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Use of Materials Derived From Cattle in Human Food and Cosmetics; and Recordkeeping Requirements for Human Food and Cosmetics Manufactured From, Processed With, or Otherwise Containing, Material From Cattle; Final Rule and Proposed Rule

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 189 and 700

[Docket No. 2004N–0081]

RIN–0910–AF47

Use of Materials Derived From Cattle in Human Food and Cosmetics

AGENCY: Food and Drug Administration, HHS.

ACTION: Interim final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing an interim final rule (interim final rule) to prohibit the use of certain cattle material, to address the potential risk of bovine spongiform encephalopathy (BSE), in human food, including dietary supplements, and cosmetics. Prohibited cattle materials include specified risk materials, small intestine of all cattle, material from nonambulatory disabled cattle, material from cattle not inspected and passed for human consumption, and mechanically separated (MS)(Beef). Specified risk materials are the 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), and dorsal root ganglia of cattle 30 months and older; and the tonsils and distal ileum of the small intestine of all cattle. Prohibited cattle materials do not include tallow that contains no more than 0.15 percent hexane-insoluble impurities and tallow derivatives. FDA is taking this action in response to the finding of an adult cow, imported from Canada, that tested positive for BSE in the State of Washington. This action is consistent with the recent interim final rule issued by the U.S. Department of Agriculture (USDA) declaring specified risk materials and the carcasses and parts of nonambulatory disabled cattle to be inedible, unfit for human food, and prohibiting their use as human food and requiring that the entire small intestine be removed and disposed of as inedible. This action will minimize human exposure to materials that scientific studies have demonstrated are highly likely to contain the BSE agent in cattle infected with the disease. Scientists believe that the human disease variant Creutzfeldt-Jakob disease (vCJD) is likely caused by the consumption of products contaminated with the agent that causes BSE. Also in this issue of the **Federal Register**, FDA is proposing to require that manufacturers and processors of human food and cosmetics that are manufactured from, processed with, or otherwise contain material from cattle establish and maintain records sufficient to demonstrate that the food and cosmetics are in compliance with this interim final rule.

DATES: The interim final rule is effective on July 14, 2004. Submit written or electronic comments by October 12, 2004. The Director of the Office of the Federal Register approves the incorporation by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51 of certain publications in 21 CFR 189.5 and 700.27 as of July 14, 2004.

ADDRESSES: You may submit comments, identified by Docket No. 2004N–0081, by any of the following methods:

- Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.
- Agency Web site: *http://www.fda.gov/dockets/ecomments*. Follow the instructions for submitting comments on the agency Web site.
- E-mail: fdadockets@oc.fda.gov. Include Docket No. 2004N–0081 and or RIN number RIN–0910–AF47 in the subject line of your e-mail message.
- FAX: 301–827–6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD–ROM submissions]: Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the agency name and Docket No. or Regulatory Information Number (RIN) for this rulemaking. All comments received will be posted without change to *http://www.fda.gov/dockets/ecomments*, including any personal information provided. For detailed instructions on submitting comments and additional information on the rulemaking process, see section V in the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to *http://www.fda.gov/dockets/ecomments* and/or the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Rebecca Buckner, Center for Food Safety and Applied Nutrition (HFS–306), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740, 301–436–1486.

SUPPLEMENTARY INFORMATION:

I. Background

On January 26, 2004, the Department of Health and Human Services announced new safeguards to strengthen existing firewalls against transmission of bovine spongiform encephalopathy (BSE) in the United States. This interim final rule, will protect the food and cosmetic supply from materials that may carry a risk of transmitting BSE. Consumption of products contaminated with agent that causes BSE has been linked to a human disease. The United States is currently protected from the spread of BSE by import controls, increased surveillance for the disease in the cattle population, FDA's 1997 ruminant feed regulation, and the United States Department of Agriculture's (USDA's) ban on specified risk materials and certain other cattle material in human food. This interim final rule complements USDA's ban for FDA-regulated human food and cosmetics.

A. Transmissible Spongiform Encephalopathies

Transmissible spongiform encephalopathies (TSEs) are fatal neurodegenerative disorders, which have been identified in humans and a number of animal species (e.g., cattle, sheep, goats, elk, deer, cats, and mink), but primarily in ruminants (cattle, sheep, elk, deer). TSEs are characterized by a long incubation period, then a shorter course of neurological symptoms, followed by death (Ref. 1). Postmortem histopathology of the brain tissue from humans and animals with TSEs is characterized by a sponge-like appearance of the brain and deposits of abnormal forms of certain cell-associated proteins (normal prion proteins) in the brain. In some TSEs, deposits of abnormal prion proteins are detected in other nervous and non-nervous tissues, such as the spinal cord, peripheral nerves, intestine, spleen, lymph nodes, and bone marrow (Refs. 2 to 6).

TSEs in humans include sporadic CJD, variant Creutzfeldt-Jakob disease (vCJD), Gerstmann-Straussler-Scheinker syndrome, kuru, fatal familial insomnia, and sporadic fatal insomnia (Ref. 7). Nonhuman TSEs include BSE in cattle, scrapie in sheep and goats, transmissible mink encephalopathy (TME) in mink, feline spongiform encephalopathy (FSE) in cats, and chronic wasting disease (CWD) in deer and elk (Ref. 7). Scrapie and CWD occur, and TME has occurred, in the United States. On December 23, 2003, USDA diagnosed BSE in an adult cow

in the United States that had come from Canada.

The pathogenesis of TSEs is poorly understood. Resistance of TSE agents to physical and chemical treatments that would destroy most nucleic acids makes conventional micro-organisms, such as bacteria and viruses, less likely causes (Ref. 8). The prion theory suggests that the infectious agents of TSEs are abnormally folded forms of normal prion proteins, and is the most widely accepted explanation (Ref. 9). Normal prion protein genes are found widely in nature. In mammals, normal prion proteins are primarily expressed in neurons, but also can be found in other tissues in lower concentrations, depending on the mammalian species (Ref. 10). It is not well understood how the abnormal folding of prion proteins occurs, why hosts cannot efficiently dispose of or develop immunity to these proteins, and what factors cause some TSEs.

The current lack of an antemortem diagnostic test for TSEs in either humans or animals limits surveillance for these diseases, studies of disease pathogenesis, and other research efforts. Diagnosis is confirmed by special post-mortem examination of brain tissue by identification of abnormal prion proteins in advanced stages of the disease. At earlier stages of disease development, abnormal prion proteins may not yet be present or are undetectable in brain tissue. Presently, there are no effective treatments for TSEs, and all are invariably fatal (Ref. 1).

B. Bovine Spongiform Encephalopathy

BSE is a TSE of cattle with a long incubation period (2 to 8 years), most likely acquired following consumption of an animal product containing the infectious BSE agent (Refs. 11 and 12). The British Ministry of Agriculture, Fisheries and Food (now known as the Department for Environment, Food, and Rural Affairs) first recognized BSE as a distinct disease in November 1986. The clinical signs of BSE include behavioral, gait, and postural abnormalities. The disease usually presents in cattle observed to have increased apprehension, increased reaction to sound and touch, and a swaying gait. These signs are accompanied by subtle changes in the normal behavior of the cow, such as separation from the herd while at pasture, disorientation, staring, and excessive licking of the nose or flanks. The disease progresses to stumbling and falling, and ends with seizures, coma, and death (Ref. 13).

Epidemiological studies have characterized the outbreak of BSE in the United Kingdom as a prolonged epidemic arising at various locations, with all occurrences due to a common source, and have suggested that feed contaminated by a TSE agent was the cause of the disease outbreak (Ref. 14). The subsequent spread of BSE, however, is associated with the feeding of meat-and-bone-meal from rendered BSE-infected cattle to non-infected cattle (Ref. 14). It appears likely that the BSE agent was transmitted among cattle at an increasing rate by ruminant-to-ruminant feeding until the United Kingdom ban on such practices went into effect in 1988 (Ref. 11). The United Kingdom instituted a ruminant-to-ruminant feed ban to stop the cycle of infection, restrict the geographic spread of the disease, and eliminate potential sources of new infections. Since BSE was first identified in the United Kingdom, approximately 185,000 cattle have been diagnosed with the disease there (Ref. 15). The precautionary slaughter of millions of British cows and increasingly stringent prohibitions on certain animal feeding practices appear to have slowed, but not eradicated, the BSE epidemic in the United Kingdom. In 1992 (the peak year of the epidemic), there were over 35,000 cases of BSE in the United Kingdom; in 2003, there were approximately 458 cases (Ref. 15).

The measures used to control and prevent the spread of BSE in the United Kingdom were too slowly developed or too poorly enforced to prevent the occurrence of BSE in cattle in other countries to which the United Kingdom had shipped BSE-infected cattle or cattle feed (Ref. 11). In addition to the United Kingdom, BSE has been detected in non-imported cattle in Austria, Belgium, Canada, the Czech Republic, Denmark, Finland, France, Germany, Greece, Israel, Italy, Japan, Liechtenstein, Luxembourg, the Netherlands, Poland, Portugal, the Republic of Ireland, Slovakia, Slovenia, Spain, and Switzerland (Ref. 15). On December 23, 2003, USDA diagnosed a positive case of BSE in an adult Holstein cow, born in Canada, in the State of Washington.

C. Creutzfeldt-Jakob Disease and Variant Creutzfeldt-Jakob Disease

CJD is a sporadic disease of humans that exists throughout the world with an annual incidence of approximately one case per million population (Ref. 9). The highest death rates in the United States and the United Kingdom occur in individuals between the ages of 60 and 70 (Ref. 16). Death generally occurs after less than a year of progressive neurological deterioration (Ref. 9). Early symptoms typically include changes in sleeping and eating patterns, followed by inappropriate behavior and eventual dementia, lack of coordination, and myoclonic spasms. CJD is always fatal (Ref. 16). The cause of sporadic CJD is not fully understood, but genetic susceptibility may play a role (Ref. 9). CJD has been inadvertently transmitted between humans during medical treatment or diagnostic procedures via contaminated neurosurgical instruments, transplants of dura mater and corneas, injection of pituitary extract, and cross-contamination from medical personnel who handled tissues from patients with CJD (Ref. 9).

In April 1996, British scientists reported a previously undetected new variant of CJD (vCJD) in young patients, with symptoms somewhat different from sporadic CJD (Refs. 17 and 18). All cases of vCJD had histopathologic evidence of spongiform changes in the brain, but also showed formation of ''florid'' plaques (a core of amyloid protein with surrounding halos of vacuoles) not typically seen in other forms of CJD (Ref. 9). Clinically, vCJD usually begins with a psychiatric presentation, such as depression, anxiety, nightmares or hallucinations. These symptoms are followed by memory impairment, then dementia in the late stages. The clinical course may last up to 2 years before death occurs (Ref. 19).

Because scientific evidence suggests that the presence and infectivity of abnormal prion proteins in vCJD share some characteristics with those abnormal prion proteins found in cattle with BSE, scientists have concluded that exposure to the BSE agent is the most plausible explanation for the occurrence of vCJD (Refs. 20 to 23). Monkeys (genetically the closest animal model to humans) inoculated with samples of brain from BSE-infected cattle have been found to develop a TSE that is histopathologically similar to vCJD (Ref. 24), as have mice inoculated or fed with BSE-infected tissue (Ref. 25). Studies have shown that abnormal prion proteins from vCJD patients are molecularly similar to abnormal prion proteins from BSE-infected cattle, but different from abnormal prion proteins from patients with CJD (Ref. 19). Although the exact route of exposure is not known, most scientists believe that vCJD in humans is caused by consumption of cattle products contaminated with the agent that causes BSE (Refs. 16, 26, and 27).

Since 1996, approximately 150 probable and confirmed cases of vCJD have been reported in the United Kingdom. In addition, one case of vCJD each has been reported in Ireland and

Canada, both of which are believed to be related to BSE exposure in the United Kingdom. The one reported case of vCJD in the United States is also believed to be related to United Kingdom BSE exposure (Ref. 10). In addition, there have been seven vCJD cases in France and one in Italy (Ref. 10). Because the incubation period for vCJD in humans may range from 5 to 20 years, some epidemiological models have projected that many more (600–3000) cases of vCJD caused by consumption of BSE-contaminated cattle products may occur in the United Kingdom in the future (Ref. 28).

D. BSE Risk Assessments

In 1998, USDA asked the Harvard Center for Risk Analysis (HCRA) and the Center for Computational Epidemiology at Tuskegee University to evaluate United States measures to prevent the spread of BSE to animals and humans if it were to occur in this country. The Harvard-Tuskegee risk assessment (referred to below as the Harvard-Tuskegee study) was published in November 2001, revised in 2003, and determined that the United States was highly resistant to any proliferation of BSE or a similar disease (Ref. 29). The risk assessment model also demonstrated that certain new control measures could reduce the small risk even further.

The Harvard-Tuskegee study involved a probabilistic simulation model to determine the consequences of introducing BSE into the U.S. cattle population. This simulation indicated that, in a hypothetical situation in which 10 infected cattle were imported into the United States, on average only four new cases of BSE would arise, and the disease would be eliminated in 20 years. The Harvard-Tuskegee study determined that these new cases of BSE would most likely arise in the United States from incomplete compliance with FDA's ruminant feed regulation (see III.A of this document), and also concluded that an epidemic of BSE in this country resulting from scrapie, CWD, or another TSE is unlikely.

The Harvard-Tuskegee study estimated the number of cattle infectious doses that might be available for human exposure, but it did not estimate the likelihood of human disease from this exposure because the relationship between the two is not known. According to the study, the estimated total infectivity available for human exposure from the importation of 10 infected cattle is 35 cattle infectious doses over 20 years. The Harvard-Tuskegee study determined that the greatest sources of infectivity to consumers are direct consumption of cattle brain and spinal cord and also meat from advanced meat recovery systems that contains central nervous system tissue. The Harvard-Tuskegee study did not address potential human exposure to the BSE agent through food containing ingredients of cattle origin, such as gelatin, beef stocks, extracts, and flavorings or cosmetics.

The Harvard-Tuskegee study identified three pathways that could lead to cattle or human exposure to the BSE agent: (1) Noncompliance with FDA's ruminant feed regulation prohibiting the use of certain proteins in feed for cattle and other ruminants; (2) rendering of animals that die on the farm, and use (through illegal diversion or cross-contamination) of the rendered product in ruminant feed; and (3) the inclusion of high-risk tissues from cattle, such as brain and spinal cord, in products for human oral consumption. Evaluation of potential risk mitigation measures in the study found that a prohibition against rendering of animals that die on the farm would reduce the potential cases of BSE following hypothetical exposure by 82 percent. In addition, a ban on specified risk materials (SRMs) including brain, spinal cord, and vertebral column from inclusion in human and animal food would reduce potential BSE cases in cattle by 88 percent and potential human exposure to BSE by 95 percent. The Harvard-Tuskegee study also noted the value of ensuring that low-risk cattle tissues are not cross-contaminated with high-risk tissue.

In 2003, after the discovery of a case of BSE in a cow in Canada, the USDA asked HCRA to evaluate the implications of the hypothetical previous introduction of BSE in the United States from Canada. The HCRA model indicated that the potential for spread of BSE among cattle and the potential for human exposure to BSE increase as the time period lengthens between the introduction of infected Canadian cattle and FDA's issuance of the ruminant feed regulation in 1997 (i.e., there is more potential for spread of BSE if the infected cattle were imported from Canada in 1990 versus 1996). In the worst case scenario involving importation of five infected animals from Canada, BSE would be eliminated from the United States with high probability by 2020 (Ref. 30).

E. Specified Risk Materials

1. List of Infective Tissues

Data on the distribution of BSE infectivity in tissues are incomplete, and there are ongoing experiments with cattle to confirm and update earlier data (Refs. 2 to 6 and 31). In a pathogenesis study in which cattle tissues were assayed for infectivity following intracerebral inoculation of tissues from cattle orally exposed to the BSE agent, distal ileum and spinal cord were found to harbor infectivity as early as 6 months post-inoculation for distal ileum and 32 months post-inoculation for spinal cord (Refs. 3 and 4). In one experiment, cattle were experimentally infected with BSE through consumption of the brains of cattle with BSE. Infectivity in the tissues of the cattle consuming the brains was evaluated by mouse bioassay. In the mouse bioassay, infectivity was detected in brain, spinal cord, dorsal root ganglia (clusters of nerve cells attached to the spinal cord that are contained within the bones of the vertebral column), trigeminal ganglia (clusters of nerve cells connected to the brain that lie close to the exterior of the skull), and distal ileum. All of the central nervous system (CNS) tissues were found to be infective in animals 32 to 40 months after exposure to the BSE agent, which in some cases could be months before anticipated onset of clinical signs of illness. This study was done with relatively few animals (n=30), and the experimental conditions do not reflect field conditions of disease transmission. Therefore, a second phase of the experiment was initiated, and will continue for several more years, to determine if any of the tissues that initially did not appear to be infective actually contain low levels of infection. Preliminary results from this study have indicated that tonsil, at 10 months after exposure, carries a low level of infectivity (Ref. 31).

In cattle infected with BSE under field conditions, infectivity has been found in the brain, spinal cord, and retina of the eye in animals with clinical disease (Ref. 31). The Scientific Steering Committee of the European Union (Ref. 27) has reported on the proportion of total infectivity in various tissues. They estimate that, in an animal with clinical disease, approximately 64 percent of the infectivity is in the brain, 26 percent is in the spinal cord, 4 percent is in the dorsal root ganglia, 2.5 percent is in the trigeminal ganglia, and 3 percent is in the distal ileum. The eyes are estimated to contain less than 1 percent of the infectivity.

Based on the information presented previously and consistent with the USDA's regulation (69 FR 1862, January 12, 2004; discussed in section II of this document), we have determined that the tissues with the highest risk of harboring BSE infectivity (the SRMs) are

the 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), and dorsal root ganglia of animals 30 months and older, and tonsil and distal ileum of cattle of all ages. Though the skull and the vertebral column have not been shown to harbor BSE infectivity, they contain tissues that have been shown to be infectious; therefore, we are including the skull and the vertebral column in the list of SRMs. We are not including the vertebrae of the tail, the transverse processes of the thoracic and lumbar vertebrae, and the wings of the sacrum as SRMs with the rest of the vertebral column, because they do not contain spinal cord or dorsal root ganglia.

2. Animal Age at Which Tissues Become Infective

As discussed in the previous section, most tissues that harbor BSE infectivity have been shown to do so in animals more than 30 months after exposure to the agent. The exceptions are tonsils, which have been shown to harbor infectivity at low levels at 10 months post-exposure, and the distal ileum, which has been shown to harbor infectivity as early as 6 months post-exposure. In a study of the BSE epidemic in the United Kingdom, Dealler and Lacey (Ref. 32) noted that only 29 of 5,470 animals younger than 36 months of age developed BSE, with the peak number of cases occurring between 48 and 60 months of age. At the height of the BSE epidemic in the United Kingdom when thousands of animals were being diagnosed with BSE each year, fewer than 20 animals younger than 30 months were confirmed with the disease (Ref. 33). The youngest animal with a confirmed case of BSE was 20 months old (Ref. 15).

Though animals younger than 30 months can develop BSE, it is a very rare occurrence, based on epidemiological and experimental evidence. Therefore, we have concluded that 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), and dorsal root ganglia should be considered SRMs only in cattle 30 months and older.

We are aware that there have been documented cases of BSE in animals younger than 30 months, and that some tissues become infectious before the animal exhibits clinical signs. As mentioned previously, during the height of the BSE epidemic in the United Kingdom, a small number of animals younger than 30 months showed signs of the disease. More recently, Japan has reported cases of BSE in 21- and 23-month-old animals, discovered during testing of animals presented for slaughter. As the science and epidemiology on this issue develop, FDA may find it necessary to modify the age period for SRM removal through future rulemaking.

Based on experimental evidence, we have concluded that the tonsil and distal ileum of the small intestine of all cattle should be considered SRMs.

F. Small Intestine

To ensure effective removal of the distal ileum, USDA is requiring that the entire small intestine be removed and disposed of as inedible product. FDA is also prohibiting the use of the entire small intestine in FDA-regulated food and cosmetics as prohibited cattle material. We are doing so because: (1) It is difficult to distinguish one end of the small intestine from the other once the organ has been removed from the animal, (2) there is no international agreement on how much of the small intestine should be removed to ensure that the distal ileum is separated from the upper part of the intestine, and (3) there is no way for a manufacturer or processor to document that the distal ileum was adequately removed since there is no international consensus on the issue. USDA has solicited comment on whether processors may be able to effectively remove just the distal ileum. FDA requests comment on this issue as it affects FDA's rule.

G. Mechanically Separated (MS)(Beef)

MS(Species) is a standardized food defined by the USDA in 9 CFR 319.5 (see section IV.A of this document for definition of MS(Beef)). The standard does not limit the amount of spinal cord and dorsal root ganglia that can contaminate vertebral column used to produce the product. Consequently, MS(Beef) may contain concentrated amounts of such tissues. Because we have concluded that spinal cord, dorsal root ganglia and vertebral column are all SRMs, we are designating MS(Beef) as a prohibited cattle material.

H. Nonambulatory Disabled Cattle

Experience has shown that nonambulatory disabled cattle (see section IV.A of this document for definition) are the population at greatest risk for harboring BSE. Surveillance data in the European Union in 2002 showed that there were 29 positive/10,000 tests for BSE among healthy-appearing cattle of all ages and 148 positive/10,000 tests for BSE among nonambulatory animals of all ages (Ref. 34). In Switzerland, sampling of particular populations of cattle revealed that BSE-positive animals were 49 to 58 times more likely to be found in the nonambulatory population than in the population selected for passive slaughter surveillance (Ref. 35). The Harvard-Tuskegee study estimated that, following importation of 10 infected cattle, a prohibition against rendering animals that die on the farm (these animals are usually nonambulatory disabled) would decrease the number of new cases of BSE by 82 percent.

Because typical clinical signs of BSE cannot always be observed in nonambulatory disabled cattle, and because evidence has indicated these cattle are more likely to have BSE than apparently healthy cattle, FDA is designating material from nonambulatory disabled cattle as prohibited cattle materials.

I. Cattle Not Inspected and Passed for Human Consumption

For cattle that are not inspected (see section IV.A of this document for definition), there is no information as to their suitability for use in human food and cosmetics in general, and as to their disease status and potential for harboring BSE in particular. In addition, such cattle are likely to have died on the farm or en route to slaughter, and these animals are not eligible for inspection by the USDA. Therefore, these cattle are at higher risk of harboring undetected BSE. For cattle that are inspected but not passed, a regulatory authority (USDA or other) has made a determination that they are not appropriate for use in human food. Such a determination may be based, among other things, on evidence of a neurological disorder associated with a higher risk of BSE. Moreover, material from cattle not inspected or inspected and not passed for human consumption is prohibited from human food by USDA. By requiring that material from cattle for use in FDA-regulated human food and cosmetics be inspected and passed for human consumption, we are minimizing the risk of exposure to the agent that causes BSE, and extending the protections offered by the USDA or the appropriate regulatory authority in other countries to FDA-regulated human food and cosmetics.

J. BSE Testing for Food Safety Purposes

No practical antemortem tests for BSE exist. The currently available postmortem tests, although useful for disease surveillance (i.e., determining the rate of disease in the population of

cattle), are not appropriate as food safety indicators. This is, in part, due to limitations on the existing testing methods, which rely on the use of brain tissue. Experimental evidence demonstrates that certain potentially infective tissues, such as distal ileum and tonsil, are the first tissues to accumulate infectivity in the incubation period, and this is prior to any infectivity being demonstrated in brain tissue (Refs. 3, 36, and 37). Therefore, tests conducted on brain tissue may not reflect accurately the potential infectivity in other tissues that develop infectivity earlier, such as distal lieum. Development of effective food safety indicators will require improved understanding of the pathogenesis of the disease and improved laboratory methods.

K. Dietary Supplements

Some dietary supplements contain cattle-derived materials (e.g., liver powder, brain, ovaries, eye tissue, mammary tissue, adrenal gland, hypothalamus) or substances derived from these tissues. On March 13, 2003 (68 FR 12158), FDA proposed current good manufacturing practice (CGMP) regulations for dietary ingredients and dietary supplements. In the proposal, we recognized that animal-derived ingredients in dietary supplements present important public health and safety issues and that some dietary supplements contain material from cattle that may contain the infective agent that causes BSE. We also stated that, in the absence of broadly applicable or validated diagnostic tests available to manufacturers to identify BSE-infected animals or materials, the agency is considering whether to set forth specific requirements designed to prevent the use of materials derived from certain animals from regions that may present a risk of BSE. Further, in the proposal we sought comment, among other things, on whether we should include in the final rule specific requirements for manufacturing, packing, or holding all animal-derived dietary ingredients, including cattle-derived ingredients, whether or not they originate from areas with BSE. FDA will respond to those comments in a final dietary supplement CGMP rule and consistent with the provisions of this rule, which applies to all human food, including dietary supplements.

L. Cosmetics

Cosmetics may be made from a variety of cattle-derived ingredients. Tallow derivatives, particularly fatty acids and glycerin, are the predominant bovine ingredient used by the cosmetic industry. Additionally, ingredients sometimes include albumin, brain extract, brain lipid, cholesterol, fibronectin, sphingolipids, collagen, keratin, and tallow. Cattle-derived ingredients serve many functions and may be used as skin conditioning agents, emollients, binders, and hair and nail conditioning agents.

There are several routes through which cosmetics contaminated with the agent that causes BSE could transmit disease to humans. Transmission of the BSE agent to humans through intact skin is not likely; however, cosmetics may be ingested or applied to cut or abraded skin or to mucosal tissues, particularly in the eye, which could provide direct routes for infection.

Although injection into the eye does not represent normal human contact with cosmetics, experimental studies in animals may provide relevant information on potential routes of exposure. In mice, intraocular injection of scrapie caused infection along the optic nerve, which eventually spread into non-neural tissue via the lymphatic system (Ref. 38). In addition to intraocular injection, infectivity has been transmitted to animals via the conjunctiva of the eye (mucosal tissue). Scott et al. (Ref. 39) found that scrapie was induced in 42 percent of rodents by dropping a high concentration of infectivity onto the conjunctiva. Klitzman et al. (Ref. 40) suggested that kuru, a human TSE disease found only among the Fore people of New Guinea, might have been transmitted by rubbing infected human brain into eyes or cut skin, while handling and consuming infected brain during funeral rituals.

Cut or abraded skin also has been proposed as a route for contracting TSE diseases. The transmission of kuru through cut skin has been suggested and was mentioned previously (Taylor et al. (Ref. 41) and Ingrosso et al. (Ref. 42)) demonstrated increased transmission of scrapie via oral mucosal tissue. In one study, 100 percent of mice with experimentally damaged oral mucosal tissue developed scrapie through ingestion of infected material, while only 71 percent of mice with intact mucosa developed the disease (Ref. 41). In addition, Pammer et al. (Ref. 43) and Sugaya et al. (Ref. 44) noted that epithelial cells, dendritic cells, and keratinocytes (the primary cell types found in the epidermis) have been found to contain infectious prion protein, indicating that these cells are potential targets for peripheral infection with a TSE disease.

Use of BSE-contaminated cosmetics could provide a means of human infection via several routes discussed previously. Many cosmetics are typically applied in the area of the eye (mascara, eye brow pencil, eyeliner, eye lotion, and eye makeup remover) and almost any cosmetic, including shampoo, can get into the eye via eye rubbing or incorrect application. Any cosmetic product, but particularly shaving creams and gels and lotions, may be applied to cut or abraded skin. Many products may come in contact with mucosal tissue via rubbing. Cosmetics that are ingested, such as lipstick, dentifrices, mouthwash, and breath fresheners, would have the same route of infection as the feeding studies mentioned previously, if the cosmetics were contaminated with the agent that causes BSE.

M. Tallow and Tallow Derivatives

Tallow is an animal-derived hard fat that has been heat processed; most tallow is derived from cattle. Any risk of BSE transmission from tallow is a result of protein that is present as an impurity in the tallow. Taylor et al. (Refs. 45 and 46) found in rendering studies with abnormal prion protein that the prion protein did not preferentially migrate into the fat fraction, but remained with the protein fraction. Therefore, there is no reason to believe that tallow is likely to contain unusually high amounts of prion protein as a constituent of the insoluble impurities fraction that remains in tallow after rendering. Taylor et al. (Refs. 45 and 46) also reported that the various rendering processes used for tallow production in the United Kingdom were sufficient to produce tallow that did not result in infection when injected into the brains of mice, even though the starting material was highly spiked with the scrapie agent. Wilesmith et al. (Ref. 47) noted that the geographical variation in the incidence of BSE in the United Kingdom was not consistent with the use of tallow in cattle feed and concluded that the most likely source of infection in cattle was BSE-contaminated meat and bone meal.

The Office International des Epizooties (OIE), the international animal health standard setting body, categorizes tallow with insoluble impurities of no more than 0.15 percent as protein-free tallow and indicates that tallow that meets this standard can be safely consumed by animals regardless of the starting materials (Ref. 48). There is thought to be a 10- to 10,000-fold increase in the amount of infectious material needed to cause illness in humans as compared with cattle because of the species barrier, though the European Commission's Scientific Steering Committee cautioned that this

range is uncertain and in a unlikely, but worst case scenario, the species barrier may not exist (Ref. 49). FDA's Transmissible Spongiform Encephalopathy Advisory Committee (TSEAC) considered the safety of tallow and tallow derivatives in 1998 (Ref. 50). Members of the Committee indicated that tallow is a food with negligible or no risk of transmitting BSE to humans or animals.

Based on the research and the opinions noted previously, we are permitting tallow to be used in human food and cosmetics if it contains no more than 0.15 percent hexane-insoluble impurities or otherwise complies with these regulations. We believe we are adequately protecting human health by requiring a tallow standard for human food and cosmetics that is as protective as the standard recommended by OIE to prevent BSE in cattle.

Tallow derivatives are produced by subjecting tallow to chemical processes (hydrolysis, trans-esterification, and saponification) that involve high temperature and pressure. The TSEAC considered tallow derivatives in 1998 (Ref. 50) and determined that the rigorous conditions of manufacture are sufficient to further reduce the BSE risk in tallow derivatives. In addition, the OIE also recommends that derivatives of protein-free tallow be freely traded among countries because they pose insignificant BSE risk to animals (Ref. 48). Because we believe that tallow has negligible risk of transmitting BSE, and tallow derivatives undergo additional processing, we do not believe that tallow derivatives pose a risk of transmitting the agent that causes BSE to humans.

II. USDA Interim Final Rule

On January 12, 2004, in response to the diagnosis of BSE in a cow in the United States, USDA published a series of interim final rules including ''Prohibition of the Use of Specified Risk Materials for Human Food and Requirements for the Disposition of Non-Ambulatory Disabled Cattle'' (69 FR 1862). The rule declares that SRMs are inedible and unfit for food and prohibits their use as human food. The rule designates the following as SRMs: The 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), and dorsal root ganglia of cattle 30 months of age and older, and the tonsils and distal ileum of the small intestine of all cattle. To ensure the distal ileum is completely removed, the entire intestine must be removed and disposed of as inedible. The rule also declares that MS(Beef) is unfit for food and inedible. In addition, the rule requires that all nonambulatory disabled cattle presented for slaughter be condemned and not used in human food. Furthermore, the rule requires that establishments that slaughter cattle or that process the carcasses or parts of carcasses of cattle maintain daily records sufficient to document the implementation and monitoring of procedures for removal, segregation, and disposition of SRMs. Finally, the rule deems all age-associated SRMs (all SRMs except tonsil and distal ileum) to be from animals 30 months or older unless an establishment can demonstrate that the materials are from an animal that was younger than 30 months of age at the time of slaughter.

In this interim final rule, FDA is extending similar protections to FDA-regulated human food and cosmetics. The USDA's interim final rule will reduce but will not, by itself, eliminate the availability and use of prohibited cattle materials in domestic and imported FDA-regulated human food and cosmetics. Domestically, generally human food that contains meat only in a relatively small proportion or that historically has not been considered by consumers to be products of the meat food industry (e.g., soup stock, beef flavors and extracts, gelatin), is not produced under USDA inspection (see definition of ''meat food product'' in 21 U.S.C. 601(j)) and may be physically available for use in FDA-regulated human food and cosmetics. Further, even when excluded from human food produced in USDA-inspected establishments, prohibited cattle materials may leave the establishments for inedible rendering or destruction. These materials, which previously have not been explicitly prohibited in human food and cosmetics by FDA, might then be used in FDA-regulated human food or cosmetics. For example, prohibited cattle materials leaving a USDA-inspected facility might not be denatured sufficiently to preclude their use in FDA-regulated human food and cosmetics.

Under the Food Safety and Inspection Services' (FSIS') rule, SRMs, small intestine from all cattle, and material from nonambulatory disabled cattle must be designated as inedible. However, certain products, such as gelatin and collagen (which are both covered by the provisions of this rule) used in FDA-regulated human food and cosmetics, have traditionally been produced from cattle material deemed inedible by the USDA. Therefore, such a designation by the USDA may not be enough to preclude use of prohibited cattle materials in FDA-regulated products without additional regulation by FDA. Further, some cattle are not slaughtered under continuous USDA inspection (e.g., some are sent directly to rendering). Cattle material from these animals, such as brains or bones which include SRMs, could end up as starting material for human food, such as meat extracts or gelatin, respectively. Furthermore, if prohibited cattle materials were used in FDA-regulated human food or cosmetics, the rule would facilitate FDA's ability to use the enforcement mechanisms of the Federal Food, Drug, and Cosmetic Act (the act) that apply to adulterated products (e.g., seizure) to prevent human exposure to the prohibited cattle materials.

Imported products also may contain the types of materials prohibited by the USDA, but which would not fall within the scope of the USDA's import regulations either because of the nature of the products or their country of origin. Specifically, although both FSIS and Animal and Plant Health Inspection Service (APHIS) impose BSE-related prohibitions, these prohibitions collectively do not cover all FDA-regulated human food and cosmetics. FSIS' restrictions, contained in its interim final rule described earlier in this document, do not apply to importation of dietary supplements, cosmetics, and FDA-regulated human food not considered to be ''meat food products'' under the Federal Meat Inspection Act (21 U.S.C. 601(j)).

APHIS' BSE-related restrictions on imports do not cover gelatin for human use (beyond requiring a permit) or cosmetics, and apply only to a limited number of countries (9 CFR 94.18).

III. FDA Actions on BSE

A. The FDA Ruminant Feed Regulation

In the **Federal Register** of June 5, 1997 (62 FR 30936), FDA published a regulation that prohibits, with some exceptions, the use of protein derived from mammalian tissues in feed for cattle and other ruminant animals (21 CFR 589.2000) (ruminant feed regulation). FDA published the ruminant feed regulation because of findings that ruminants had been fed protein derived from animals in which TSEs were found and that consumption of this protein may cause TSEs in ruminants. The regulation was intended to prevent the establishment and amplification of BSE in the United States and thereby minimize any risk to animals and humans. FDA currently is

considering changes to further strengthen the regulation.

B. FDA Guidance

During the past decade, we have communicated with the public and manufacturers, applicants, importers, and processors of FDA-regulated human food and cosmetics about appropriate steps to increase product safety and minimize the risk of products being contaminated with the BSE agent. Most of our communications have been in the form of letters and guidance to industry and import alerts.

• November 1992—We wrote to manufacturers of dietary supplements to alert them to the developing concern about TSEs in animals and CJD in humans and recommended that they investigate the geographic sources of any bovine and ovine material used in their products. We suggested that manufacturers develop plans to ensure, with a high degree of certainty, that bovine and ovine materials used in their products were not from countries where BSE exists (''BSE countries'' specified by USDA's APHIS in 9 CFR 94.18) or from sheep flocks (foreign or domestic) infected with scrapie.

• August 1994—We published a notice in the **Federal Register** (59 FR 44592, August 29, 1994) entitled ''Bovine-Derived Materials; Agency Letters to Manufacturers of FDA-Regulated Products.'' The notice published the November 1992 letter previously described and, additionally, letters to manufacturers of FDA-regulated drugs, biologics, and medical devices (December 1993), products for animals (August 17, 1994), and manufacturers and importers of dietary supplements and cosmetics (August 17, 1994). The letter to the manufacturers and importers of dietary supplements and cosmetics included our recommendation that firms manufacturing or importing dietary supplements or cosmetics containing specific bovine tissues ensure that the tissues do not come from cattle born, raised, or slaughtered in BSE countries.

• October 1994—We issued Import Alert 17–04, which allowed for the detention, without examination, of bulk shipments of high-risk bovine tissues and tissue-derived ingredients from BSE countries. When FDA issued Import Alert 17–04 in 1994, the list of BSE countries included the United Kingdom, France, Ireland, Oman, Switzerland, and Portugal. We have updated this alert whenever APHIS has revised the list of countries in 9 CFR 94.18.

• May 1996—We sent a letter to manufacturers and importers of dietary supplements and cosmetics stating that FDA strongly believed that manufacturers should take immediate and concrete steps to reduce the potential risk of human exposure to the BSE infectious agent.

• October 1997—We published a notice of availability (62 FR 52345, October 7, 1997) of a guidance for industry entitled ''The Sourcing and Processing of Gelatin to Reduce the Potential Risk Posed by Bovine Spongiform Encephalopathy (BSE) in FDA-Regulated Products for Human Use.'' In the guidance FDA recommends, among other things, that gelatin processors ensure that slaughterhouses that supply cattle bones for gelatin production remove heads, spines, and spinal cords as the first procedure following slaughter.

IV. Description of Interim Final Rule and Legal Authority

A. Definitions

In new §§ 189.5(a) and 700.27(a) (21 CFR 189.5(a) and 21 CFR 700.27(a)) we are defining the following terms for the purposes of this regulation:

1. *Prohibited cattle materials* means specified risk materials, small intestine of all cattle, material from nonambulatory disabled cattle, material from cattle not inspected and passed, or MS(Beef). The phrase ''prohibited cattle materials'' includes all of the individual categories of materials and tissues prohibited by this rulemaking. Prohibited cattle materials do not include tallow that contains no more than 0.15 percent hexane-insoluble impurities and tallow derivatives.

2. *Inspected and passed* means that the product has been inspected and passed for human consumption by the appropriate regulatory authority, and at the time it was inspected and passed, it was found to be not adulterated. This definition is consistent with the USDA's definition in 9 CFR 301.2.

3. *Mechanically Separated (MS)(Beef)* means a meat food product that is finely comminuted, resulting from the mechanical separation and removal of most of the bone from attached skeletal muscle of cattle carcasses and parts of carcasses, that meets the specifications contained in 9 CFR 319.5, the USDA regulation that prescribes the standard of identity for MS(Species). This definition of MS(Beef) is consistent with the term as used by the USDA in its recent interim final rule (69 FR 1862) prohibiting its use in human food.

4. *Nonambulatory disabled cattle* means cattle that cannot rise from a recumbent position or that cannot walk, including, but not limited to, those with broken appendages, severed tendons or ligaments, nerve paralysis, fractured vertebral column or metabolic conditions. This definition of nonambulatory disabled cattle is consistent with the definition of nonambulatory disabled livestock in the USDA's interim final rule (69 FR 1862) requiring that nonambulatory disabled cattle be condemned and not used as human food.

5. *Specified risk material (SRM)* means the 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), and dorsal root ganglia of cattle 30 months and older, and the tonsils and distal ileum of the small intestine of all cattle. This definition of SRMs is the same as that used by the USDA in its interim final rule (69 FR 1862) declaring SRMs to be inedible and prohibiting their use in human food.

6. *Tallow* means the rendered fat of cattle obtained by pressing or by applying any other extraction process to tissues derived directly from discrete adipose tissue masses or to other carcass parts and tissues. Tallow must be free of prohibited cattle material or must contain not more than 0.15% hexane-insoluble impurities determined by the method for ''hexane-insoluble matter,'' pp. 464–465, the Food Chemicals Codex, 5th Ed. (2003), incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, or another method equivalent in accuracy, precision, and sensitivity to the method in the Food Chemicals Codex. You may obtain copies of the above-referenced method from the Division of Dairy and Egg Safety (HFS–306), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740, or you may examine a copy at the Center for Food Safety and Applied Nutrition's Library, 5100 Paint Branch Pkwy., College Park, MD, or at the Office of the Federal Register, 800 North Capitol St., NW., Suite 700, Washington, DC.

7. *Tallow derivative* means any chemical obtained through initial hydrolysis, saponification, or trans-esterification of tallow; chemical conversion of material obtained by hydrolysis, saponification, or trans-esterification may be applied to obtain the desired product.

B. Requirements for Prohibited Cattle Materials

USDA recently declared SRMs and MS(Beef) unfit for food and inedible and prohibited their use in human food. USDA also required that all nonambulatory disabled cattle

presented for slaughter be condemned and not used in human food and that small intestine of all cattle be removed and disposed of as inedible. To ensure that the SRMs, small intestine of all cattle, MS(Beef), and material from nonambulatory disabled animals are not incorporated into FDA-regulated human food and cosmetics, we are similarly prohibiting the use of SRMs, small intestine of all cattle, MS(Beef) and material from nonambulatory disabled cattle in human food and cosmetics. We are also prohibiting material from cattle not inspected and passed. We are defining these five categories of material as prohibited cattle materials.

Scientists believe that the human disease vCJD is likely caused by the consumption of products contaminated with the agent that causes BSE. The relationship between the agent that causes BSE and human cases of vCJD has been described in section I.C of this document. Contamination of products with infected cattle CNS tissue is believed to have led to the development of vCJD in humans (Refs. 16, 26, and 27).

Currently, no practical method for testing products for the agent that causes BSE is available and, therefore, we do not have a means of distinguishing products that contain infectious material from products that do not. Consumers also often are not able to determine which products contain prohibited cattle materials and which products do not. For example, rendered products including brain and spinal cord may become ingredients in soups, broths, meat flavors, extracts, dietary supplements and cosmetics, where their presence may not be indicated as such on the label. Furthermore, consumers have no way to determine whether animal material in a human food or cosmetic was sourced from nonambulatory disabled cattle or from cattle that were not inspected and passed for human consumption.

In addition to being unable to test for infectious material in products, we also do not know the infectious dose for humans. Despite widespread exposure in the United Kingdom to BSE-contaminated meat products, only a very small percentage of the exposed population has been diagnosed with vCJD to date. However, ongoing experiments indicate that the infectious dose for cattle is very low. One gram of affected cattle brain homogenate is sufficient to cause BSE in more than 50 percent of calves exposed by mouth. Five years after oral consumption of lower doses of brain material, 2 of 15 calves fed 0.1 gram had developed BSE, and 1 of 15 fed 0.01 gram had developed the disease. This experiment is ongoing (Ref. 51). There is thought to be a 10- to 10,000-fold increase in the amount of infectious material needed to cause illness in humans, as compared with cattle, because of the species barrier (Ref. 49).

We know that consumption of contaminated material has caused illness in humans, although we do not know the infectious dose, and we cannot test to determine which products contain infectious material. Therefore, we have provided in § 189.5(b) that no human food shall be manufactured from, processed with, or otherwise contain prohibited cattle materials, and in § 700.27(b) that no cosmetic shall be manufactured from, processed with, or otherwise contain, prohibited cattle materials.

FDA is applying these requirements for prohibited cattle materials to all products or ingredients of products manufactured in the U.S. or imported into the U.S. In an advanced notice of proposed rulemaking, entitled ''Federal Measures to Mitigate BSE Risks: Considerations for Further Actions,'' published by APHIS, FSIS, and FDA in this issue of the Federal Register, FSIS is seeking comment on the issue of equivalence and BSE requirements. Likewise, FDA requests comment on standards to apply when determining another country's BSE status, providing an exemption for ''BSE-free'' countries, and how to determine that countries meet any standards that might be developed. FDA intends to work with USDA in developing a harmonized U.S. position on exempting other countries from our respective requirements related to BSE.

C. Tallow and Tallow Derivatives

Tallow is defined in §§ 189.5(a)(6) and 700.27(a)(6) as ''the rendered fat of cattle obtained by pressing or by applying any other extraction process to tissues derived directly from discrete adipose tissue masses or to other carcass parts and tissues.'' Tallow derivatives are defined in §§ 189.5(a)(7) and 700.27(a)(7) as ''any chemical obtained through initial hydrolysis, saponification, or trans-esterification of tallow or the chemical conversion of material obtained by hydrolysis, saponification, or trans-esterification.'' For the reason described in section I.K of this document, we provide in §§ 189.5(a)(1) and 700.27(a)(1) that tallow with no more than a 0.15 percent hexane-insoluble impurities and tallow derivatives are not considered prohibited cattle materials under this rule. We are requiring in §§ 189.5(a)(6) and 700.27(a)(6) that you measure the hexane-insoluble impurities in tallow by the method for ''hexane-insoluble matter'' described in the 5th edition of the Food Chemicals Codex (Institute of Medicine, National Academies of Science) and incorporated by reference into this rule or by another method that is at least equivalent in accuracy, precision and sensitivity to the method described in the Food Chemicals Codex, 5th edition. Tallow that contains more than 0.15 percent hexane-insoluble impurities may be used if it complies with the requirements for cattle materials in § 189.5 for human food and § 700.27 for cosmetics.

We note that, regardless of its purity level, tallow to be used in human food and cosmetics is subject to the other provisions of the act and is adulterated, for example, if it has been prepared, packed or held under insanitary conditions whereby it may have become contaminated with filth (21 U.S.C. 342(a)(4)).

D. Records Access Requirements

We are requiring in §§ 189.5(c) and 700.27(c) that manufacturers and processors of human food and cosmetics that are manufactured from, processed with, or otherwise contain, material from cattle must make existing records relevant to compliance with this rule available to FDA for inspection and copying. We believe that records documenting the absence of prohibited cattle materials in human food and cosmetics are critical for manufacturers, processors, and FDA to ensure compliance with the prohibitions on the use of prohibited cattle materials in this interim final rule. Once material is removed from cattle, we may not be able to obtain the information necessary to determine whether it is prohibited cattle materials. There is currently no way to test reliably for the presence of the BSE agent or for the presence of prohibited cattle materials. Therefore, manufacturers and processors of human food and cosmetics must depend on records from the suppliers of cattle material to demonstrate that their supplier's cattle material does not contain prohibited cattle materials.

The agency believes that recordkeeping and records access requirements are necessary immediately. The agency, however, recognizes that recordkeeping systems cannot be put into place immediately and, therefore, to include recordkeeping requirements in this interim final rule could result in manufacturers and processors immediately being in violation of the adulteration provisions of the act with respect to human food and cosmetics because of their failure

immediately to establish and maintain the necessary records as of the effective date of this interim final rule. For that reason, we are proposing record establishment and maintenance requirements in a separate rulemaking, rather than including them in this interim final rule. Accordingly, in this issue of the **Federal Register**, we are proposing to require that those manufacturers and processor establish and maintain records to demonstrate compliance with this rule (see ''Recordkeeping Requirements for Human Food and Cosmetics Manufactured From, Processed With, or Otherwise Containing Material from Cattle''). Although the agency is pursuing a separate rulemaking on recordkeeping, we believe that some records may already be maintained that could provide the agency with valuable compliance information before a final rule on recordkeeping is issued as a result of the separate rulemaking. Therefore, we are requiring in this interim final rule that FDA be able to access already existing records that may demonstrate, or be relevant to, compliance with this rule.

E. Scope of the Interim Final Rule

The prohibitions contained in § 189.5 (b) apply to all FDA-regulated human food, except tallow and tallow derivatives. ''Human food'' is ''food'' as that term is defined in section 201(f) of the act (21 U.S.C. 321(f)), except for animal food. Specifically, ''human food'' is: (1) Articles used for food or drink for man, (2) chewing gum, and (3) articles used for components of any such article. ''Human food'' includes, but is not limited to, food additives, including substances that migrate into food from food packaging and other articles that contact food, color additives, dietary supplements and dietary ingredients, and infant formula.

The prohibitions contained in § 700.27 (b) apply to all FDA-regulated cosmetics. ''Cosmetic'' is defined in section 201(i) of the act (21 U.S.C. 321(i)) 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.

In 21 CFR 701.20, FDA explains the criteria articles must meet to be considered ''soap'' under section 201(i) of the act.

F. Legal Authority

FDA is issuing these regulations under the adulteration provisions in sections 402(a)(2)(C), (a)(3), (a)(4), (a)(5), 601(c), and under section 701(a) of the act (21 U.S.C. 342(a)(2)(C), (a)(3), (a)(4), (a)(5), 361(c), and 371(a)). Under section 402(a)(3) of the act, a food is deemed adulterated ''if it consists in whole or in part of any filthy, putrid, or decomposed substance, or if it is otherwise unfit for food.'' ''Otherwise unfit for food'' is an independent clause in section 402(a)(3). It does not seem to require that a food be filthy, putrid, or decomposed for it to be ''otherwise unfit for food.'' We conclude that a food can be ''otherwise unfit for food'' based on health risks. We seek comments on this interpretation. Because of the discovery of a BSE positive cow in the United States and the possibility of disease transmission to humans from exposure to material from infected cattle, prohibited cattle materials (SRMs, small intestine of all cattle, MS(Beef), material from nonambulatory disabled cattle, and material from cattle not inspected and passed) may present a risk to human health. Under our interpretation of section 402(a)(3), these materials are unfit for food. Under section 402(a)(4) of the act, a food is adulterated ''if it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health.'' The failure to ensure that food is prepared, packed, or held under conditions in which prohibited cattle materials do not contaminate the food constitutes an insanitary condition whereby it may have been rendered injurious to health and thus renders the food adulterated under section 402(a)(4). Under section 402(a)(5) of the act, food is deemed adulterated if ''* * * it is, in whole or in part, the product * * * of an animal which has died otherwise than by slaughter.'' Some cattle are not inspected and passed because they have died before slaughter. Material from these cattle that die otherwise than by slaughter is adulterated under section 402(a)(5).

We are also relying on the food additive provision in section 402(a)(2)(C) of the act. Any substance whose intended use results or may reasonably be expected to result in it becoming a component of food is a food additive unless, among other things, it is the subject of a prior sanction (explicit approval for a specific use by USDA or FDA prior to September 6, 1958), or is generally recognized as safe (GRAS). The regulations under 21 CFR 181.1(b) provide that, if scientific data or information shows that the use of a prior-sanctioned ingredient may be injurious to health and, thus, in violation of section 402 of the act, FDA can prohibit use of the ingredient in food. Prior sanctions are described in 21 CFR part 181. FDA is not aware of any prior sanctions that relate to the present use of prohibited cattle materials. However, to the extent any prior sanctions exist for the use of prohibited cattle materials in food, they are hereby revoked.

A determination that a substance added directly or indirectly to a food is GRAS for its intended use is generally based on specific information regarding the composition of the substance, its use, method of preparation, methods for detecting its presence in food, and information about its functionality in food as determined by experts qualified by scientific training and experience to evaluate the safety of such a substance (21 CFR 170.35). A substance added to food becomes GRAS as a result of a common understanding about the substance throughout the scientific community familiar with the safety of such substances. The basis of expert views may be either scientific procedures, or, in the case of a substance used in food prior to January 1, 1958, experience based on common use in food (§ 170.30(a)) (21 CFR 170.30(a)). Substances that are GRAS based on use prior to January 1, 1958, must be currently recognized as safe based on their pre-1958 use (See *United States* v. *Naremco*, 553 F.2d 1138 (8th Cir. 1977); compare *United States* v. *Western Serum*, 666 F.2d 335 (9th Cir. 1982)).

General recognition of safety based upon scientific procedures requires the same quantity and quality of scientific evidence as is required to obtain approval of a food additive regulation for the ingredient (§ 170.30(b)). (See *United States* v. *Naremco*, 553 F.2d at 1143). A substance is not GRAS if there is a genuine dispute among experts as to its recognition (An Article of Drug * * * Furestrol Vaginal Suppositories, 251 F. Supp 1307 (N.D. Ga. 1968), aff'd, 415 F.2d 390 (5th Cir. 1969)). It is not enough, in attempting to establish that a substance is GRAS, to establish that there is an absence of scientific studies that demonstrate the substance to be unsafe; there must be studies that show the substance to be safe (*United States* v. *An Article of Food* * * * *CoCo Rico*, 752 F.2d 11 (1st Cir. 1985)). Conversely, a substance may be ineligible for GRAS status if studies show that the substance is, or may be, unsafe, or if there is a conflict in studies.

Expert opinion that prohibited cattle materials are GRAS would need to be supported by scientific literature, and

other sources of data and information, establishing that there is a reasonable certainty of no harm from the material under the intended conditions of use. Expert opinion would need to address topics such as whether BSE infectivity can be detected and whether it is reasonably certain that the BSE agent will not be transmitted through prohibited cattle materials. The burden of establishing that a substance is GRAS is on the proponent of the substance. (See *CoCo Rico*, *supra*).

For the reasons discussed in section I of this document, the agency is declaring that prohibited cattle materials are not GRAS by qualified experts for use in human food and, therefore, are food additives. Section 402(a)(2)(C) of the act deems food adulterated ''if it is, or it bears or contains, any food additive which is unsafe within the meaning of section 409 * * *.'' Under section 409(a) (21 U.S.C. 348(a)), a food additive is unsafe unless a food additive regulation or an exemption is in effect with respect to its use or its intended use. As a result, because neither a food additive regulation, nor an exemption, is in effect for prohibited cattle materials intended for use in human food, such materials, with the exception of dietary ingredients in dietary supplements, are adulterated under section 402(a)(2)(C) of the act, and their presence in food renders the food adulterated.

Dietary supplements are considered food under the act and are included in this rule. However, the food additive definition in section 201(s)(6) of the act exempts from regulation as a food additive ''an ingredient described in paragraph (ff) in, or intended for use in, a dietary supplement.'' An ingredient described in section 201(ff) is a dietary ingredient. Therefore, a dietary ingredient, within the meaning of section 201(ff), is not subject to regulation as a food additive. FDA notes that, under this rule, ingredients containing prohibited cattle materials, and dietary supplements containing such ingredients, would be adulterated food under section 402(a)(3) and (a)(4) of the act, as unfit for food and as food prepared, packed, or held under insanitary conditions whereby it may have been rendered injurious to health. Such dietary ingredients would also be adulterated under section 402(a)(5) of the act if sourced from an animal that died other than by slaughter.

Under section 601(c) of the act, a cosmetic is adulterated ''if it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health.'' The failure to ensure that a cosmetic is prepared, packed, or held under conditions in which prohibited cattle materials do not contaminate the cosmetic constitutes an insanitary condition whereby it may have been rendered injurious to health and, thus, renders the cosmetic adulterated under section 601(c).

Under section 701(a) of the act, FDA is authorized to issue regulations for the act's efficient enforcement. A regulation that requires measures to prevent human food from being unfit for food, from being or bearing an unsafe food additive, from being the product of an animal that died otherwise than by slaughter, and to prevent human food and cosmetics from being held under insanitary conditions, allows for efficient enforcement of the act. The regulations require that manufacturers and processors of human food and cosmetics that are manufactured from, processed with, or otherwise contain, material from cattle make existing records available to FDA for inspection and copying. Once material is removed from cattle, we may not be able to obtain the information necessary to determine whether it is prohibited cattle material. For example, we would not know from examination of a spinal cord whether the source animal was over 30 months of age at the time of slaughter or whether it was inspected and passed. Therefore, the records access requirement is necessary for the efficient enforcement of this rule. Failure to comply with this rule's records access requirement renders the affected food and cosmetics adulterated under sections 402(a)(4) and 601(a) respectively.

V. Issuance of an Interim Final Rule, Immediate Effective Date, and Opportunity for Public Comment

We are issuing this rule as an interim final rule, effective immediately, with an opportunity for public comment. Section 553(b)(3)(B) of the Administrative Procedure Act (5 U.S.C. 553(b)(3)(B)) provides that, when an agency for good cause finds that notice and public procedure are impracticable, unnecessary, or contrary to public interest, the agency may issue a rule without providing notice and public comment. FDA has determined that there is good cause under 5 U.S.C. 553(b)(3)(B) and 21 CFR 10.40(d) because the discovery of BSE in a cow in the United States requires regulations in place immediately to impose restrictions on the use of cattle material in human food and cosmetics to further reduce the possibility of transmission of vCJD. Further, under 5 U.S.C. 553(d)(3), we find good cause to make the rule effective immediately. It is imperative that we act quickly to impose these restrictions on the use of cattle material in human food and cosmetics to further reduce the possibility of transmission of vCJD and ensure that there is consistent protection of the U.S. food supply by imposing upon FDA-regulated products the same restrictions related to BSE imposed upon USDA-regulated products.

FDA invites public comment on this interim final rule. The comment period on this interim final rule will be 90 days. The agency will consider modifications to this interim final rule based on comments made during the comment period. Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this interim final rule. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

This interim final rule applies to human food and cosmetics manufactured from, processed with, or that otherwise contain, material from cattle slaughtered on or after its effective date. Human food and cosmetics under the act include their components and the rule applies to these components. FDA realizes that it may be difficult, in certain instances, for manufacturers and processors to comply immediately with all of the provisions of this interim final rule. We may consider this in enforcing the rule.

FDA will address comments received and confirm or amend this interim final rule in a final rule.

VI. Analysis of Economic Impacts of the Interim Final Rule Use of Materials Derived From Cattle in Food and Cosmetics

A. Interim Final Regulatory Impact Analysis

FDA has examined the economic implications of this interim final rule as required by Executive Order 12866. Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages;

distributive impacts; and equity). Executive Order 12866 classifies a rule as significant if it meets any one of a number of specified conditions, including: Having an annual effect on the economy of $100 million, adversely affecting a sector of the economy in a material way, adversely affecting competition, or adversely affecting jobs. A regulation is also considered a significant regulatory action if it raises novel legal or policy issues. FDA has determined that this interim final rule is not an economically significant regulatory action.

1. Need for Regulation

The FSIS' interim final rule requires that specified risk materials, small intestine from all cattle, tissue from nonambulatory disabled cattle, and MS(Beef) not be used for human food. Specified risk materials include the brain, skull, eyes, trigeminal ganglia, spinal cord, vertebral column (excluding the vertebrae of the tail, the transverse process of the thoracic and lumbar vertebrae, and the wings of the sacrum), and dorsal root ganglia of cattle 30 months and older, and the tonsils and distal ileum of the small intestine of all cattle. The FSIS interim final rule requires that all of the prohibited materials be destroyed or sent to inedible rendering.

FDA, in response to the finding of an adult cow that tested positive for BSE in the State of Washington and to be consistent with the USDA in regulating cattle products that could potentially transmit BSE, is issuing this interim final rule for FDA-regulated food and cosmetics that may contain cattle material of concern. Specifically, this interim final rule regulates cattle materials that may be used in human foods (e.g., dietary supplements, food additives, color additives, infant formula) and cosmetics.

This interim final rule will not affect the incidence of BSE in cattle, which is addressed in other FDA regulations. This interim final rule will serve as a safeguard to reduce human exposure to the agent that causes BSE that may be present in cattle-derived products from domestic and imported sources. If BSE-infected cattle or cattle material is prevented from use in human food by the requirements in this rule (e.g., the requirement that cattle materials be sourced from inspected and passed animals) this interim final rule will reduce human risk by reducing human exposure to infectious materials (i.e., prohibited cattle materials).

2. Interim Final Rule Coverage

This interim final rule prohibits the use of ''prohibited cattle materials.'' These include SRMs (brain, skull, eyes, trigeminal ganglia, spinal cord, vertebral column (excluding the vertebrae of the tail, the transverse process of the thoracic and lumbar vertebrae, and the wings of the sacrum), and dorsal root ganglia of cattle 30 months and older (including rendering of these materials), and the tonsils and distal ileum of the small intestine of all cattle), small intestine of all cattle, tissue from nonambulatory disabled cattle, tissue from cattle not inspected and passed for human consumption, and MS(Beef) in all FDA-regulated human food and cosmetics.

Under this interim final rule, tallow with no more than 0.15 percent hexane-insoluble impurities or that meets the requirements of § 189.5(b) (human food) or § 700.27(b) (cosmetics) may be used in food or cosmetics. In addition, tallow derivatives are exempt from the requirements of this rulemaking. The provisions for tallow and tallow derivatives in this interim final rule are in accordance with the best guidance from the OIE and FDA's TSEAC. The interim final rule provides in §§ 189.5(c) and 700.27(c) that manufacturers and processors of human food or cosmetics that are manufactured from, processed with, or otherwise contains cattle material must make records relevant to compliance with this rule available to FDA for inspection and copying.

3. Regulatory Options Considered

In response to the concern over BSE in food and cosmetics, FDA considered three regulatory options:

- No new regulation (baseline).
- Prohibit the use of prohibited cattle materials in human food and cosmetics and require access to existing records relevant to determine compliance.
- Prohibit the use of prohibited cattle materials in human food and cosmetics and require establishment, maintenance, and access to records demonstrating that prohibited cattle materials are not used in human food and cosmetics.

*Option 1: No new regulation.*We use this option as the baseline. By definition, no costs and benefits are associated with the baseline.

Option 2: Prohibit the use of prohibited cattle materials in human food and cosmetics and require access to existing records relevant to determining compliance.

This option would prohibit the use of prohibited cattle materials in all FDA-regulated food, including dietary supplements, and cosmetics, and would require that manufacturers and processors make existing records related to compliance with the rule available to FDA for inspection and copying.

The prohibition would cover the same materials prohibited by the FSIS interim final rule and also materials from cattle that are not inspected and passed for human consumption. Because SRMs, small intestine of all cattle, nonambulatory disabled cattle and MS(Beef) are subject to the USDA's disposition requirements (e.g., destruction or rendering for purposes other than human food), we assume that generally these materials are not likely to be widely available for use in the manufacture of FDA-regulated human food and cosmetics. The manufacturers and processors of products currently using materials that are considered SRMs (e.g., the brain, skull, spinal cord) would presumably be able to continue to use these ingredients, but exclusively from cattle younger than 30 months of age. The manufacturers of FDA-regulated human food products that use rendered material would continue to use rendered material that is the product of edible rendering (e.g., edible tallow). The manufacturers and processors of products using the tonsils and the small intestine of all cattle, material from nonambulatory disabled cattle, material from cattle not inspected and passed for human consumption, and MS(Beef) would need to find substitutes for these ingredients. We assume that the recent USDA rulemaking has already led many of these manufacturers to search for alternative ingredients.

We do not have adequate information to quantify the cost of ingredient switching for human foods and request data on this subject. To the extent that this option leads to increased use of alternative ingredients, exposure to prohibited cattle materials will be reduced. Without a complete records requirement, however, the incentives to ensure that alternative ingredients are used are reduced. Access to existing records, as required by this option, would not increase the costs of this interim final rule, but would be beneficial in ensuring that acceptable cattle material is used in the manufacture of food and cosmetics.

Manufacturers of cosmetics that currently use inedible rendered materials, including tallow containing more than 0.15 percent hexane-insoluble impurities, would have to find alternative ingredients. We assume that they would switch to edible cattle rendered material, or perhaps non-cattle inedible rendering, to continue production. While we do not have

specific price information for all cattle material, edible or inedible, used in cosmetics, we were able to determine that prime edible tallow from cattle is 4 cents more per pound than inedible tallow from cattle ($0.1575 per lb. vs. $0.1975 per lb.) (Ref. 52). In comparison, the alternative fats white grease and yellow grease are less expensive than even inedible tallow ($0.01 to $0.02 per lb. less), while lard is more expensive than edible tallow ($0.06 more per lb.).

Because edible cattle material is more expensive than inedible material, the costs for inputs into cosmetic production would increase for those producers that currently use inedible cattle material and must switch to edible cattle material. FDA does not have information on the specific number of ingredient substitutions that will be made in cosmetics production as a result of this interim final rule. We assume that the increased costs of edible cattle material as an ingredient in cosmetic production would, at least in part, be passed along to cosmetics' consumers in the form of higher prices for finished products. It is unlikely that the price increases for the cosmetic inputs or for the finished products would be large enough to substantially decrease the amounts of the affected products sold. FDA requests comments on this assumption.

Even though FDA does not have a specific list of cosmetics that currently use inedible rendering as an input in production, we do have information from the year 2000 on the U.S. consumption of inedible tallow and greases used in soap, lubricants, and fatty acids (Ref. 53). We expect that these three ingredients represent a good portion of the inedible rendering that is used to produce cosmetics.

Tallow is the generally accepted term for the rendered fat from ruminant carcasses, while grease is a more generic term that could be used to describe rendered pork fat (white grease), used restaurant grease (yellow grease), or lower quality tallow (also called yellow grease). To estimate the portion of inedible tallow from cattle in the inedible tallow and greases category, we looked at the percentage of total production of inedible tallow and greases that represented inedible tallow for the year 2000, and found that inedible tallow represented 54 percent of the mixture.

Table 1 of this document shows the usage of inedible tallow and greases by category (soap, lubricant, or fatty acid), the consumption that represents the cattle portion of the material (inedible tallow) and the calculated additional costs—about $18 million—of these potential cosmetic inputs. The cost of cosmetic ingredient switching shown in table 1 represents an upper bound estimate of costs. Some cosmetic products likely use tallow derivatives, exempt from this rulemaking, or already use cattle-derived ingredients that are considered edible. Because we do not have precise information on how many cosmetic products use tallow with more than the maximum level of insoluble impurities or other inedible cattle material as ingredients, we estimate the costs of cosmetic ingredient switching to be between $0 and $18 million.

TABLE 1.—INEDIBLE TALLOW USAGE & PRICE PREMIUM FOR EDIBLE TALLOW

U.S. Consumption of Inedible Tallow & Greases, 2000	lbs	Consumption in lbs That represents Tallow Only	Price Premium for Edible Tallow = $0.04/lb
Total inedible Tallow and greases usage	3,654,200,000		
- in soap	147,620,000	79,714,800	$3,188,592
- in lubricants	102,300,000	55,242,000	$2,209,680
- in fatty acids	583,000,000	314,820,000	$12,592,800
Total increased cost of cosmetic inputs			$17,991,072

Regulatory option 2 would decrease the likelihood of human exposure to BSE in several ways. First, by making clear that prohibited cattle material cannot be used in FDA-regulated human food and cosmetics, option 2 would create an additional regulatory barrier, beyond existing regulations, between consumers and food and cosmetics potentially contaminated with BSE. Second, by deeming human food and cosmetics manufactured from, processed with, or otherwise containing, prohibited cattle materials to be adulterated, option 2 would clarify FDA's ability to prohibit importation of prohibited cattle materials. Imported products, such as gelatin, beef extracts, and dietary supplements, may contain the types of materials prohibited by the USDA, but may not fall under the scope of the USDA's import restrictions.

The benefits of this interim final rule are the value of the public health benefits. The public health benefit is the reduction in the risk of the human illness associated with consumption of the agent that causes BSE.

If we define the baseline risk as the expected annual number of cases of vCJD per year, then the annual benefits of prohibiting prohibited cattle materials for use in foods and cosmetics would be:

(baseline annual cases of vCJD - annual cases of vCJD under FDA interim final rule) x (value of preventing a case of vCJD).

An alternative way to characterize benefits is:

Reduction in annual cases in vCJD under FDA interim final rule x (value of preventing a case of vCJD)

We do not know the baseline expected annual number of cases, but based on the epidemiology of vCJD in United Kingdom we anticipate much less than one case of vCJD per year in the United States. Because the interim final rule will reduce rather than eliminate risk of exposure to BSE infectious materials, the reduction in the number of cases will be some fraction of the expected number. The value of preventing a case of vCJD is the value of a statistical life plus the value of preventing a year-long or longer illness that precedes certain death for victims of vCJD. In a recent rulemaking regarding labeling of trans fatty acids (68 FR 41433, July 11, 2003), we used a range of $5 to $6.5 million for the value of a statistical life. The value of preventing a vCJD case would be even higher because of the significant medical costs associated with the illness (Ref. 54). We estimate that the value of preventing a single case of vCJD ranges

from $5.7 to $7.1 million. This estimate includes direct medical costs, reduced ability of the ill person to function at home and at work, and the cost of premature death.

As discussed earlier in this document, the Harvard-Tuskegee study has stated that a ban on specified risk materials, including cattle brains, spinal cord and vertebral column, from inclusion in human and animal food would reduce the very few potential BSE cases in cattle by a further 88 percent and potential human exposure to infectivity in meat and meat products by a further 95 percent. This interim final rule, in conjunction with the USDA's interim final rule, will help achieve this reduction in potential human exposure. This interim final rule will also reduce potential human exposure to BSE infection in human food not covered by the Harvard-Tuskegee study. For example, this interim final rule will help ensure that a domestically produced or foreign-produced dietary supplement or ingredient contains cattle material (e.g., brain) from animals of an appropriate age.

Summary of Costs and Benefits of Interim Final Rule

The social cost of this interim final rule, which we approximate by multiplying the difference in ingredient prices by the pre-regulation quantity of ingredients, will be borne by producers and consumers of affected products. If demand is inelastic compared with supply, consumers will bear most of the social cost. If supply is inelastic compared with demand, producers will bear most of the social cost. The ready availability of alternatives for the prohibited ingredients, and the small number of products currently using them, implies that the social costs of this rule will likely be small for foods. The social costs for cosmetics will be greater. We estimate that the cost of ingredient switching for cosmetics will range from a lower bound of $0 to an upper bound of $18 million. The benefit of this interim final rule is that its requirements will—by reducing exposure to potentially infective materials—provide a safeguard against a case of vCJD occurring in humans if cattle infected with BSE enter the human food or cosmetic supply.

Option 3: Prohibit the use of prohibited cattle materials in human food and cosmetics and require establishment, maintenance, and access to records demonstrating that prohibited cattle materials are not used in human food and cosmetics.

Option 3, like option 2, prohibits the use of prohibited cattle materials in human food, including dietary supplements, and cosmetics. We explained in the discussion of option 2 that the USDA's prohibitions are not sufficient, by themselves, to ensure that prohibited cattle materials are not used in FDA-regulated food and cosmetics. Therefore, FDA must be able to determine whether prohibited cattle materials are used in the human food and cosmetics it regulates. Option 3 requires manufacturers and processors of FDA-regulated human food and cosmetics manufactured from, processed with, or otherwise containing cattle material to establish, maintain, and provide access to records documenting that prohibited cattle materials are not used in their products. Under this option, records would not be not required for human food or cosmetics containing tallow derivatives because tallow derivatives are not prohibited cattle material. The marginal difference between options 2 and 3 presented in this interim final rule is the requirements to establish and maintain records for cattle-derived materials in Option 3. The requirement of records for cattle-derived materials is the subject of an FDA proposed rulemaking published elsewhere in this issue of the **Federal Register**. Thus, Option 3 of this interim final rule represents the impacts of the requirements for the interim final rule and for the proposed recordkeeping requirement. The impact of only the recordkeeping requirement for cattle-derived materials used in food and cosmetics is fully explained elsewhere in this issue of the **Federal Register**.

Without these records, FDA may not be able to determine the age of cattle material, such as brain or spinal cord, once it is separated from the source animal. In addition, without records, the agency may not be able to determine the inspectional status of the source animals. This regulatory option would require that the manufacturer or processor retain records for 2 years after using cattle material in food or cosmetics. Records must be kept at the manufacturing or processing establishment or another reasonably accessible location.

The costs of option 3 are the $0 to $18 million ingredient switching costs calculated for option 2, plus the recordkeeping costs. We assume that some records must be created for each shipment of materials from a slaughterhouse or rendering facility to an FDA-regulated facility. We also assume that all supporting information is known by the slaughter or rendering facility. The USDA's interim final rule requires that establishments that slaughter cattle or that process the carcasses or parts of carcasses of cattle maintain daily records sufficient to document the implementation and monitoring of procedures for removal, segregation, and disposition of SRMs.

Although most FDA-regulated human food does not use a large quantity of cattle material, certain products contain substantial amounts. Some fats and oils (e.g., oleo margarine and shortening) use edible tallow and its derivatives; ice cream, yogurt, candies, flavorings, marshmallows, and mayonnaise use gelatin; and some soups, mixed entrees, cake mixes and pasta use a range of cattle material (Refs. 55 and 56).

Using establishment data from the FDA Small Business Model (which includes information on all establishments in a manufacturing sector regardless of size) (Ref. 57), FDA estimated that 132 establishments produce fats and oils, 181 establishments produce spreads, 127 establishments produce flavoring extracts, 40 establishments produce canned soups and stews, 625 establishments produce non-chocolate candy, 88 establishments produce yogurt, and 451 establishments produce ice cream. FDA cannot verify that all of these establishments actually use cattle materials that fall under the jurisdiction of this interim final rule; many may not. It is likely that all of the 132 establishments that produce fats and oils currently use tallow derivatives, not tallow, so FDA assumes that no records would be required to be kept by this establishment group. We assume that only 25 percent of the establishments from the remaining production sectors listed previously actually produce human food that is manufactured from, processed with, or otherwise contains material from cattle and therefore would be required to keep records under this option. We include only 25 percent of the establishments in our estimates because most of the manufacturers likely do not use cattle-derived ingredients in their products. FDA requests comments on this assumption.

FDA research shows that 25 establishments with U.S. addresses supply cattle-derived ingredients that are used in cosmetics (Ref. 58). These cattle-derived ingredients include albumin, brain extract, brain lipids, cholesterol and cholesterol compounds, fibronectin, sphingolipids, spleen extract, tallow, and keratin and keratin compounds. FDA research also shows that 22 foreign establishments may export these cattle-derived ingredients to U.S. cosmetic manufacturers. The U.S. cosmetic manufacturers would be required to obtain records from the foreign establishments under this

option. We therefore include these foreign establishments when we estimate the recordkeeping costs of the regulatory options in the interim final rule. Imported cosmetic products represent about 10 to 20 percent of the cosmetics products on U.S. store shelves (Refs. 59, 60, and 61). The burden of this interim final rule to foreign cosmetics input suppliers and manufacturers will be less than the burden on domestic cosmetics producers. The burden will be less for foreign cosmetics manufacturers because Europe currently imposes some requirements similar to this rule.

FDA does not have enough information on the types of cattle material used by the 47 domestic and foreign cosmetics establishments to know how often tallow derivatives (exempt from the definition of prohibited cattle materials and, therefore, exempt from the requirements under this option) are the only cattle-derived ingredient used in these products. We estimate that 75 percent (or 35) of the 47 cosmetics establishments would have to keep records for their cattle-derived ingredients. We estimate that only 75 percent will keep records because many cosmetics use tallow derivatives as their only cattle-derived material and such materials are exempt from this rulemaking. FDA requests comments on this assumption.

From FDA's dietary supplement database (Ref. 62), we are able to tell that there are 162 dietary supplement brand names that use cattle material as ingredients in their products. We assume that each brand name represents a facility that produces multiple dietary supplement products containing cattle-derived ingredients; therefore we assess recordkeeping costs for all 162 brand names. We do not have information to determine if any of the dietary supplement manufacturers use tallow derivatives (exempt from all requirements under this option) as their only cattle-derived ingredient.

Recordkeeping Costs

The USDA's BSE interim final rule requires those establishments that slaughter cattle or that process the carcasses or parts of carcasses of cattle maintain daily records sufficient to document the implementation and monitoring of procedures for removal, segregation, and disposition of SRMs. This USDA requirement would reduce the startup costs of the recordkeeping required under this option.

Recordkeeping costs include one-time costs and recurring costs. One-time costs include the costs of designing records and training personnel in the maintenance of the records. The recurring costs are the costs of ensuring that appropriate records document the absence of prohibited cattle risk materials in human food and cosmetics. The costs of retaining records and planning for an FDA request for records access are estimated to be zero. We estimate these costs to be zero becasue current business practices already dictate that records for a second year is assumed to be greater than the marginal cost of doing so. Although there is no specific time period for providing records when requested, FDA notes that records requestes costs are zero when FDA gives the records submitter 24 hours to comply. These cost estimates are consistent with cost estimates used in FDA's proposed recordkeeping requirements in ''Establishment and Maintenance of Records Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002'' (68 FR 25188, May 9, 2003).

We assume that the one-time training burden incurred for each facility is the equivalent of 1 month's on-the-job training or approximately 1/3 of an hour. This time includes both the training required for personnel to learn how to verify that shipments contain the appropriate records, and also the training required for personnel to learn how to file and maintain those records. Given current business practices, we know personnel are familiar with recordkeeping. Therefore, the requirement to maintain additional records is expected to be learned quickly. This training burden for recordkeeping is consistent with the recordkeeping training burden in the analysis for the proposed recordkeeping rule (68 FR 25188; May 9, 2003) and the records maintenance burden used in the analysis of the Juice HACCP rule (66 FR 6138; January 19, 2001). Consistent with the analysis conducted for the proposed recordkeeping rule (68 FR 25188; May 9, 2003), FDA assumes an hourly cost of an administrative worker, $25.10 per hour, which has been doubled from $12.55 wage per hour to include overhead costs. This cost, $25.10 per hour, applies to all labor costs.

We use the FDA Labeling Cost Model to estimate the one-time records design costs per facility of $1,190 per stockkeeping unit (SKU) (Ref. 63). It is likely that facilities using cattle-derived ingredients, whether the ingredients are for human food or cosmetics, will take advantage of their economies of scope and produce more than one product with these ingredients. It is probable that each establishment has several SKUs associated with products containing cattle-derived ingredients that will now require recordkeeping. To account for additional products and SKUs we multiply the record design costs per facility by 1.5 for a total design cost per facility of $1,785 ($1,095 in labor costs and $690 in capital costs).

We multiplied the cost per product per SKU by 1.5 to account for the additional records design required for the additional SKUs. The record design cost for the first affected product or SKU will be more expensive than the marginal cost of adding records for additional SKUs. This marginal cost of record design for additional SKUs could be negligible or it could come close to doubling the costs; we therefore pick 1.5, the midpoint of one and two, to be the cost multiplier.

Consistent with the analysis conducted for the proposed recordkeeping rule implementing the 2002 Bioterrorism Act, this record design cost is assumed to be shared between two facilities—the upstream facility and the downstream facility—as both will need to be involved in record production that meets the needs of both the supplier and customer for the cattle-derived ingredient.

Unlike the Bioterrism Act proposed recordkeeping rule, we do not have direct information on all the facilities covered; we do not have data on the number of slaughter plants or renderers that supply cattle material for human food and cosmetic manufacturers and processors under FDA jurisdiction. FDA does, however, have some information on the number and type of downstream facilities that receive this material. Using information on the number of human food and cosmetic manufacturers that may use cattle-derived ingredients subject to this interim final rule, we can account for the total shared records costs by assuming that each food manufacturer or processor facility listed in the table below procures ingredients from one upstream slaughter plant or renderer. We assume each manufacturing facility maintains an exclusive contractual relationship with one ingredient supplier for calculation purposes. Even if multiple input suppliers are utilized by the manufacturing facility, the marginal record set-up costs would decrease for additional suppliers. Once the facility has learned what records are required, it is less costly to keep records on additional input suppliers. FDA requests comment on this assumption.

Information on food producing facilities in Table 2 represent U.S. facilities; dietary supplement numbers account for both domestic and foreign facilities; cosmetics numbers account

for both domestic and foreign input suppliers.

TABLE 2.—FIRST-YEAR RECORDS COSTS

Type of Product Using Cattle Material	Number of Facilities Estimated to Use Cattle Materials	Costs Per Facility for Designing Records	Costs Per Facility for Training (1/3 hour * $25.10 per hour)	Total Setup Costs
Canned soups and stews	10	$1,785	$8.37	$17,934
Fats and oils	0			
Flavoring extracts	32	$1,785	$8.37	$57,388
Spreads	45	$1,785	$8.37	$80,702
Candy	156	$1,785	$8.37	$279,766
Yogurt	22	$1,785	$8.37	$39,454
Ice cream	113	$1,785	$8.37	$202,651
Dietary supplements	162	$1,785	$8.37	$290,526
Cosmetics	35	$1,785	$8.37	$62,768
Color additives	0			
Total	575	$1,785	$8.37	$1,031,189

The recurring recordkeeping cost is the cost of ensuring that appropriate records document the absence of prohibited cattle materials in human food and cosmetics.

The framework for estimating the amount of time required for FDA-regulated facilities to ensure that the records for each shipment of materials is based on the regulatory impact analysis of the proposed recordkeeping requirements in ''Establishment and Maintenance of Records Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002.'' In that analysis we estimated that 30 minutes per week would be required to ensure that records on each shipment to and from a facility contain adequate information of the contents of the package, as well as adequate information on the transporter, supplier, and receiver.

The recordkeeping requirements of this regulatory option will cover only a small fraction of all ingredients used in the human food and cosmetic manufacturing processes and only require that records of cattle-derived ingredient origin from the input supplier be verified and maintained by a food or cosmetic manufacturer or processor. Because this recordkeeping requirement is less complex than the recordkeeping requirements under the Bioterrorism Act and affects fewer ingredients, we estimate the per facility burden to be about one-half of the burden estimated for the Bioterrorism Act recordkeeping rule (68 FR 25188, May 9, 2003): 15 minutes per week, or 13 hours per year. FDA assumes that this recordkeeping burden will be shared between two entities (i.e., the slaughter plant and the manufacturer or processor of finished products containing cattle-derived ingredients).

Table 3 shows the recurring recordkeeping costs for human food and cosmetic manufacturers and processors. As stated earlier, information on food producing facilities in Table 3 represents U.S. facilities; dietary supplement numbers account for both domestic and foreign facilities; cosmetics numbers account for both domestic and foreign input suppliers.

TABLE 3.—RECURRING ANNUAL RECORDS COSTS

Type of Product (From Raw or Rendered Material That Needs Accompanying Documentation)	Number of Facilities	Annual Costs Per Facility of Ensuring That Appropriate Records Accompany Each Shipment Received (13 hours * $25.10/hour)	Total Recurring Annual Costs
Canned soups and stews	10	$326.30	$3,263
Fats and oils	0		
Flavoring extracts	32	$326.30	$10,442
Spreads	45	$326.30	$14,684
Candy	156	$326.30	$50,903
Yogurt	22	$326.30	$7,179

TABLE 3.—RECURRING ANNUAL RECORDS COSTS—Continued

Type of Product (From Raw or Rendered Material That Needs Accompanying Documentation)	Number of Facilities	Annual Costs Per Facility of Ensuring That Appropriate Records Accompany Each Shipment Received (13 hours * $25.10/hour)	Total Recurring Annual Costs
Ice Cream	113	$326.30	$36,872
Dietary supplements	162	$326.30	$52,861
Cosmetics	35	$326.30	$11,421
Color additives	0		
Total	575	$326.30	$187,625

The benefits of this option are the same as the benefits of option 2—the value of the public health benefits. The public health benefit is the reduction in the risk of the human illness associated with consumption of the agent that causes BSE. With this option, however, requiring the establishment and maintenance of records provides an additional safeguard to prevent exposure to potentially infected materials.

B. Regulatory Flexibility Analysis

FDA has examined the economic implications of this interim final rule as required by the Regulatory Flexibility Act (5 U.S.C. 601–612). If a rule has a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires agencies to analyze regulatory options that would lessen the economic effect of the rule on small entities. FDA does not believe that this interim final rule will have a significant economic impact on a substantial number of small entities.

For this interim final rule, the only cost is for those human food and cosmetic facilities that will need to switch to alternative ingredients. While food facilities may incur search costs as well as higher ingredient costs, the ready availability of alternatives for prohibited ingredients, and the small number of products currently using them, implies that these costs will be negligible for foods.

Cosmetic facilities are more likely than food facilities to experience substantial ingredient switching costs as a result of this interim final rule. As shown previously, we estimate that 35 cosmetics establishments will be affected by this interim final rule. If ingredient switching costs are closer to FDA's estimated upper bound of $18 million than to the lower bound of 0, the average cost per establishment will be about $500,000. We do not know if any of the affected establishments are small businesses. This cost would, however, be a significant economic impact for small cosmetics businesses. If the actual costs are closer to the lower bound, then the economic impact will not be significant.

Because switching ingredients is the source of the reduction in exposure to potentially infective materials, it is necessary to apply the rule's provisions to all establishments equally. We have, however, allowed small businesses some flexibility by not requiring the establishment and maintenance of records in this interim final rule. In a companion rulemaking, we propose record establishment and maintenance requirements and ask for comments on their effect on small businesses.

C. Unfunded Mandates

Title II of the Unfunded Mandates Reform Act of 1995 (Public Law 104–4) requires cost-benefit and other analyses before any rulemaking if the rule would include a ''Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year.'' The current inflation-adjusted statutory threshold is $115 million. FDA has determined that this interim final rule does not constitute a significant rule under the Unfunded Mandates Reform Act.

D. SBREFA Major Rule

The Small Business Regulatory Enforcement Fairness Act of 1996 (Public Law 104–121) defines a major rule for the purpose of congressional review as having caused or being likely to cause one or more of the following: An annual effect on the economy of $100 million or more; a major increase in costs or prices; significant adverse effects on competition, employment, productivity, or innovation; or significant adverse effects on the ability of U.S.-based enterprises to compete with foreign-based enterprises in domestic or export markets. In accordance with the Small Business Regulatory Enforcement Fairness Act, the Office of Management and Budget (OMB) has determined that this interim final rule is not a major rule for the purpose of congressional review.

VII. Paperwork Reduction Act Analysis

This interim final rule does not contain information collection provisions that are subject to review by the OMB under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). Therefore, clearance by OMB under the Paperwork Reduction Act of 1995 is not required.

VIII. Environmental Impact Analysis

FDA has carefully considered the potential environmental effects of this interim final rule and of three possible alternative actions. In doing so, the agency focused on the environmental impacts of its action as a result of disposal of unused cattle byproducts (e.g., dead animals and slaughter byproducts) that need to be handled after the rule becomes effective.

The environmental assessment (EA) considered each of the alternatives in terms of the need to provide maximum reasonable protection of human health without resulting in a significant impact on the environment. The EA considered environmental impacts related to landfill, incineration, composting, and land burial. The additional waste that might result from the selected action would be an extremely small amount compared to the total amount of waste generated by the cattle industry.

The agency has concluded that the interim final rule will not have a significant impact on the human environment, and that an environmental impact statement is not required. FDA's finding of no significant impact (FONSI) and the evidence supporting that finding, contained in an EA prepared

under 21 CFR 25.40, may be seen in the Division of Dockets Management (see **ADDRESSES**) between 9 a.m. and 4 p.m., Monday through Friday. FDA invites comments and submission of data concerning the EA and FONSI.

IX. Federalism

We have analyzed this interim final rule in accordance with the principles in Executive Order 13132. We have determined that the interim final rule does not contain policies that have substantial direct effects on the states, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we have concluded that the interim final rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement has not been prepared.

X. References

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List of Subjects

21 CFR Part 189

Food additives, Food packaging, Incorporation by reference.

21 CFR Part 700

Cosmetics, Packaging and containers, Incorporation by reference.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 189 and 700 are amended as follows:

PART 189—SUBSTANCES PROHIBITED FROM USE IN HUMAN FOOD

■ 1. The authority citation for 21 CFR part 189 continues to read as follows:

Authority: 21 U.S.C. 321, 342, 348, 371.

■ 2. Part 189 is amended by redesignating subparts B and C as subparts C and D, respectively, and by adding a new subpart B to read as follows:

Subpart B—Prohibited Cattle Materials

Sec.

189.5 Prohibited cattle materials.

Subpart B—Prohibited Cattle Materials

§ 189.5 Prohibited cattle materials.

(a) *Definitions.* The definitions and interpretations of terms contained in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) apply to such terms when used in this part. The following definitions also apply:

(1) *Prohibited cattle materials* means specified risk materials, small intestine of all cattle, material from nonambulatory disabled cattle, material from cattle not inspected and passed, or MS(Beef). Prohibited cattle materials do not include tallow that contains no more than 0.15 percent hexane-insoluble impurities and tallow derivatives.

(2) *Inspected and passed* means that the product has been inspected and passed for human consumption by the appropriate regulatory authority, and at the time it was inspected and passed, it was found to be not adulterated.

(3) *Mechanically Separated (MS)(Beef)* means a meat food product that is finely comminuted, resulting from the mechanical separation and removal of most of the bone from attached skeletal muscle of cattle carcasses and parts of carcasses, that meets the specifications contained in 9 CFR 319.5, the regulation that prescribes the standard of identity for MS (Species).

(4) *Nonambulatory disabled cattle* means cattle that cannot rise from a recumbent position or that cannot walk, including, but not limited to, those with broken appendages, severed tendons or ligaments, nerve paralysis, fractured vertebral column or metabolic conditions.

(5) *Specified risk material* means the 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), and dorsal root ganglia of cattle 30 months and older and the tonsils and distal ileum of the small intestine of all cattle.

(6) *Tallow* means the rendered fat of cattle obtained by pressing or by applying any other extraction process to tissues derived directly from discrete adipose tissue masses or to other carcass parts and tissues. Tallow must be free of prohibited cattle material or must contain not more than 0.15 percent hexane-insoluble impurities as determined by the method for ''hexane-insoluble matter,'' p. 465, in the ''Food Chemicals Codex,'' 5th Ed. (2004), incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, or another method equivalent in accuracy, precision, and sensitivity to the method in the Food Chemicals Codex. You may obtain copies of the method from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418 (Internet address *http://www.nap.edu*) and the Division of Dairy and Egg Safety (HFS–306), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD

20740. Copies may be examined at the Center for Food Safety and Applied Nutrition's Library, 5100 Paint Branch Pkwy., College Park, MD 20740, or at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202–741–6030, or go to: *http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html*.

(7) *Tallow derivative* means any chemical obtained through initial hydrolysis, saponification, or trans-esterification of tallow; chemical conversion of material obtained by hydrolysis, saponification, or trans-esterification may be applied to obtain the desired product.

(b) *Requirements.* No human food shall be manufactured from, processed with, or otherwise contain, prohibited cattle materials.

(c) *Records.* Manufacturers and processors of human food that is manufactured from, processed with, or otherwise contains, cattle material must make existing records relevant to compliance with this section available to FDA for inspection and copying.

(d) *Adulteration.* (1) Failure of a manufacturer or processor to operate in compliance with the requirements of paragraphs (b) or (c) of this section renders human food adulterated under section 402(a)(4) of the act.

(2) Human food manufactured from, processed with, or otherwise containing, prohibited cattle materials is unfit for human food and deemed adulterated under section 402(a)(3) of the act.

(3)*Food additive status.* Prohibited cattle materials for use in human food are food additives subject to section 409 of the act, except when used as dietary ingredients in dietary supplements. The use or intended use of any prohibited cattle material in human food causes the material and the food to be adulterated under section 402(a)(2)(C) of the act if the prohibited cattle material is a food additive, unless it is the subject of a food additive regulation or of an investigational exemption for a food additive under § 170.17 of this chapter.

PART 700—GENERAL

■ 3. The authority citation for 21 CFR part 700 continues to read as follows:

Authority: 21 U. S. C. 321, 331, 352, 355, 361, 362, 371, 374.

■ 4. Section 700.27 is added to read as follows:

§ 700.27 Use of prohibited cattle materials in cosmetic products.

(a) *Definitions.* The definitions and interpretations of terms contained in section 201 of the act apply to such terms when used in this part. The following definitions also apply:

(1) *Prohibited cattle materials* means specified risk materials, small intestine of all cattle, material from nonambulatory disabled cattle, material from cattle not inspected and passed, or MS(Beef). Prohibited cattle materials do not include tallow that contains no more than 0.15 percent hexane-insoluble impurities and tallow derivatives.

(2) *Inspected and passed* means that the product has been inspected and passed for human consumption by the appropriate regulatory authority, and at the time it was inspected and passed, it was found to be not adulterated.

(3) *Mechanically Separated (MS)(Beef)* means a meat food product that is finely comminuted, resulting from the mechanical separation and removal of most of the bone from attached skeletal muscle of cattle carcasses and parts of carcasses that meet the specifications contained in 9 CFR 319.5, the regulation that prescribes the standard of identity for MS (Species).

(4) *Nonambulatory disabled cattle* means cattle that cannot rise from a recumbent position or that cannot walk, including, but not limited to, those with broken appendages, severed tendons or ligaments, nerve paralysis, fractured vertebral column or metabolic conditions.

(5) *Specified risk material* means the 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), and dorsal root ganglia of cattle 30 months and older and the tonsils and distal ileum of the small intestine of all cattle.

(6) *Tallow* means the rendered fat of cattle obtained by pressing or by applying any other extraction process to tissues derived directly from discrete adipose tissue masses or to other carcass parts and tissues. Tallow must be free of prohibited cattle risk material or must contain not more than 0.15 percent hexane-insoluble impurities determined by the method for ''hexane-insoluble matter,'' p. 465, in the ''Food Chemicals Codex,'' 5th Ed. (2004), incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, or another method equivalent in accuracy, precision and sensitivity to the method in the Food Chemicals Codex.. You may obtain copies of the method from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418 (Internet address *http://www.nap.edu*) and the Division of Dairy and Egg Safety (HFS–306), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740. Copies may be examined at the Center for Food Safety and Applied Nutrition's Library, 5100 Paint Branch Pkwy., College Park, MD 20740, or at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202–741–6030, or go to: *http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html*.

(7) *Tallow derivative* means any chemical obtained through initial hydrolysis, saponification, or trans-esterification of tallow; chemical conversion of material obtained by hydrolysis, saponification, or trans-esterification may be applied to obtain the desired product.

(b) *Requirements.* No cosmetic shall be manufactured from, processed with, or otherwise contain, prohibited cattle materials.

(c) *Records.* Manufacturers and processors of cosmetics that are manufactured from, processed with, or otherwise contain, cattle material must make existing records relevant to compliance with this section available to FDA for inspection and copying.

(d) *Adulteration.* Failure of a manufacturer or processor to operate in compliance with the requirements of paragraph (b) or (c) of this section renders a cosmetic adulterated under section 601(c) of the act.

Dated: July 8, 2004.

Lester M. Crawford,

Acting Commissioner of Food and Drugs,

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