

are linked to hazards that are inherent to foods (e.g., microbial contamination and contamination with macroscopic filth).

The proposed dietary supplement CGMPs are modeled after the food CGMPs in part 110 in that they cover the scope of practices related to the receiving, inspecting, quality control operations, packaging, segregating, processing, storing, and distribution of dietary ingredients and dietary supplements. Dietary supplements require many of the same types of sanitary practices and other practices as conventional food production in order to produce a product that is not adulterated; dietary supplements are subject to many of the same hazards as are conventional foods. However, dietary supplements have their own set of unique requirements as a result of the characteristics and hazards due to their "hybrid" nature, e.g., dietary supplements can be considered as falling somewhere along the continuum between conventional foods on the one hand and drugs on the other. Thus, the CGMPs for dietary supplements need to address the characteristics and hazards of dietary supplements, the operations and processes used to manufacture dietary supplements, particularly those necessary to ensure the identity, purity, quality, strength, and composition claimed on the label.

Dietary supplements, unlike conventional foods, contain ingredients that are consumed in very small quantities, for example, in a tablet or capsule. Such ingredients may be intended to have an anticipated, specific physiological response. Such ingredients are more "drug-like" than "food-like," in part, because very small changes in the strength, purity, or quality of the ingredient can have significant, and possibly adverse, health consequences to those who ingest it. Thus, the dietary supplement CGMPs, by necessity, need to include provisions related to identity, purity, strength, quality, and composition of the product so that the dietary supplement "food" product will be manufactured in a manner that will not result in adulteration.

Further, plant products that are used to produce dietary supplements may be ground or in a powder and not easily recognized compared to conventional food that is readily identifiable (e.g., one can readily distinguish between white flour and white sugar, but not between ground plaintain and ground *D. lanata*). Thus, for the manufacturer to be sure that the dietary supplement contains the correct ingredient and the amount of the ingredient that is intended, the

manufacturer must test or examine the ingredient using appropriate methods. The "modeled after" language in section 402(g) of the act provides the agency with the flexibility to devise CGMPs that make sense for dietary supplements, and that are based on the same principles as food CGMPs in part 110, i.e., to prevent adulteration related to insanitary conditions or other conditions that may be necessary to prevent adulteration, given the nature of the specific food product and the characteristics of, and hazards inherent in, that food.

The scope of the legal authority for the proposed dietary supplement CGMPs includes the legal authorities upon which the food CGMPs are based. For example, section 402(a)(3) of the act states that 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." Section 402(a)(4) of the act states that a food is deemed 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." While section 402(a)(3) of the act focuses on the food itself, section 402(a)(4) of the act focuses on the conditions under which the food is prepared, packed, or held. Courts have adopted a broad reading of section 402(a)(4) of the act when we have taken actions to advance the public health (see *U.S. v. Nova Scotia Food Products Corp.*, 568 F. 2d 240, 248 (2d Cir. 1977)). The agency tentatively concludes that the authorities that it relied on for its umbrella CGMPs in part 110 for food are relevant to the authorities that it needs for this proposed rule for dietary supplement CGMPs. In addition, section 409 of the act is another provision that is relevant to dietary supplement CGMPs. Section 409 of the act addresses circumstances under which a food may be deemed adulterated based on the use of a food additive. Section 409 of the act is relevant to good manufacturing practices for foods, including dietary supplements, because a food would be deemed adulterated if it contained a food additive that was not used in a manner consistent with the statutory and regulatory requirements under section 409 of the act (see sections 402(a)(2)(C) and 409 of the act). Although Congress explicitly excluded "dietary ingredients," as defined in section 201(ff) of the act, from the definition of food additive, (see section 201(s)(6) of the act), ingredients other than dietary ingredients in a dietary supplement are subject to regulation as

a food additive under section 409 of the act, unless they are subject to an exception to the definition of "food additive" under section 201(s) of the act.

Moreover, dietary ingredients and dietary supplements may contain pathogenic bacteria or viruses that pose serious public health and safety concerns (Ref. 36). Botanical dietary ingredients are living plants that may contain different microorganisms. These include *Lactobacillus*, *Leuconostoc*, *Pseudomonas*, and *Xanthomonas* species and molds. Potential pathogens such as *Listeria monocytogens*, *Pseudomonas aeruginosa* and *Enterobacteriaceae* may also be present. Secondary microbial contamination from soil (*Bacillus cereus*, *Clostridium perfringens* and mycotoxin-producing molds, etc.), animal feces (*Salmonella* and *Shigella* spp., *Escherichia coli*) and handling (*Staphylococcus aureus*) can also occur during harvesting, processing, and transportation (Ref. 36). Animal-derived dietary ingredients or dietary supplements may also pose a risk. For example, bovine colostrum, the lacteal secretion which precedes milk after a cow gives birth, is a substance that is used in dietary supplements and 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 or undulant fever. Glands and other animal tissues may contain the infective agent that causes transmissible spongiform encephalopathy (TSE) if they originate from an animal infected with the disease (Ref. 37).

We have authority to issue regulations under section 361 of the PHS Act. The Secretary delegated authority to the Commissioner of FDA (the Commissioner) to exercise the functions vested in the Secretary under section 361 of the PHS Act (see 21 CFR 5.10(a)(3)). This authority authorizes the Commissioner to issue and enforce regulations that, in the Commissioner's judgment, are necessary to prevent the introduction, transmission, or spread of communicable diseases from one State to another. Because this authority is designed to eliminate the introduction of diseases from one State to another, the Commissioner may exercise the authority over the disease-causing substance within the State where the food is manufactured, packaged, or held. The Commissioner, therefore, assumes the authority to issue regulations under the PHS Act to assure that foods are manufactured, packaged, and held under conditions that will prevent the introduction, transmission,