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CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

August 8, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, MD 20852

Re: Docket No. 96N-0417, Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Dietary Ingredients and Dietary Supplements

Dear Sir or Madam:

The Consumer Healthcare Products Association welcomes the opportunity to comment on the above captioned proposed rule issued by the Food and Drug Administration in the March 13, 2003 Federal Register. CHPA is the 122-year-old trade association representing manufacturers of dietary supplements and over-the-counter medicines. CHPA members manufacture dietary supplements that would be affected by the proposed rule.

CHPA supports rules governing the regulation of dietary supplements as a special type of food. Indeed, the association has long advocated Good Manufacturing Practices for dietary supplements. This includes our comments to the agency on the 1997 Advance Notice of Proposed Rulemaking, comments on CFSAN's annual priorities, and in speeches or remarks in other forums. The Dietary Supplement Health and Education Act envisioned food-modeled GMPs for dietary supplements and we continue to support that approach. CHPA believes such an approach is consistent with industry's objective: to produce quality products that meet consumer expectations and demands.

CHPA makes the following comments to the proposed rule:

1. **The proposed rule appears to under-estimate the costs of the requirements.** While we are not able to provide precise information at this time to assist the agency in refining its economic analysis impact of the rule, and while we recognize the difficulty in making accurate assessments, the proposed rule appears to dramatically under-estimate the financial impact on firms – large, small, or in between – of the extensive requirements envisioned. It is, however, with cooperation from industry that better economic assessments can be made, including evidence to support the conclusions of the economic assessment.

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2. **CHPA supports adoption and use of a systems-based approach to product quality that controls critical points in the process.** The proposed rule stresses a prescriptive process by which many of the manufacturing controls and testing requirements are specified in detail. Sections 111.35(g); 37; 45(a)(2), (6), and (8)(i); 50; and 70 represent examples in which the proposed rule lists out extensive testing requirements and step-by-step actions. 111.50(c) alone includes 14 different types of information to be included in the batch records which could be recorded in other places. In addition, the proposed regulations create unnecessary redundancy in testing between suppliers and manufacturers and the requirement to test every batch of finished product is overly burdensome, costly and not needed if the process is properly validated. While this type of approach may provide guidance to industry for the control of some quality manufacturing systems, the specificity of such a detailed approach may not be applicable to all process systems for dietary supplements. The net result is that instead of assuring quality, some critical process control steps may be overlooked or not included in such an approach.

   Instead, the proposed rule should focus on the expected outcome of the processes. The agency should look to the principles of an outcome-based quality approach which reflects not only modern quality control thinking but also leads to better and more effective quality control system design. We are aware that the agency has used such a principle-based approach through Hazard Analysis and Critical Control Points (HACCP) in the juice manufacturing and seafood areas and we encourage consideration of these types of system design principles for dietary supplements. Under such a principle-based approach, industry would be responsible for developing and defining written procedures for each stage of the process – including raw material certification, production, and finished product analysis – and a written plan for qualifying this process. This type of approach focuses on the critical quality steps in the process and would be a more effective and efficient system for testing. CHPA is willing to work with the agency in exploring an outcomes or systems based approach to quality management of dietary supplement products.

   We recognize that our support for a quality systems approach departs from our June 6, 1997 comments on the advance notice of proposed rulemaking. But as the agency has increasingly recognized in other areas, such an approach both better encapsulates modern quality control thinking and allows flexibility as science and quality advance. (For example, FDA's "Summary Progress Report – Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach," notes the agency's intent to determine pathways to better integrate advances in quality management techniques, including quality systems approaches, into the agency's regulatory standards and systems. See www.fda.gov/cder/gmp/21stcenturysummary.htm.) The prescriptive approach taken in the proposed rule has the unintended effect of being more likely to stifle innovation that might otherwise *improve* quality.

3. **While use of ingredients which are generally recognized as safe (GRAS) is appropriate, the proposed rule should allow other formally recognized benchmarks to fill the same need.** Proposed 111.35(d) indicates that any substance in a dietary supplement other than a "dietary ingredient" should be listed as a food additive, listed as a color additive, authorized by a prior sanction, or generally recognized as safe (GRAS). In the latter case, the agency proposes that a claim that a non-dietary ingredient is GRAS be supported by an explanation (or be supported by a citation to a regulation). The agency's preamble notes that "you could not use our response to your GRAS notification as your basis for asserting compliance . . . because an FDA response letter is not the same as your explanation." See 68 Fed. Reg. 12196 (March 13, 2003).

   We believe the approach of requiring companies to self-certify through a determination in their own files the GRAS status of a non-dietary ingredient is unnecessary to assure the quality and safety of such ingredients. Instead, FDA should allow firms to use GRAS notification letters just as the remainder of the food industry does, using the approach of the April 17, 1997 proposed rule (62 Fed. Reg. 18938). Having each firm duplicate the same determination repeatedly eliminates the usefulness of allowing firms to use a GRAS notification as a form of supplier-to-manufacturer assurance.

   Further, the proposed rule should be broadened to allow other formally recognized benchmarks, or surrogates, for GRAS listing, as a method of determining the GRAS status. Such benchmarks or surrogates could include:

   - Substances listed in the USP/NF
   - Substances listed in the Food Chemical Codex
   - Substances listed in the American Pharmaceutical Association's "Handbook of Pharmaceutical Excipients"
   - Substances listed in FDA's "Inactive Ingredient Guide"

   Substances that are included in these references are generally regarded as safe based on a history of common use. It would seem reasonable for the agency to similarly recognize these substances as suitable for use in dietary supplements.

4. **CHPA agrees that the use of proven manufacturing technologies, processes and testing and other procedural control mechanisms can adequately provide assurance to prevent adulteration and misbranding.** We encourage the agency to promote the use of technology, efficiency and consequently economic incentives for industry to continually improve quality as an additional measure for compliance. The agency notes that the proposed rule seeks to establish a framework in which decisions about producing a dietary supplement are left to the manufacturer, but where the production process includes measures designed to ensure dietary supplements are manufactured in a manner that will prevent adulteration. See 68 Fed. Reg. 12194 (March 13, 2003). We agree with this view and recommend consideration of our points 2 and 7.

We would therefore advocate that the agency effectively reconcile a rule which allows either the extensive testing envisioned in the proposal, or, in the alternative, a documented process control system. The Council for Responsible Nutrition, another trade association representing the dietary supplement industry, has discussed elements of a rigorous process control system in discussions with and comments to the agency, and we commend them. Such a system would include a supplier certification program (including verification, audits, and supplier qualification); identity testing of incoming ingredients; documented in-process control procedures (both master and batch); verification of ingredient additions and yield; and, perhaps most importantly, data to demonstrate that the process consistently delivers the expected results.

5. **CHPA supports inclusion of expiration dating and stability testing in the rule.** Given the discussion of optional expiration dating (which would require stability testing to support such dating) in the Advance Notice of Proposed Rulemaking, we were surprised that such a provision was not included in the proposed rule. Both nutrition labeling regulations and the Dietary Supplement Health and Education Act require that dietary supplements meet their labeled potency throughout their shelf life (see 21 CFR 101.9(g)(4), and 21 USC 343(s)(2)(D) or (E)). But to establish that shelf life, expiration dating and stability testing are needed.

   Consumers frequently expect, if not demand, expiration dating, as do many retailers, and many dietary supplement products already use expiration dates.

   Finally, 21 USC 342(g) envisions, when necessary, expiration dating within GMPs.

   CHPA, therefore, supports inclusion of expiration dating and stability testing in the rule. Such requirements should allow a variety of scientifically sound approaches, such as accelerated stability testing, to establish expiration dates.

6. **We are concerned with the proposed rule's record retention and access requirements.** The record retention and access requirements in the proposed rule exceed those which are common for foods, and appear more like drug requirements. Congress was quite clear in 21 USC 342(g)(2) that dietary supplement GMPs should be modeled on food GMPs, not drug. Apart from limited special circumstances, such as low acid canned foods, which are more likely to involve a risk of recall, or clear statutory authority, such as record retention and access requirements under the Bioterrorism Act (e.g., one-up/one-down shipment records), the proposed rule represents a departure from FDA's past approaches and is not within the agency's inspection authority.

   We urge the agency to revisit and limit proposed 111.125 to more closely model a food GMP approach.

The plain intent of the Food, Drug and Cosmetic Act's factory inspection provision further underscores the limited nature of FDA's access authority for food and dietary supplements. 21 USC 374(a) is very broad and extensive as to records access for drugs, restricted devices, and infant formula. In contrast, records access for food (and dietary supplements) is more circumscribed.

7. **Flexibility in approaches can lead to the same end without creating a conflict between a systems approach and a testing approach.** As noted throughout several aspects of these comments, different approaches, when well designed and rigorously implemented, can support a quality system that delivers quality products. Developing a systems approach, contrasted with spelling out a detailed checklist of requirements and testing to support them, need not be seen as entirely contradictory. They are rather two different perspectives that look toward the same quality end. On the basis of meeting that quality end, then, having the flexibility to demonstrate that a systems approach plan is met can be done either through plan control point documentation *or* by having extensive, firm-specific and identified testing documentation. A HACCP-inspired approach and a more traditional 'specification and test' approach need not be seen as mutually exclusive.

Conclusion. Finally, CHPA looks forward to continued cooperation with the agency as plans are made to finalize GMPs for dietary supplements. Having quality systems and quality assurance in place remains the goal of all. We would also hope that the agency considers the need for training seminars involving both impacted firms and FDA field officers as implementation approaches. We would welcome the opportunity to work with the agency and other interested parties toward that end.

Respectfully submitted,

F. Razzaghi

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DB/FR/DCS/mm

cc: Karen Strauss, CFSAN (HFS-821)
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