

cleaned food contact surfaces that when evaluated for efficacy, yield a reduction of 5 logs, which is equal to 99.999 percent reduction of representative disease microorganisms of public health significance. Because dietary supplements are consumed without further processing, and for consistency with other agency definitions and standards, we are persuaded to propose the FDA "Food Code" definition of "sanitize." The agency believes that there may be a number of agents that can reduce the number of microorganisms present on contact surfaces. A tolerable level of risk may be achieved by interventions that have been validated to achieve a cumulative 5-log reduction in the target pathogens. However, we do not specify the manner in which the risk is reduced. The proposed requirement mandates that you validate that the control measures are both appropriate to their operation and scientifically sound. In many cases, processors may rely on a written certification from the equipment manufacturer or may obtain a written scientific evaluation of a process, especially in cases where two or more control measures are used to accomplish the 5-log reduction in the target pathogen, to ensure that the process is adequate to destroy microorganisms of public health significance or to prevent their growth. The agency requests comments on its approach to pathogen reduction. In particular, the agency requests comments on whether all contact surfaces should be subject to proposed § 111.3 "sanitize."

Proposed § 111.3 defines "theoretical yield" as "the quantity that would be produced at any appropriate step of manufacture or packaging of a particular dietary ingredient or dietary supplement, based upon the quantity of components or packaging to be used, in the absence of any loss or error in actual production." We would complement this definition by defining "actual yield" in proposed § 111.3 as "the quantity that is actually produced at any appropriate step of manufacture or packaging of a particular dietary ingredient or dietary supplement." Comparing theoretical yields to actual yields may help identify deviations or problems in the manufacturing or packaging process. To illustrate this point, you should understand that the theoretical yield is the quantity or amount that you expect to see at a particular step, while the actual yield is the quantity or amount that you actually obtain at a particular step.

Proposed § 111.3 defines "water activity" as "a measure of the free moisture in a component, dietary

ingredient, or dietary supplement and is the quotient of the water vapor pressure of the substance divided by the vapor pressure of pure water at the same temperature." The proposed definition is consistent with the definition at § 110.3(r) and 21 CFR 113.5(w) and 114.5(h). Water activity can play an important role in promoting microbial growth, and that, in turn, can play a part in the contamination of your components, dietary ingredients, and dietary supplements.

Proposed § 111.3 defines "we" as meaning the U.S. Food and Drug Administration.

Proposed § 111.3 defines "you" as "a person who manufactures, packages, or holds dietary ingredients or dietary supplements." "You" is the recommended "plain language" term designed to make regulations easier to understand. In this proposed rule, "you" refers to any person, within the meaning of section 201(e) of the act, who engages in any activity covered by this proposed rule. You should note that "you" includes, but is not limited to, the owner of the manufacturing firm as well as supervisors responsible for ensuring that these CGMPs are followed. In other words, "you" can be the person who owns the dietary ingredient or dietary supplement company as well as persons who work for the company.

#### 4. Do Other Statutory Provisions and Regulations Apply? (Proposed § 111.5)

Proposed § 111.5 would require that you comply with the regulations in proposed part 111, and with other applicable statutory provisions, and regulations under the act, related to manufacturing, packaging, or holding dietary ingredients or dietary supplements. Other statutory provisions or regulations that may apply to the manufacture, packaging, or holding of dietary ingredients or dietary supplements include, but are not limited to: (1) The PHS Act to prevent the introduction, transmission, or spread of communicable diseases; (2) part 110 ("Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Human Food"); (3) part 113 (21 CFR part 113) ("Thermally Processed Low-Acid Foods Packaged in Hermetically Sealed Containers"); (4) part 123 (21 CFR part 123) ("Fish and Fishery Products"); (5) parts 70 through 82 (21 CFR parts 70 through 82) (for color additives); and (6) parts 170 through 189 (21 CFR parts 170 through 189) (for food additives). For example, a manufacturer who produces a dietary supplement that includes fish and fishery products, such as fish oil, would have to comply with HACCP regulations

as required by part 123 as well as these CGMP provisions, if this rule is finalized, that apply to the dietary supplement. These other statutory provisions and regulations may apply because of the type of manufacturing process used or the type of ingredient in the dietary supplement.

Certain dietary ingredients, *e.g.*, an animal-derived ingredient, may require certain manufacturing, packaging, and holding practices because, without such practices, they may pose serious public health and safety concerns related to the transmission of communicable disease. For purposes of this discussion, the term "animal-derived dietary ingredient" refers to materials, substances, tissues, body fluids, or body secretions from animals, birds, reptiles, insects, and other living creatures and substances that may be derived from them. We do not consider human tissues and other parts of humans, other than human milk, to be eligible to be a dietary ingredient under section 201(ff) of the act because such products have not been used as a "dietary substance for use by man to supplement the diet by increasing the total dietary intake" (21 U.S.C. 321(ff)(1)(E)).

Certain animal-derived dietary ingredients, as well as the handling practices associated with such ingredients, may pose serious public health and safety risks, and therefore, may require regulations. Animal-derived materials, substances, and tissues have the potential to cause serious illnesses or injuries when ingested. For example, bovine colostrum is a substance that is used in dietary supplements (Ref. 46). Bovine colostrum which is the lacteal secretion which precedes milk after a cow gives birth, likely presents the same potential health risks as does milk. Bovine milk may contain pathogenic organisms capable of causing diseases in man such as tuberculosis, undulant fever, and gastrointestinal disease (Ref. 47). Such milk must be pasteurized in accordance with 21 CFR 1240.61. We have proposed a specific requirement at § 111.65(c)(5) that would require that you sterilize, pasteurize, freeze, refrigerate, control hydrogen-ion concentration (pH), control humidity, control water activity, or use any other effective means to remove, destroy, or prevent the growth of microorganisms and to prevent decomposition. This requirement, which would apply to bovine colostrum for use in a dietary supplement, is necessary to remove certain potential health risks. Milk also may contain contaminants, such as drug residues if the cow has been treated with such substances prior to beginning lactation,