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June 5, 1997

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Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Dr., rm1-23
Rockville, MD 20857

RE: Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Dietary Supplements. (Docket No. 96N-0417)

Dear Sir or Madam:

Perrigo Company appreciates this opportunity to comment on the Food and Drug Administration's Advance Notice of Proposed Rulemaking (ANPR) concerning Good Manufacturing Practice (GMP) requirements for Dietary Supplements, published in the Federal Register of February 6, 1997, 62 Fed. Reg. 5700. In the ANPR, FDA requested comments on a draft document submitted by the dietary supplement industry concerning proposed GMPs for dietary supplements. FDA said that it will consider this draft as a possible framework for its development of GMPs. In addition, the agency sought responses to several other related issues.

Perrigo is a leading store brand manufacturer of over-the-counter products and produces low-cost, high quality alternatives to national brand products. Perrigo's subsidiary, Perrigo of South Carolina, Inc., is a leading producer and distributor of private label dietary supplement products.

Perrigo shares FDA's commitment that consumers should receive safe and effective products and commends FDA for its efforts. Perrigo recommends that FDA adopt the industry

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draft submission ("draft") without change (Perrigo was directly involved in its preparation), except for those modifications proposed by the Council for Responsible Nutrition (CRN) and the Nonprescription Drug Manufacturers Association (NDMA) which Perrigo also supports. The industry draft is based on sound scientific principles and years of industry practice.

The following are Perrigo's responses to FDA's questions.

I. Proper Identification of Dietary Supplement Ingredients

In the ANPR, FDA requested comments on appropriate testing requirements to provide positive identification of dietary supplement ingredients. Perrigo recommends that FDA adopt the draft's proposal. Specifically, according to paragraph (c)(7)(iv) of the section on Production and Process controls:

> Each lot of raw material shall undergo at least one test by the manufacturer to verify its identity. Such tests may include any appropriate test with sufficient specificity to determine identity, including chemical and laboratory tests, gross organoleptic analysis, microscopic identification, or analysis of constituent markers.

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62 Fed. Reg. At 5705. No particular identification test is described because, in light of the number and variety of dietary supplements and due to the constant changes and improvements in analytical methodology, designation of a specific test will be severely limiting and inadequate. Although recognizing that GMPs should require identification of the ingredients used in dietary supplements, Perrigo agrees with the industry position that setting a specific test is not prudent. Rather, FDA should defer to dietary supplement manufacturers to establish acceptable means by which to identify the ingredients in their products. If FDA determined it appropriate to provide any more guidance to industry, it could do so through the guidance document development process.

II. Certification that a dietary ingredient is free from contamination.

FDA requested industry comment on whether "a certification will provide assurance that dietary ingredients are not contaminated, or whether specific testing requirements are necessary and would effectively ensure the safety and wholesomeness of these products." 62 Fed. Reg. At 5708. The agency noted that, "many ingredients used in dietary supplements do not have a history of food use in the United States, and thus, the potential for contamination with microorganisms or filth is unknown." Id. At 5707.

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Perrigo contends that a supplier's certification should be sufficient to provide assurances that the dietary ingredients are not contaminated. We respectfully disagree with the implication that an ingredient's lack of historical use in food suggests that it is adulterated or unsafe. Certainly, the reverse is not true; product with a long history of use does not guarantee that a particular product will be free from contamination.

All dietary ingredients sold in the United States before the enactment of the Dietary Supplement Health and Education Act (DSHEA) in 1994 are presumed to be safe. Any new dietary ingredient introduced since that time must be thoroughly evaluated for its safety. Therefore, each manufacturer must take appropriate steps to prevent contamination or adulteration of any ingredient. The potential for adulteration has very little to do with a history of food use in the United States and almost everything to do with the company's handling of the ingredient throughout the process of producing a final product. FDA must keep in mind that it is in the manufacturer's best interest to ensure that all ingredients used in its final dietary supplement product are free from contamination. Thus, if a manufacturer finds acceptable a supplier certification, FDA should be satisfied.

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III. Verification of compliance with GMPs

FDA asked whether FDA should require manufacturers to "establish procedures to document that the procedures prescribed for the manufacture of a dietary supplement are followed on a continuing or day-to-day basis." 62 Fed. Reg. At 5708. Perrigo asserts that a specific documentation requirement in this case will be redundant because there are numerous record keeping requirements elsewhere in the GMPs proposed in the industry draft. See, e.g., paragraph (b)(11) of section on Equipment and Utensils; paragraphs (a)(iii) and (b) of section of Quality Control and Laboratory Operations; paragraphs (a) and (b) of section on Production and Process controls; paragraph (c) of section on Warehousing, Distribution and Post-Distribution Procedures. Compliance with these record keeping and documentation requirements will address FDA's concern. Thus, a separate documentation as proposed by FDA, is unnecessary.

IV. Adverse event reporting

FDA requested comments on whether dietary supplement GMPs should require "reports of injuries or illnesses to a firm be evaluated by competent medical authorities to determine whether follow up action is necessary to protect the public health." 62 Fed. Reg. At 5708. Perrigo recommends against this requirement. Neither the adverse event reporting regulation for foods nor OTC drugs require medical review of each and every complaint. Rather, the company

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evaluates the complaint and, if necessary, it will seek the opinion of a medical reviewer; the decision is left to the company. Similarly, FDA should defer to the dietary supplement manufacturer to review each complaint carefully and to handle the matter appropriately and responsibly. There is no reason for FDA to impose a new requirement of dietary supplement, where it has not done for other FDA-regulated products.

In addition, this proposed requirement will be extremely burdensome to dietary supplement manufacturers and a waste of medical resources if every report of injury or illness must be automatically reviewed by a medical authority. There are a variety of reasons for complaints, many of which have no merit or are found to be unrelated to the product. Thus, FDA should defer to the company to evaluate and assess how to handle complaints.

V. Hazard Analysis Critical Control Points (HACCP)

The FDA has asked "whether certain, or all, of the requirements for manufacturing and handling dietary ingredients and dietary supplements may be more effectively addressed by a regulation based on the principles of Hazard Analysis and Critical Control Points (HACCP), rather than the system outlined in the industry submission." 62 Fed. Reg. At 5708.

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Perrigo along with most of the industry was not familiar with the HACCP process, therefore along with the NDMA and CRN we have been researching HACCP. Through this research no clear advantage has been observed for choosing a HACCP program over a GMP program. Because there is no clear advantage to using a HACCP program and Perrigo has experience with a GMP program, we do not believe the HACCP approach is the best way to proceed. Perrigo also supports the NDMA's comments on this issue.

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In conclusion, Perrigo recommends that FDA adopt the industry proposal on dietary supplement GMPs as modified by the NDMA and CRN comments. We also encourage FDA to consider our responses to its questions, which we have based on sound science and established industry practice.

Perrigo appreciates the opportunity to comment on the ANPR. Please feel free to contact me at (616) 673-1125 if there are any questions or if Perrigo can provide FDA with additional information.

Sincerely yours,

Tim Hertzler
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