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SUBMITTED VIA E-MAIL fdadockets@oc.fda.gov
AND OVERNIGHT COURIER

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

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

Dear Sir/Madam:

Weider Nutrition Group, Inc. (Weider) submits the following comments on the Food and Drug Administration's (FDA's) proposed regulations for good manufacturing practices (CGMPs) in the manufacturing, packaging, or holding of dietary supplements.

Weider develops, manufactures, markets, distributes, and sells branded and private-label vitamins, nutritional supplements and sports nutrition products in the United States and throughout the world. The Company offers a broad range of capsules and tablets, powdered drink mixes, ready-to-drink beverages and nutrition bars, consisting of approximately 775 stock-keeping units (SKUs) domestically and internationally. Weider manufactures some products and purchases other finished products for wholesale distribution.

Weider continually seeks to improve its manufacturing practices to increase operating efficiency and enhance product quality. Appropriate CGMPs for dietary supplements will benefit consumers and achieve the purposes of DSHEA so long as the CGMPs, the FD&C Act, and FDA regulations pertaining to dietary supplements are appropriately enforced.

The final rule for CGMPs should be limited to the statutory authority conferred upon FDA to regulate dietary supplements. ETSI Pipeline Project v. Missouri, 484 U.S. 495, 517 (1988)("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.'"). For this reason, the CGMPs for dietary supplements should be modeled after CGMPs for conventional foods. 21 U.S.C. §342(g)(2) ("The Secretary may by regulation prescribe good manufacturing practices for dietary supplements. Such regulations shall be modeled after current good manufacturing practice regulations for food and may not impose standards for which there is no current and generally available analytical methodology.").

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The emphasis of CGMPs should be well-controlled manufacturing processes rather than exhaustive finished-goods testing. To test every finished product for every ingredient would be redundant of in-process controls and add costs without commensurately greater assurances of identity, purity, quality, strength and composition. Higher costs would result in higher prices, less consumption, and more illness with higher health care expenses. Rigorous in-process controls may justify auditing of finished-goods for identity, purity, quality, strength, and composition.

Furthermore, FDA lacks authority to require finished product testing for dietary supplements where conventional food CGMPs do not require finished goods testing. See FDC Act § 402(g)(2). FDA has exceeded its authority in requiring finished batch testing for dietary supplements.

Written procedures are the cornerstone of good manufacturing practices and should be required for the following areas: cleaning and maintenance of equipment and utensils, receipt and handling of raw materials, finished goods specifications and release criteria, reprocessing materials to meet specifications, and control procedures for labeling and packaging, and equipment calibration. Weider believes that reliance on implementation of written procedures will be more efficient and less-expensive than reliance on finished goods testing.

The proposed CGMPs would not permit manufacturers to rely on a vendor's certificate of analysis for a raw material as evidence that the material complies with specifications and labeling requirements. Manufacturers should be permitted to rely on a certificate of analysis based on a qualified vendor's actual test of the lot or batch of the material shipped so long as the manufacturer verifies the identity of the material upon receipt. Manufacturers should be permitted to rely on a vendor certification program to qualify vendors. By vendor certification and reliance on vendors' certificates of analysis, manufacturers may reduce redundant quality testing of ingredients and costs without compromising quality or risk of adulteration.

Contrary to the proposed rule, CGMPs should not require that all components be an authorized food additive, authorized by prior sanction, an FDA listed color additive, or GRAS for use in a dietary ingredient or dietary supplement, when the component is not found in the finished product. 68 F.R. page 12257. The proposed rule defines a component as "any substance intended for use in the manufacture of a dietary ingredient or dietary supplement including those that may not appear in the finished dietary ingredient or dietary supplement." 68 F.R. page 12252. Many dietary supplements could not meet this requirement. For example, Vitamin C predominantly is manufactured by the Reichstein Process, which uses palladium as a catalyst. Until use of palladium as a catalyst is sanctioned by FDA, the decades old Reichstein Process would result in per se adulterated Vitamin C even though though the "component" palladium is not found in the finished good. The final CGMPs should not require that components that are not found in the finished goods in a material amount be subject to the same GRAS requirements as a dietary ingredient or dietary supplement.

FDA's proposed CGMPs 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 made available to FDA during an inspection. See 21 C.F.R. § 111.125(c). 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 failure to make available for inspection 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 records 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). 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).

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 CGMP requirements impose a three year recordkeeping requirement on firms. See 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. 670 (2002). Therefore, to the extent that records must be kept for dietary supplement CGMPs, the records need only be kept for a maximum of two years.

In short, the dietary supplement CGMP recordkeeping regulation exceeds the agency's statutory inspection authority. The regulation must comply with the limited records inspection authority under Section 306(a) of the Bioterrorism Act.

Weider's additional comments on specific provisions of the proposed CGMPs are attached hereto and are incorporated herein.

In conclusion, Weider Nutrition supports FDA's efforts to promulgate CGMPs for dietary supplements within the statutory authorization granted by Congress, thereby promoting availability of unadulterated dietary supplements to support public health and reduce burgeoning health care costs.

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Attachment

Comments Solicited by the Preamble

Pg. 36 A voluntary label statement that a dietary supplement complies with CGMP should be allowed. There are several third party organizations such as USP and NNFA that have proposed or established GMPs that are as or more rigorous than those proposed by the FDA. Any such statement that characterizes the nature of the GMP compliance should be allowed.

Pg. 43 Written procedures should be required for operations that impact on the strength, purity and quality of the dietary supplements. Specifically for the cleaning, setup, and maintenance of equipment, inspection and handling of incoming components and packaging material, manufacturing and quality operations, as well as calibration and laboratory operations. Written procedures promote consistency and clearly lay out expectations, facilitate training and provide reference for individuals in performing their job functions.

Pg. 67 Certifications from suppliers do not necessarily ensure that the component has the identity, strength, purity and quality required. Certificates of Analysis in conjunction with a supplier certification program and/or CoA verification program can provide those assurances. In the pharmaceutical industry skip lot testing, with the exception of identity testing, is common for active and non-active ingredients. Identity testing of every lot should be a minimum requirement.

Pg. 84 Written procedures for the verification of equipment, and records of verifications for equipment, should be required. Verifications should consist of confirmation of materials of construction for product contact surfaces, service ratings of installed motors, and verification of required controls for the operation of the equipment is the extent of the requirement. Timers and other measurement devices are covered under the calibration requirements.

Pgs. 110 &122 The regulations promulgated by the USDA provide adequate control over the use of animal tissues that might contain microorganisms, specifically viruses, of public health concern. Certifications by suppliers, government agencies (foreign or domestic), and/or manufacturers are the responsibility of the firm accepting them to verify the existence of procedures and records that support the certifications.

VII.C.3.b Small entities should not be given a longer period to come into compliance with the proposed CGMPs. Weider believes that the larger manufacturers and most of the manufacturers that fit the definition of small already comply with most of the proposed GMPs for business reasons. Firms not already substantially complying with the proposed GMPs are likely responsible for the majority of adulterations and/or recalls that the

proposed regulations are intended to limit/eliminate. To give such "outliers" more time to come into compliance will not serve the public health premise for the regulations.

Comments on the Proposed CGMP Provisions

§111.1 The proposed regulation should eliminate the term Dietary Ingredient, which is not defined in the Act. Manufacturers of dietary ingredients would still be subject to 21 CFR part 110 for conventional foods. The proposed dietary supplement CGMPs are so different and burdensome than for conventional foods that suppliers of dietary ingredients for use in food would exclude sales to dietary supplement manufacturers.

111.3 Definition of Batch: Drug regulations specify that product meets strength, purity and efficacy. Why do supplements have additional requirement for quality and composition? Quality is implied by conformance to the other criteria. Purity, when dealing with some botanical ingredients may be subjective.

Definitions for the following terms would be beneficial:

Control Point means any point, step, or stage in the manufacturing process where control is necessary to prevent adulteration.

Scientifically valid analytical method means an officially published method (AOAC, USP, American Herbal Pharmacopoeia), or is based on scientific data or results published in scientific journals, references, or text books or supported by proprietary research.

111.12(a)(b) The phrase "education, training, and experience *or any combination thereof*" be added to the regulation.

111.13(b) The requirement for supervisors to be qualified by training and experience is too broad and open to subjective interpretation during inspection. Persons meeting the requirements of the supervisor's job description generated by the firm are by definition "qualified."

111.20(d)(1) Smooth hard surfaces should be "required only where necessary to ensure that adequate cleaning requires washing of walls and ceilings to prevent cross contamination from batch to batch of dietary supplements." To require more poses an undue economic and logistical burden to no beneficial end.

11.25(b)(1) Calibration is necessary only for those instruments needed to prevent adulteration and ensure that specifications for identity, purity, quality, strength and composition are met. Some instruments are used only for

operational efficiency or cost control and have no direct bearing on product quality. The regulation could refer to "instruments and controls you use to generate data required by the master manufacturing record or specifications," or require the quality control unit to prepare a critical instrument list for the instruments that require calibration.

111.25(e)(1) Written procedures for disassembling, cleaning and re-assembling major equipment should be required. These procedures should describe the appropriate cleaning agent and method of cleaning as well as specify the intervals and schedule for cleaning equipment. Records of the cleaning, maintenance and use for major pieces of processing equipment should be required. Written procedures promote consistency and clearly lay out expectations, facilitate training and provide reference for individuals in performing their job functions.

111.30(a)(2) The requirements of 21 CFR 110.40 reflect the level of assurance that equipment is adequate for its intended use. This proposed section of the GMPs is overly prescriptive compared to conventional food GMPs without justification.

111.30(b)(1) The requirement for the Quality Control Unit to approve calibrations, inspections and checks of equipment required for this section is too prescriptive. Adequately qualified persons outside of the Quality Control Unit meets the spirit of this requirement. The Quality Control Unit should perform audits of the records generated to ensure the appropriate calibrations, inspections and checks are being adequately performed at the required intervals.

111.35(a) Written procedures for production and process controls should be written and followed. Without written procedures, an adequate basis for controlling the production process or for employee training and supervision likely will not exist.

111.35(d)(3) This provision is redundant of the general provision that other applicable laws and regulations must be observed. At a maximum, this section might state "Other substances used in dietary supplements must comply with the statutory and regulatory provisions of the FD&C act. It is not feasible to require that the starting materials used by the bulk ingredient manufacturers be GRAS or approved food additives. Many raw materials are not in fact food grade substances or approved food ingredients until after processing.

111.35(g)(1) As an alternative, a well controlled process plus one identity test should be permitted to substitute for a requirement to test each batch for all specifications. Acceptance of a certificate of analysis, plus one identity test should also be permitted where the vendors process has been audited

or verified and where it has been established that the certificate of analysis is based on appropriate testing by the vendor.

111.35(i) Written procedures for reprocessing should be established and followed for reprocessing material into usable product. We believe the use of written procedures facilitates training, increases consistency and provides references for people in performing their assigned functions.

111.35(i)(4)(iii) The Quality Control Unit should have authority to determine the fitness for use of all material that has been rejected previously. There should not be any exclusions as such for microbial contamination or heavy metals if adequate re-processing can meet specifications.

111.35(k) Written procedures and specifications should be established and followed describing the tests or examinations needed to assure the quality and purity of the finished product. It should be recognized that testing performed by suppliers or by another qualified laboratory may be accepted, provided the reliability of the testing has been verified and an adequate certificate of analysis has been supplied.

111.37 The Quality Control Unit should be free to designate what functions are performed by whom. Some "quality" functions are better left to the operational unit with periodic auditing performed by QC.

111.37(b)(11) Requiring reserve samples of in-process material presents an undue burden in terms of storage requirements and higher costs to no incremental benefit. Stability and safety issues render the usefulness of stored samples questionable. This requirement should be eliminated.

111.40 Written procedures should be established and followed for the receipt, identification, examination, handling, sampling, testing, and approval or rejection of raw materials.

111.40(a)(2) The phrase "perform testing, as needed" is too vague and implies that testing is always necessary. This should be re-phrased to say, "perform testing, if necessary," to allow for the acceptance of a certificate of analysis that has been verified by vendor certification process and/or verification to be accurate.

111.40(b) Written procedures should be established and followed for the receipt, identification, examination, handling, sampling, testing, and approval or rejection of labeling and packaging materials to ensure consistency and eliminate uncertainty as to requirements.

111.50(c)(4) Records for the cleaning and maintenance of major pieces of equipment are kept in log books for the equipment and should not be included in the

batch record, except possibly for a verification that appropriate cleaning and/or maintenance was done.

111.50(d)(2) QC must have the authority to release batches where there is a deviation from the specifications where the deviation does not impact the product's suitability for use. For example, instances of intended overage of an ingredient for stability but actual content is below specifications but meets label claim. After an adequate investigation to ensure there is no underlying quality issues, QC should have the option of releasing the material with a shortened expiration date. Also in cases where a specification is not significant to the product's overall quality such as tablet thickness, QC should have the authority to release the product for distribution.

111.50(f) QC should have the authority to allow reprocessing if there is a valid process for correcting the defect.

111.50(g) As above, in cases where a specification is not significant to the product's overall quality such as tablet thickness, QC should have the authority to release the product for distribution.

111.50(h) The requirement must be modified to take into account the expiration date of the product. A blanket three-year storage requirement imposes unnecessary costs for products that may be dated for shorter periods. We believe this section should be re-written to express the requirement as a function of the manufacturing date or expiration date. For example, three years from the manufacturing date or 1 year beyond the expiration date. Moreover, FDA lacks authority to impose this regulation.

111.65(d) The Quality Unit must have the authority to allow the usage of material that has failed to meet specifications where it deems the defect will not significantly affect the overall quality of the finished product even if reprocessing is not an option. For example, where a material fails to meet particle size specifications that are designed to maximize the efficiency of processing of the material, but ultimately does not impair strength, the quality unit should have the authority to release the material for use.

111.70 Written procedures must be established and followed to ensure that the correct labels and packaging material are issued and used.

111.95 Written procedures must be established and followed for handling consumer complaints. We do not believe that there should be two systems for handling complaints. All complaints should be handled in a consistent manner.