP) Database?

The Voluntary Cosmetic Registration Program (VCRP) is an FDA post-market reporting system for use by manufacturers, packers, and distributors of cosmetic products that are in commercial distribution in the United States. There are two parts to the VCRP, one for registering establishments and another for filing formulations. You may participate in both parts of the program or only one part. No fees are required to participate in this voluntary program.

The VCRP does not apply to cosmetic products for professional use only, such as products used in beauty salons, spas, or skin care clinics. It also does not apply to hotel samples or free gifts or cosmetic products you make in your home to sell to your friends.

To learn more and participate in the VCRP, see "Voluntary Cosmetic Registration Program (VCRP)" http://www.fda.gov/Cosmetics/GuidanceComplianceRegulatoryInformation/VoluntaryCosmeticsRegistrationProgramVCRP/default.htm

Where can I find information on importing and exporting cosmetics?

Importing:

For an overview, see "Cosmetic Imports"
http://www.fda.gov/Cosmetics/InternationalActivities/ImportsExports/CosmeticImports/default.htm
Additional resources listed at this page include "Federal Agencies Issue Draft Guidance for Industry Good Importer Practices" http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm109063.htm and Import Surveillance
http://www.fda.gov/Cosmetics/InternationalActivities/ImportsExports/CosmeticImports/ImportSurveillance/default.htm, for links to Import Alerts and recent Import Refusals related to cosmetics.

Exporting:

For answers to regulatory questions and information about export certificates, see "Cosmetic Exports" http://www.fda.gov/Cosmetics/InternationalActivities/ImportsExports/CosmeticExports/default.htm

Does FDA offer assistance to small businesses?

Yes. For information, visit “Small Business Assistance”
http://www.fda.gov/ForIndustry/SmallBusinessAssistance/default.htm