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BY FACSIMILE AND FEDERAL EXPRESS

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive
Room 1-23
Rockville, MD 20857

Re: Current Good Manufacturing Practice for Dietary Supplements [Docket No. 96N-0417]

Ladies/Gentlemen:

On behalf of our client National Nutritional Foods Association ("NNFA"), a trade association of manufacturers, distributors and retailers of dietary supplements and other natural food products, we submit the following comments on FDA's above-referenced Advance Notice of Proposed Rulemaking ("ANPR") relating to Current Good Manufacturing Practice ("CGMP") in Manufacturing, Packing or Holding Dietary Supplements (62 Fed. Reg. 5700-5709, Feb. 6, 1997).

SUMMARY OF COMMENTS

NNFA supports the principle of promulgating CGMP regulations for dietary supplements. However, upon further consideration of the initial draft set forth in the ANPR, NNFA believes that certain aspects of the proposal need to be modified to bring the rules more in accord with the CGMP regulations for conventional foods, and to permit compliance by small as well as large manufacturers. NNFA does not favor a HACCP approach for dietary supplements. We address concrete issues below, followed by responses to the nine specific questions posed by FDA in the ANPR.

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A. Comments on Proposal

1. Need for Regulations

NNFA takes the position that CGMP rules for dietary supplements are desirable, not only to fulfill an intent of the Dietary Supplement Health and Education Act of 1994 ("DSHEA") (21 U.S.C. §342(g)), but also to provide uniform standards for the supplement industry regarding the production of safe and quality products.

As mandated by DSHEA, any CGMP regulations for dietary supplements must be modeled on the existing CGMP rules for conventional foods in 21 C.F.R. Part 110. As such, CGMP rules for dietary supplements should be general in nature (as the food CGMP's are), and should include more specific standards only for tests necessary to assure the identity, potency and quality of individual dietary ingredients and dietary supplements.

NNFA further maintains that any CGMP standards issued by FDA should be promulgated by notice-and-comment rulemaking. While DSHEA permits but does not require rulemaking, the procedural safeguards afforded by the Administrative Procedures Act are essential to protect the supplement industry's interests in this area..

2. Reliance on Supplier Certifications

Subsection (c)(7)(v) of the Production and Process Control section, which would allow manufacturers of dietary supplements to rely upon certificates of analyses from suppliers of raw materials (dietary ingredients) for product specifications other than identity, should be modified to delete the requirement that a manufacturer "establish the reliability of the supplier's analyses." This additional provision defeats the purpose of permitting a manufacturer to rely on a Certificate of Analysis to ensure that a given dietary ingredient meets such specifications. It is also highly impractical, because raw material suppliers are unlikely to permit on-site inspection and validation of their production methods.

3. "Plant Management" Language Not Appropriate

The Personnel section would provide that "plant management" shall take particular measures and precautions regarding employees involved in dietary supplement production. Not only is the term "plant management" undefined, but it has implications for individual criminal liability under the Park standard applicable to violations of the Federal Food, Drug, and Cosmetic Act ("FD&C Act"). Any CGMP regulations adopted should be written in terms of what the requirements are, not

who is responsible for the requirements. Responsibility is an enforcement discretion matter that should not be part of CGMP rules.

4. "Supervision" Needs Clarification

The provision in subsection (d) of the Personnel section that "[R]esponsibility for assuring compliance" by "all personnel" with "all" CGMP requirements "shall be clearly assigned" likewise has inappropriate Park implications. Further, compliance with each and every CGMP requirement cannot be absolutely insured. While assignment of particular duties to qualified personnel can be an appropriate CGMP standard, the terms "responsibility", "assurance" and "all" should be deleted from this subsection.

5. Changes to Quality Control and Laboratory Operations Section

(a) If subsection (a) (i) in the Quality Control and Laboratory Operations section is adopted, "equipment" should be included as an item over which the quality control unit has authority to approve or reject.

(b) If expiration dating subsection (c) (1) of the same section is adopted, the language "meets label claim" should be substituted for "meets established specifications."

6. Instrument and Control Accuracy

The proposed requirement in Subsection (a)(8) of the Equipment and Utensils section that all instruments and controls used in all aspects of dietary supplement manufacturing should be accurate strongly implies a validation requirement. Since validation is a standard applicable to drug but not to food CGMP, clarification is needed that this section does not mandate any validation.

7. Master and Batch Control Records

(a) Such records, if ultimately required, should be kept only for the manufacture of finished dietary supplement products, not for dietary ingredient raw material components, which are typically received from outside suppliers. Subsection (a) of the Production and Process Controls section should be modified accordingly.

(b) The definition of a "batch" should be distinguished from the definition of a "lot." A lot is generally a larger amount of raw material from which one or more individual batches are made. The Definitions section should be amended accordingly.

8. "Intent" to Provide Label Claim

(a) The requirement in Subsection (a)(2)(ii) of the Production and Process Controls section that each batch be formulated with the "intent to provide" 100% of a dietary ingredient once again implicates potential criminal liability, since intent to defraud or mislead is an element of a felony penalty under the Section 303(c) of the FD&C Act. If this provision is adopted, a different term than "intent" should be used.

(b) The term "amount" should be substituted for "weight or measure" in this and other provisions of the document, for clarity and simplification.

9. Deviations

The requirement in subsection (a)(3) of the Production and Process Controls section that any deviation from written specification, standards, test procedures or laboratory control mechanisms be recorded and justified is, again, a provision from the drug but not the food CGMP regulations. It should be deleted.

10. Microbiological Testing

Subsection (c)(7)(ii) of the Production and Process Controls section would mandate microbiological tests for each raw material "liable to microbiological contamination that is objectionable in view of its intended use." This is too vague and open-ended a standard for when microbiological testing is required. A more specific standard is desirable (e.g., testing required "when microbiological contamination is reasonably possible, based on the source and method of manufacture of the raw material").

11. Metal Content

While subsection (d)(9) of the Production and Process Controls section would require effective measures against inclusion of metal in a finished dietary supplement product, certain dietary

ingredients (e.g., selenium) are metals. Dietary ingredients of metal origin should be explicitly excluded from the application of this subsection.

12. Lot Numbers

Subsection (e)(6) of the Production and Process Controls section would require assignment of lot numbers that permits determination of "the history of the manufacture and control of the batch." This language is somewhat vague; again, more specificity is advisable (e.g., "determination of the dates of manufacture of the batch, and of the production and process controls used in connection therewith").

13. Complaint Files

Subsection (d) of the Warehousing, Distribution and Post-Distribution Procedures section would require maintenance of records of complaints. Clarification is needed that maintenance of such files will not require production of such files during an FDA inspection, since section 704 of the FD&C Act does not authorize FDA to have access to such files, and they are not required by the food CGMP regulations.

14. Implementation

A minimum of 18 months from the date of publication of any final CGMP regulations should be the effective date for compliance. Many small manufacturers will need lead time to purchase equipment and establish procedures for such procedures as dietary ingredient identity testing.

B. Responses to Specific FDA Questions

1. Defect Action Levels Inappropriate

(a) While DAL's provide a useful bright line for regulatory purposes in the food area, they are FDA-created enforcement guidelines which are not part of the food CGMP's. Also, the ANPR's provision that DAL's will be established when "necessary and feasible to do so" does not address who makes this determination (FDA? individual companies? trade associations?) For these

reasons, NNFA submits that DAL's are not appropriate for inclusion in CGMP regulations for supplements.

(b) The ANPR's statement that botanical ingredients in dietary supplements may result in greater consumer exposure to such ingredients is incorrect. Generally, botanical ingredients are present in dietary supplements in approximately the same amounts normally consumed in conventional foods. In addition, where supplements contain extracts or concentrates of botanical ingredients, the methods used to extract or concentrate the botanicals serve to remove materials which might have caused consideration of the need for establishing a DAL.

2. Identity Tests

If adopted, the proposed requirement for a dietary supplement manufacturer to conduct identity tests to verify the identity of incoming lots of dietary ingredients (subsection (c)(7)(iv) of the Production and Process Controls section) should be amended to state specifically that any appropriate, verifiable analytical methods can be utilized. This is particularly apt where an identity test for a particular ingredient (e.g., ingredients in many botanical products) is not contained in an official compendium (e.g., USP, NF). Acceptable methodology should include voluntary methods such as those contained in the AOAC, as well as other less formal methods. Traditional organoleptic methods and other sensory methods should also be acceptable.

3. No Broad Adulteration Standard

Throughout the ANPR, standards are set forth to prevent dietary ingredients or dietary supplements "from becoming adulterated." FDA also specifically questions whether the supplier certification against filth or microorganism content that are authorized by the food GMP's need to be supplemented by additional testing for other substances, such as pesticide residues.

NNFA maintains that a broad "from becoming adulterated" criterion goes beyond the proper purpose of CGMP regulations. The statutory purpose of the drug CGMP purpose in the FD&C Act is confined to providing assurance of product identity, strength, quality and purity (21 U.S.C. §351(a)(2)(B)). The food GMP's are primarily intended to prevent product contamination. However, to broaden the purpose of CGMP's for dietary supplements to preclude all of the many different types of adulteration provided by the FD&C Act goes well beyond the appropriate scope of CGMP rules. It also is too high a standard for manufacturers, who can and should only be held responsible for acts over which they have control.

4 & 5. Procedure and Illness or Injury Documentation Exceed Food CGMP

Subsection (a)(3) of the Quality Control and Laboratory Operations section would require that all responsibilities and procedures applicable to product quality control "shall be established in writing and followed ..." Also, FDA seeks comment on whether dietary supplement manufacturers should be required to establish procedures for evaluating and documenting illness or injury reports.

Neither of these provisions are contained in the food CGMP regulations. Under the directive of DSHEA that dietary supplement CGMP rules be modeled on the food CGMP rules, they should be deleted. An illness or injury evaluation requirement is part of the much more stringent drug CGMP's. As for quality control documentation, there is unwarranted potential criminal liability if a CGMP rule requires all such procedures to be in writing. It is sufficient if a dietary supplement manufacturer is required utilize appropriate quality control procedures. Adoption of written QC SOP's should be voluntary.

6. No GRAS Evaluation

FDA's query whether dietary supplement manufacturers should be required to evaluate the safety of dietary ingredients should clearly be answered in the negative. A GRAS list of dietary ingredients was explicitly considered during negotiations on DSHEA, and rejected. Manufacturers of supplements containing new dietary ingredients are required to comply with the 75 day prior substantiation and notification requirement of DSHEA. This is the safety assessment decided on by Congress for supplements, and it cannot be expanded absent an explicit statutory change. Moreover, manufacturers of dietary supplements are responsible for the safety of their products under product liability law principles.

7. Computer Controls

Computer hardware and software are simply specialized plant equipment, and therefore need no additional level of regulation.

8. HACCP Inappropriate

NNFA opposes adoption of a Hazard Analysis Critical Control Points system for dietary supplements. While a HACCP system is flexible, food industry experience with HACCP is

very limited, and it has never been utilized in the dietary supplement industry. Moreover, unlike CGMP's, HACCP lacks particular standards designed to assess identity, strength and quality on an ingredient-by-ingredient and a product-by-product basis, which is a vital part of any regulatory system governing dietary supplement manufacturing.

9. One Set of CGMP Standards

NNFA appreciates the agency's recognition of the segmentation and specialization of the dietary supplement industry. Nonetheless, the Association believes that there should be a single, uniform set of CGMP standards that can be met by both small and large manufacturers, and by different segments (raw material as well as finished products manufacturers) within the industry. Broad standards that can be met by the various companies in the industry are preferable to distinct rules for particular types of companies. In addition, since customers routinely request continuing FDA guarantees, CGMP's have contractual implications, and all dietary supplement manufacturers should be able to meet any CGMP regulations that are adopted.

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NNFA stands ready to engage in continued cooperation with FDA in the development workable CGMP rules for dietary supplements. We trust our comments will be useful in this regard.

Respectfully submitted,

NATIONAL NUTRITIONAL FOODS ASSOCIATION

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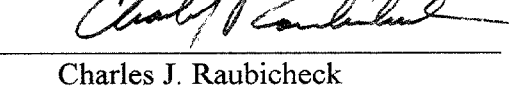
By 
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