August 11, 2003

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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 Practices in Manufacturing, Packing, or Holding Dietary Ingredients and Dietary Supplements

Dear Sir/Madam:

Nutraceutical Corporation (Nutraceutical) submits the following comments on the Food and Drug Administration's (FDA's) proposed regulations for current good manufacturing practices (CGMPs) in the manufacturing, packaging, or holding of dietary ingredients and dietary supplements. Nutraceutical is one of the largest manufacturers and marketers of dietary supplement products in the United States, with over 3,000 SKUs of dietary supplements manufactured, bottled or distributed in or from our facilities. Nutraceutical and other responsible manufacturers have already implemented effective CGMPs based in large part on prior industry submissions, including the use of third-party auditors to verify compliance, and, therefore, serve as a valuable source of information as to what will work and what will not work with respect to the proposed rule.

We are aware that the National Nutritional Foods Association (NNFA) and the Council for Responsible Nutrition (CRN) have submitted or are in the process of submitting detailed, comprehensive comments on the dietary supplement CGMPs proposal. In the case of NNFA, we have reviewed the actual copy submitted but in the case of CRN, we have not yet reviewed the final copy. We do not intend to duplicate the work of NNFA and CRN; therefore, we are providing below our comments only on the more salient issues they addressed and on certain issues where our views may differ from theirs. We note that we have not had the opportunity to complete our own economic analysis or review the comments of other industry participants. Accordingly, at the outset we wish to note and request that Nutraceutical be given the opportunity to submit further comments within 28 days of the date of this letter (or such longer period as FDA may grant to other parties), based on our completion of the foregoing steps.

Industry has been anxiously awaiting the publication of the dietary supplement CGMPs. The CGMPs, as currently drafted, will require all companies involved in the manufacture, holding, or packaging of dietary supplements or dietary ingredients to adhere to certain uniform practices that will better ensure the quality and safety of all dietary supplement products. Final dietary supplement CGMPs are

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needed to provide a level playing field and to eliminate the unacceptable practices of some companies that have damaged the reputation of the industry. However, to make the CGMPs effective, FDA must enforce the final rule; otherwise, those companies currently ignoring FDA dietary supplement regulations will continue to do so, to the detriment of responsible manufacturers and consumers.[1]

Nutraceutical commends FDA's efforts to work with industry and its efforts to create the proposed dietary supplement CGMPs, and these efforts must continue. However, as explained below, FDA has unfortunately ignored the CGMPs proposed by industry and has exceeded its statutory authority in proposing some of the CGMPs.[2] Specifically, FDA has proposed dietary supplement CGMPs that are the same as or that more closely resemble the drug CGMPs than the food CGMPs, which contravenes Congress' express mandate that the dietary supplement CGMPs be modeled after the food CGMPs. Furthermore, FDA does not have the statutory authority to require finished product testing or to require "citations" or "explanations" for generally recognized as safe (GRAS) ingredients, nor does FDA have the unfettered authority to inspect and copy dietary supplement CGMP records.

In addition, it is counter-productive and unfair to extend the compliance date for small businesses to three years, and it is illogical to impose dietary supplement CGMP requirements on raw material suppliers. We also believe it would be unfair to publish in the final rule a requirement for expiration dating, as has been requested by both NNFA and CRN, and such a requirement would not be consistent with food CGMPs in any case. Finally, Nutraceutical

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[1] In the preamble, FDA stresses public health concerns based on several examples of adulterated, misbranded or mislabeled dietary supplements as one of the primary reasons for the proposed CGMPs. 68 Fed. Reg. 12,158, 12,161-63 (Mar. 13, 2003). FDA also implies that dietary supplements are not subject to FDA regulation, and suggests that these examples of adulteration are the result of the inability of FDA to regulate dietary supplements. Id. at 12,161-62. We object to FDA's continued assertion that dietary supplements are "unregulated" or that FDA does not have authority to remove adulterated products from the market or prosecute irresponsible manufacturers or marketers. We also wish to point out that a rigorous enforcement program by FDA will do more to prevent adulteration than the mere existence of dietary supplement CGMPs, and that the purpose of dietary supplement CGMPs should be to improve and harmonize processes and sanitation (which is the primary purpose of food CGMPs) rather than prevent adulteration.

[2] These comments do not provide a comprehensive list of instances where FDA's proposal exceeds the agency's authority, but rather provide examples that will have a dramatic and negative impact on industry without any real benefit to consumers or public health.

requests that FDA clarify the testing procedures for contaminants and delete the section on consumer complaint requirements.

I. FDA Has Exceeded Its Statutory Authority With Respect to Certain CGMP Proposals

A. FDA's Proposed CGMPs Are Not Sufficiently Modeled After Food CGMPs

In Section 402(g)(2) of the Federal Food, Drug, and Cosmetic Act (FDC Act), Congress expressly restricted the scope of the dietary supplement CGMPs to those implemented for food: "Such [CGMP regulations] shall be modeled after [CGMP] regulations for food." 21 U.S.C. § 342(g)(2) (emphasis added). In the preamble to the proposed rule, FDA stated repeatedly that the dietary supplement CGMPs are "modeled after [the] food CGMPs." 68 Fed. Reg. 12,158, 12,165-67 (Mar. 13, 2003). However, the actual proposed dietary supplement CGMPs more closely resemble the drug CGMPs than the food CGMPs in many important respects. For example:

- The food CGMPs require that "[a]ny water that contacts food or food-contact surfaces shall be safe and of adequate sanitary quality," 21 C.F.R. § 110.37(a), but the proposed dietary supplement CGMPs would require that "[w]ater that contacts components, dietary ingredients, dietary supplements, or any contact surface" meet "the National Primary Drinking Water regulations prescribed by the Environmental Protection Agency under 40 C.F.R. Part 141 and any state and local government requirements," 21 C.F.R. § 111.15(d)(2)[3], which is similar to the drug CGMPs, 21 C.F.R. § 211.48(a) (requiring potable water to meet the standards prescribed in 40 C.F.R. Part 141).

- The proposed dietary supplement CGMPs would require that instruments used in the "manufacturing or testing [of] a component, dietary ingredient, or dietary supplement," and equipment used to "manufacture, package, label, and hold a dietary ingredient or dietary supplement" be calibrated and that the calibration be documented. 21 C.F.R. §§ 111.25(b)(1), (c)(1), (2), (d), (f), 111.30(a), (b)(1), (2), (c). This requirement is similar to the drug CGMPs. See 21 C.F.R. § 211.68 (requiring "[a]utomatic, mechanical, or electronic equipment . . . including computers" that are used in the "manufacture, processing, packing, and holding of a drug product" to be "routinely calibrated, inspected, or checked according to a written program," and requiring documentation of the calibration). The food CGMPs do not require calibration of instruments or equipment. See 21 C.F.R. Part 110.

- The proposed dietary supplement CGMPs would require that "each finished batch of the dietary ingredient or dietary supplement produced" be tested before release

[3] All citations to § 111 refer to the proposed CGMPs in the March 13, 2003, Federal Register.

"for distribution to determine whether established specifications for identity, purity, quality, strength, and composition are met" if there are "scientifically valid analytical methods available to conduct such testing." 21 C.F.R. § 111.35(g)(1). If there are no such scientifically valid analytical methods available for testing, then testing must be performed on incoming materials and in-process. 21 C.F.R. § 111.35(g)(2)(i), (ii). This requirement is similar to drug CGMPs, which require testing for "each batch of drug product" to determine whether "satisfactory conformance to final specifications" have been achieved. 21 C.F.R. § 211.165(a). There are no batch testing requirements in the food CGMPs. See 21 C.F.R. Part 110.

- The proposed dietary supplement CGMPs would establish elaborate packaging and labeling controls similar to the drug CGMPs. 21 C.F.R. §§ 111.70(a)-(h), 211.122, 211.125, 211.130, 211.134. The food CGMPs do not have packaging and labeling control requirements; rather, food manufacturers are only required to ensure that "[f]illing, assembling, packaging, and other operations" be conducted in a way to protect the food from contamination. 21 C.F.R. § 110.80(b)(13).

- The proposed dietary supplement CGMPs have extensive holding and distribution requirements, which include the maintenance of records for returned products. 21 C.F.R. § 111.85(a)-(e). The drug CGMPs have similar requirements. See 21 C.F.R. §§ 211.142, 211.150, 211.204, 211.208. The warehousing and distribution requirements for food CGMPs only require that the "[s]torage and transportation of finished food" be under conditions that will protect the food from contamination and deterioration. 21 C.F.R. § 110.93.

- The proposed dietary supplement CGMPs would require records of consumer complaints, 21 C.F.R. § 111.95(e), as do the drug CGMPs, 21 C.F.R. § 211.198(b). The food CGMPs do not include consumer complaint handling requirements. See 21 C.F.R. Part 110.

- The proposed dietary supplement CGMPs would mandate extensive recordkeeping requirements, similar to the drug CGMPs. See 21 C.F.R. §§ 111.25(f) (calibration records), 111.30(c) (automatic, mechanical, or electronic equipment records), 111.35(o) (production and process control records), 111.37(d) (quality control records), 111.40(c)(2) (component, dietary supplement, packaging, and label receiving records), 111.45(d) (master manufacturing records), 111.50(i) (batch production records), 111.60(b)(3) (laboratory examination and testing records), 111.70(h) (packaging and label operations records), 111.85(f) (returned dietary ingredient and dietary supplement records), 111.125 (general recordkeeping regulation); 21 C.F.R. Subpart J (Records and Reports for Drug Products). The food CGMPs do not explicitly require records.

FDA has attempted to rationalize the overreaching nature of the proposed dietary supplement CGMPs by stating that

> 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 . . . . 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. . . .
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> 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.

68 Fed. Reg. at 12,166 (emphasis added). This explanation for the more stringent dietary supplement CGMPs is an admission that the proposed dietary supplement CGMPs were modeled after the drug CGMPs, not the food CGMPs. Further, the argument that dietary supplements are not "food-like" because they contain basically the same ingredients as found in food but in small quantities is illogical. Finally, there is no support for the concept that dietary supplements are different from foods[4] based on physiologic effects or because of safety concerns. Numerous conventional foods are expected to have similar responses, as evidenced by the growing number of conventional food health claims.[5] Consumers rely on the information in the Nutrition Facts boxes of conventional foods to ensure that they are getting enough fiber, calcium, folic acid, and other nutrients known to provide health benefits, yet FDA does not require drug-like CGMPs for conventional foods. With respect to safety, errors in food ingredients, such as the inadvertent addition of peanuts, milk, or eggs, are a much more significant public health problem than the "very small changes in the strength, purity, or quality" of dietary supplement ingredients.

Whether dietary supplements are more "drug-like" than "food-like" is irrelevant for purposes of drafting the dietary supplement CGMPs. Congress specified that the dietary supplement CGMPs model the food CGMPs, not the drug CGMPs. Congress could have directed the agency to use the drug CGMPs as a model or provided FDA with broader or

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[4] Congress expressly specified that dietary supplements "shall be deemed to be a food within the meaning of this Act." FDC Act § 201(ff), 21 U.S.C. § 321(ff).

[5] See, e.g. 21 C.F.R. §§ 101.72 (calcium and osteoporosis health claim), 101.79 (folate and neural tube defects health claim), and 101.81 (soluble fiber and coronary heart disease health claim).

unrestricted authority to promulgate CGMP regulations for dietary supplements, but Congress did not.

The courts have consistently reined in FDA's attempts to promulgate regulations that exceed the scope of the agency's statutory authority. In FDA v. Brown & Williamson Tobacco Corp., the Supreme Court rejected FDA's attempt to regulate the commercial distribution of cigarettes. 529 U.S. 120 (2000). More recently, the United States Court of Appeals for the Second Circuit found that FDA's regulation requiring unit-dose packaging for iron supplements exceeded the scope of FDA's authority to regulate dietary supplement products under the FDC Act. Nutritional Health Alliance v. FDA, 318 F.3d 92 (2d Cir. 2003). "Regardless of how serious the problem an administrative agency seeks to address, . . . it may not exercise its authority 'in a manner that is inconsistent with the administrative structure that Congress enacted into law.'" Brown & Williamson, 529 U.S. at 125, quoting ETSI Pipeline Project v. Missouri, 484 U.S. 495, 517 (1988). FDA has exceeded its statutory authority by promulgating proposed dietary supplement CGMPs that go far beyond the food CGMPs, in direct violation of Congress' order.

B. FDA Lacks the Authority to Require Finished Product Testing of Dietary Supplements; Such Testing is Prohibitively Expensive in Any Case

The proposed dietary supplement CGMPs would require manufacturers to ensure through testing that each finished batch of the dietary ingredient or dietary supplement meets its established specifications for identity, purity, quality, strength, and composition. 21 C.F.R. § 111.35(g)(1). However, any mandated finished product testing for dietary supplements is outside the scope permitted by law and should be eliminated from the proposed rule. See FDC Act § 402(g)(2). The FDC Act unambiguously requires that the dietary supplement CGMPs be modeled after the food CGMPs, not the drug CGMPs. The requirement of finished batch testing of dietary supplements mirrors the drug CGMPs, not the food CGMPs, which are void of any such testing. See 21 C.F.R. §§ 111.80, 211.165(a). Therefore, FDA has exceeded its authority in requiring finished batch testing for dietary supplements.

NNFA states in its comments that finished product testing would make it impossible for small- to medium-size companies to produce multiple ingredient products. Nutraceutical would add that such testing would make certain products prohibitively expensive even for large dietary supplement manufacturers. Even though Nutraceutical has an in-house laboratory, we cannot create a multivitamin product containing dozens of ingredients, test each batch of finished goods for each ingredient, and sell the product at a price that consumers would be willing to pay for the product. It is simply too expensive to test each batch of multi-ingredient products for each ingredient.

Accordingly, instead of requiring the testing of each dietary supplement batch, FDA should permit companies to verify compliance with specifications through various means, including supplier guarantees or certifications or using an expert in CGMPs to implement a plan for compliance. The focus should be on a written plan that works for the particular product at issue, not on one scheme for the entire industry that will be very costly and unnecessary in

virtually all cases. Where batch testing might be needed, one effective and much less costly alternative would be to test several batches of finished products and then move to periodic testing. Furthermore, testing should be allowed to be performed on a product population sampling based on the contents of the package.

In sum, there are other ways for companies to ensure compliance with dietary supplement specifications that would be effective but much less costly than testing every batch. FDA should provide companies the flexibility to devise testing procedures that work for their particular products and manufacturing facilities and not unduly burden companies with specific and unnecessary testing procedures.

C. FDA Lacks the Authority to Inspect or Copy CGMP Records in the Absence of a Determination That a Product Is Adulterated

FDA's proposed dietary supplement CGMPs would require that dietary supplement firms make and maintain numerous records to reflect compliance with the CGMPs. These records include, but are not limited to, master manufacturing records (§ 111.45(d)), batch production records (§ 111.50(i)), consumer complaint records (§ 111.95(e)), and packaging and label operations records (§ 111.70(h)). The proposed recordkeeping regulation requires that all of these records be available to FDA during an inspection. 21 C.F.R. § 111.125(c). Under the proposed regulation, FDA maintains that the failure to have a required record during an FDA inspection would mean that a product is adulterated under § 402(g) of the FDC Act. 68 Fed. Reg. at 12,168. Further, according to FDA, a firm's failure to make available to FDA records covered under the proposed CGMP regulations could result in civil or criminal penalties. Id. at 12,171 ("Persons subject to regulation under the act and its implementing regulations may face civil or criminal action if they fail to comply with the act or our regulations.") (citation omitted).

FDA lacks the authority to compel the production of either food or dietary supplement CGMP records during a routine FDA inspection. Section 704(a) of the FDC Act authorizes FDA to inspect any facility where food products are manufactured or processed. Until recently, the statute only required food firms, including dietary supplement companies, to provide labeling for certain products for inspection or copying during FDA inspections. 21 U.S.C. § 374(a).

On June 12, 2002, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (the "Bioterrorism Act") was enacted. Pub. L. No. 107-188, 116 Stat. 594 (2002). The Bioterrorism Act amended Section 704 of the FDC Act to extend FDA's authority to inspect processing records of persons who manufacture, process, pack, transport, distribute, hold or import foods. Pub. L. No. 107-188, § 306(b)(1), 116 Stat. 670 (2002). However, FDA's authority to inspect or copy such records is limited to those rare instances when the Secretary has "a reasonable belief that an article of food is adulterated and presents a threat of serious adverse health consequences or death to humans or animals." Id. (emphasis added). By comparison, FDA is authorized to inspect and copy records for drug and device firms at any time during an FDA inspection, without a predetermination that a product is adulterated. 21 U.S.C. § 374(a).

Mere possible adulteration of a food is not enough to trigger FDA's inspection authority under the Bioterrorism Act. The Act's title (i.e., Bioterrorism Act) and the requirement that the food at issue pose a "serious adverse health consequence or death" indicate that Congress intended FDA to use this record inspection authority only when a food appears to have been the subject of terrorism or some other serious, related act.

The proposed dietary supplement CGMPs would impose a three year recordkeeping requirement on firms. 21 C.F.R. § 111.125(a). Under the Bioterrorism Act, however, FDA is authorized to promulgate recordkeeping regulations with a record retention period of "not longer than two years." Pub. L. No. 107-188, § 306(a), 116 Stat. 669 (2002). Therefore, to the extent that records must be kept for dietary supplement CGMPs, the records may be required to be kept only for a maximum of two years.

In sum, the proposed recordkeeping regulation in the dietary supplement CGMPs exceeds the agency's statutory inspection authority. FDA must change the regulation to reflect its limited inspection authority under Section 306(a) of the Bioterrorism Act or face possible legal challenges to this regulation.[6]

D. Proposed Section 111.35(d) Is Without Statutory Authority and Is Unnecessary and Confusing

Proposed 21 C.F.R. § 111.35(d) states that every substance or component in a dietary supplement that is not a dietary ingredient must be either an approved food additive or prior sanctioned ingredient, an approved color additive, or GRAS. If a non-dietary ingredient component is GRAS, there must be a citation to the agency's regulations or an explanation for this claim. 21 C.F.R. § 111.35(d).

This proposed regulation is unnecessary and should not be included in the proposed dietary supplement CGMPs. The law already requires that non-dietary ingredients in dietary supplements be either approved food additives, approved color additives, or GRAS. See FDC Act § 201(s). This requirement has nothing to do with good manufacturing practices, as evidenced by the absence of a similar provision in the food CGMPs. Furthermore, the requirement for a certification or explanation of GRAS substances in the proposed dietary supplement CGMPs is unnecessary and redundant. Because the law states that the dietary supplement CGMPs are to be modeled after food CGMPs, FDC Act § 402(g)(2), they should not include this provision.

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[6] A similar assertion by FDA as to its records inspection authority for devices was overruled by a court in In re Medtronic, Inc. 500 F. Supp. 536 (D. Minn. 1980) (finding that FDA exceeded its inspection authority in requiring the production of complaint file handling procedures, failure analysis procedures, and return product handling procedures for a medical device because FDA's regulations did not require such procedures to be documented).

If 21 C.F.R. § 111.35(d) is retained as part of the dietary supplement CGMPs, however, then FDA should, at the very least, remove the requirement that "[a]ny claim that a substance is GRAS, other than a dietary ingredient within the meaning of section 201(ff) of the Act . . . be supported by a citation to the agency's regulations or by an explanation for why there is general recognition of safety of the use of the substance in a dietary ingredient or dietary supplement." 21 C.F.R. § 111.35(d)(4). The requirement of a "citation" or "explanation" is unclear and, if anything, implies that there are additional requirements imposed beyond what the FDC Act requires.

II. Small Businesses Should Not Be Afforded a Three-Year Exemption from the Proposed Dietary Supplement CGMPs

FDA's Regulatory Flexibility Act (RFA) analysis revealed that the rule would have a significant economic impact on a substantial number of small entities. 68 Fed. Reg. at 12,246-47. Accordingly, under the RFA, FDA is obliged "to analyze regulatory options that would lessen" the impact. Id., 5 U.S.C. § 604(a)(5) (requiring as part of a final regulatory flexibility analysis "a description of the steps the agency has taken to minimize the significant economic impact on small entities."). To mitigate the significant costs on small entities, FDA proposed to lengthen their compliance period by two years. 68 Fed. Reg. at 12,247. Thus, the proposed rule "would be phased-in over 3 years, with large firms complying after 1 year, and both very small and small firms after 3 years." Id. This extension of the compliance period for small businesses is unreasonable and not in the public interest. Further, the extension would be unnecessary if FDA modifies the proposed dietary supplement CGMPs to provide companies with greater flexibility in achieving them. [7]

The purpose of proposed dietary supplement CGMPs is "to protect consumers from adulterated and misbranded dietary supplements due to improper manufacturing, packaging, or holding practices" and "to ensure that a dietary supplement contains what the label says it contains." Id. at 12,176. The proposed dietary supplement CGMPs, therefore, are intended serve to protect the public health by helping to prevent contamination with deleterious substances and by ensuring that consumers who require a certain level of nutrient supplementation obtain the amount of nutrients declared on supplement labels.

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[7] Alternatively, if FDA believes that three years is appropriate for compliance with the proposed dietary supplement CGMPs, that time period should be applied to all manufacturers, regardless of their size.

[9] In the preamble to the proposed dietary supplement CGMPs, FDA appears to make this point very clear: "The types of tests and when to test would be left to your discretion. The proposed rule would not specify any particular test or examination, so you would be able to decide on the appropriate methods for testing or examination that are suited to your components, dietary ingredients, and dietary supplements." 68 Fed. Reg. at 12,199 (emphasis added).

Giving small businesses additional time to comply with a rule designed to protect the public health defeats the purpose of the rule. The proposed dietary supplement CGMPs are unlike other types of rules where the public health is not directly at stake and, therefore, where compliance extensions are not unreasonable. See, e.g., 65 Fed. Reg. 38,191, 38,193 (June 20, 2000) (extending compliance with the OTC "Drug Facts" rule by one year for those companies having annual sales of less than $25,000). Furthermore, consumers will not be able to determine which dietary supplement products comply with the proposed dietary supplement CGMPs and which do not – that is, there will be no sign or symbol on the labels indicating which supplements have been manufactured according to CGMPs and which have not. It is unreasonable to reduce the economic burden on small entities at the expense of the public's health.

In addition, if FDA modifies the rule as proposed above, the costs in implementing the CGMPs would be greatly reduced, thus lessoning the economic impact on small entities. For example, giving companies flexibility in ensuring compliance with product specifications via supplier guarantees or certifications or use of a CGMP expert would greatly reduce the costs of the rule.

III. FDA Lacks the Authority to Subject "Dietary Ingredients" and Raw Material Suppliers to the Proposed Dietary Supplement CGMPs

FDA has stated that the proposed dietary supplement CGMPs should have broad application and should, therefore, apply to raw material suppliers. 68 Fed. Reg. at 12,174. It appears to us that FDA does not have the authority to impose dietary supplement CGMPs on manufacturers of dietary ingredients. Section 402(g)(1) provides that a "dietary supplement" – not a dietary ingredient – may be adulterated if it "has been prepared, packed, or held under conditions that do not meet current" CGMPs. 21 U.S.C. § 342(g)(1). Furthermore, section 402(g)(2) provides that FDA may prescribe CGMPs for "dietary supplements" – not dietary ingredients. Id. § 342(g)(2). Based on the law, it appears that FDA lacks the authority to impose dietary supplement CGMPs on companies manufacturing dietary ingredients only. Therefore, FDA has exceeded its authority in attempting to include "dietary ingredients" or raw material suppliers within the scope of the proposed dietary supplement CGMPs.

We note that even if FDA had authority to include "dietary ingredients," it only makes sense to exempt raw material suppliers from the rule. We believe that ultimately it is the party who places its label on the bottle or identifies itself as the manufacturer on the label (the Finished Product Company) that should be responsible for the identity, purity, quality, strength and composition of the product that is being sold. This means that even those Finished Product Companies that contract out the manufacturing and then place their own label on the bottle and identify themselves as the "distributor" or similar term should have final responsibility for their products. As a practical matter, the Finished Product Company is contacted by the consumer or the FDA if a quality or contamination concern arises in any case – not the raw material supplier or even the contract manufacturer – and it is the Finished Product Company who responds to these inquiries. In light of this, before marketing a product, it would only be appropriate that the

Finished Product Company have in its possession adequate documentation to verify the identity, purity, quality, strength and composition of its products.

If the rule requires that the Finished Product Company be responsible for these things, requiring raw material suppliers to follow the dietary supplement CGMPs would merely increase the costs of the raw materials without producing any real benefits. These suppliers are already responsible under food CGMPs to ensure that their starting materials are not adulterated, and when they deliver their finished raw materials with certificates of analysis, they are ensuring that the raw materials have the identity, purity, quality, strength, and composition that they purport to have. A Finished Product Company should be entitled to rely on these representations (and indeed, is entitled to rely on these representations with or without CGMPs), but should also do its own independent verification and testing, as appropriate, to ensure that it has received the proper ingredients and/or finished dietary supplement.

We also note that it would likely be very difficult if not impossible in many cases for many raw material suppliers to comply with the dietary supplement CGMPs since dietary supplements may only constitute one potential use for their ingredients, which are also used in conventional foods.

IV. Expiration Dating Requirements for Dietary Supplements Should Be Addressed in a New, Separate Rulemaking

FDA stated that it was not proposing expiration dating for dietary supplements because "scientific study" in this area "is still evolving." 68 Fed. Reg. at 12,163. Nevertheless, elsewhere in the preamble the agency invited comment as to whether a final dietary supplement CGMP rule should require expiration dating. Id. at 12,165. Although we acknowledge that both NNFA and CRN have indicated that expiration dating or "suggested use by" dating should be required for dietary supplements, we do not believe that this complex issue should be resolved in this comment period. Rather, the proposed dietary supplement CGMP regulations should be made final as soon as possible, and the issue of expiration dating should be addressed at a later time, after more scientific evidence is obtained to appropriately evaluate the issue and following appropriate comment and review by affected parties.

FDA stated that it has "insufficient scientific information to determine the biological activity of certain dietary ingredients used in dietary supplements, and such information would be necessary to determine an expiration date." Id. at 12,204. FDA also acknowledged that "official validated testing methods . . . for dietary supplements are evolving" and, therefore, there are "few official methods . . . available to assess the strength of a dietary ingredient in a dietary supplement." Id. Because there is currently a lack of information regarding expiration dating for dietary supplements, it would be illogical to require this as part of the final dietary supplement CGMP rule. Instead, FDA should propose a separate rulemaking to address expiration dating for dietary supplements after more science is developed. Only then can industry and the public intelligently comment as to how expiration dating should be implemented. Until this issue is officially addressed, however, if manufacturers currently place an expiration date or suggested

use by date on their products, then as FDA noted, the manufacturers "should have data to support that date." Id.

V. The Provision Requiring Testing for Contaminants Must Be Clarified

Section 111.35(k) requires testing or examination of components, dietary ingredients, and dietary supplements "for those types of contamination that may adulterate or may lead to adulteration." One of the "types of contamination" listed is "toxic substances." 21 C.F.R. § 111.35(k)(3). The term "toxic substances" is not defined in the proposed dietary supplement CGMPs, and FDA should define this term so that companies will know what to test for. In addition, FDA should clarify in the rule that companies are required to test only for those contaminants that can reasonably be expected to be present in their particular dietary ingredient or dietary supplement product[9]. For example, § 111.35(k) could be revised to "You must test or examine components, dietary ingredients, and dietary supplements only for those types of contamination that can reasonably be expected to adulterate or lead to adulteration of the particular component, dietary ingredient, or dietary supplement."

VI. Consumer Complaints Should Not Be Addressed by the Proposed Dietary Supplement CGMPs

FDA is proposing a complex and detailed program to review, investigate and resolve customer complaints. A fundamental flaw with the proposal is that it does not adequately define a "consumer complaint" or an "adverse event report." As noted above (in Section I), consumer complaint handling requirements do not currently exist under food CGMPs and therefore FDA does not have statutory authority to issue such requirements. However, Nutraceutical believes that this issue is important and relevant -- not only to dietary supplements, but also to conventional foods and cosmetics.

Because of this, Nutraceutical supports the development of a comprehensive system to track and analyze adverse event reports for dietary supplements, conventional foods and cosmetics. We understand that such a system is under development within FDA's Center for Food Safety and Applied Nutrition (CFSAN). This new system should replace the current patchwork of existing adverse event reporting systems. We are concerned that FDA's current proposal, which does not specifically address adverse event reporting but which does require companies to investigate consumer complaints when there is a "reasonable possibility of a relationship between the quality of a dietary supplement and an adverse event," may simply create more confusion and may contradict the overall objective of a comprehensive adverse event reporting system, which should be to develop a harmonized system for foods, cosmetics and dietary supplements.

We therefore request that this section be removed from this proposal and be dealt with separately, as part of the proposed CFSAN Adverse Event Reporting System (CAERS).

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In conclusion, while we applaud the effort to issue dietary supplement CGMPs, the text of the proposed dietary supplement CGMPs suggests that FDA may have a continued desire to ignore the Dietary Supplement Health and Education Act (DSHEA) and the mandates given by Congress to treat dietary supplements as a category of foods, and instead reclassify supplements as drugs. As noted above, evidence of this includes the fact that the rule seems to be based on drug CGMPs (rather than food CGMPs) and the continued focus on food additives, which was formerly used by the FDA as a pretext for removing dietary supplements from the market.

Furthermore, some of FDA's proposed dietary supplement CGMPs exceed FDA's statutory authority and are inflexible, overly cumbersome, and, in some cases, unnecessary or confusing. Accordingly, FDA should modify the proposed dietary supplement CGMPs to more closely resemble the food CGMPs, to provide manufacturers greater flexibility in ensuring that products meet specifications, to limit FDA's records inspection authority as provided by law, and to remove provisions that are not CGMPs, such as the provisions relating to the existing statutory requirements for GRAS substances. FDA should not extend the compliance date for small businesses but should exempt raw material suppliers from the rule, and the expiration dating of dietary supplements as well as consumer complaint handling should be addressed in a future, separate rulemaking.

Respectfully submitted,

NUTRACEUTICAL CORPORATION

Stanley E. Soper,
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