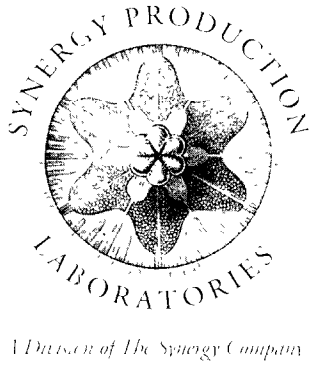

A Division of The Synergy Company

August 6, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 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 Madame,

My company fully supports the establishment of current good manufacturing practices (cGMPs) rules for dietary supplements. Responsible companies in the industry, like ours, already have effective programs in place that allow us to ensure product integrity as described in your proposed regulation. However, we are concerned that even responsible companies will be faced with costs beyond FDA's estimate due to an especially rigid and unnecessarily burdensome testing scheme and fundamental miscalculations made by the agency in its economic analysis on the impact of the proposed rule. We are also concerned that FDA's proposed cGMPs approach dietary supplements as if they were drugs, in contravention to DSHEA, which clearly intends dietary supplements to be regulated more like foods than drugs.

The following factors are critical to achieve a workable cGMP regulation: 1) supplement cGMPs should apply to the entire industry; 2) an appropriate testing regime should be required, including allowing the use of certificates of analysis, and testing at appropriate points during the manufacturing process to include statistically-based batch testing options; 3) FDA should modify sections of its proposal to be more flexible and/or to include the existing industry standard; and 4) FDA should require written procedures for certain operations, and documentation if appropriate, in key areas.

We also believe that 1) expiration or shelf-life dating should be required on product labels; 2) economic costs outlined by FDA are grossly underestimated and will have a significant and detrimental impact on the dietary supplement industry; particularly the "small and very small" as defined by FDA; and 3) the compliance periods that FDA has proposed will allow small entities adequate time to implement the rule. Our comments follow.

Supplement cGMPs should apply to the entire industry

We strongly support the FDA's proposal that this rule should apply to the entire industry, including foreign firms and raw material manufacturers. Broad application of the rule offers an additional layer of assurance that products have the identity, purity, quality, potency and composition they purport to have. Establishing that ingredients meet specification in a reliable manner at the beginning of the process, and then maintaining quality through appropriate process controls by manufacturers is the most effective and efficient manner to assure quality.

Furthermore, raw ingredient manufacturers are the only entities in the supply chain in some instances, such as with some botanicals or unique formulations, with the expertise to evaluate a raw material. We believe that by building more flexibility into some sections of the rule, bulk ingredient manufacturers that supply ingredients to the food or drug industries will be able to comply without major changes to their processes or equipment.

96N-0417

C230

2279 South Resource Boulevard, Moab, Utah 84532
Telephone 435-259-4787 • *Fax* 435-259-4919 • www.synergyproduction.com • *Email* spl@synergyproduction.com

An appropriate testing regime should be required

We support the recommendation by our trade organization, the National Nutritional Foods Association, that FDA adopt a more appropriate testing scheme to reduce the number of unnecessary tests required under the proposed rule. Flexibility in some critical areas, such as when, how and how often to test components, dietary ingredients and dietary supplements against established specifications, will allow us to develop a cGMP program that meets the mandates of the rule while still providing necessary controls. We believe these changes will lessen the economic impact and burden of the proposed rule to an acceptable level without compromising the legitimate goals of cGMPs.

The proposed rule appears to rely on an unnecessarily exhaustive and rigid testing scheme. As drafted and interpreted by virtually the entire industry, the proposed rule requires manufacturers to test every batch of finished product, if possible. If it is not possible to test the finished product, then dietary ingredients need to be tested upon receipt and throughout the manufacturing process. Testing must be performed at every level of the supply chain. Although FDA has presented this proposal as flexible, we are concerned it will eliminate many products from the marketplace that have been safety used for long periods of time. This clearly goes against the spirit and intent of the Dietary Supplement Health and Education Act (DSHEA) of 1994.

We support NNFA's recommendation that FDA modify its approach to product testing to recognize verified certificates of analysis, to allow for a statistically based approach to finished product testing, and not require unnecessarily redundant testing throughout the supply chain.

Verified Certificates of Analysis

FDA must allow for the use of verified certificates of analysis to show scientifically valid analytical testing has been conducted. Certificates of analysis are a key component of the manufacturing process, used by similar industries, and there is simply no economically feasible alternative. The final rule should require that specific and appropriate test results are provided on the certificate. Manufacturers should be required to confirm the veracity of information provided initially plus at appropriate intervals, and that their immediate supplier has an adequate cGMP program in place. Companies should not be required to do site inspections. Additionally, manufacturers should be required to test or examine raw ingredients to confirm the identity of the ingredient specified on the certificate of analysis.

Frequency and Feasibility of Testing

We agree that testing is necessary. However, we support the testing of dietary ingredients and supplements for conformity to specification based on a frequency that has been established under a statistically valid method to ensure in-process controls are adequate to assure the identity, purity, quality, potency and composition of individual dietary ingredients or dietary supplements. The availability of test methodology, the appropriateness of various points for testing dietary ingredients (i.e. identity, raw material, in-process or in the finished product) are also due additional consideration.

Testing Responsibilities

The proposed regulation does not clarify what testing obligations different companies, with different roles, have in the supply chain. We recommend that the final regulation make it clear that testing obligations fall primarily upon the manufacturer of the finished dosage form and that only one company in the chain has to perform the appropriate testing. For instance, companies which merely bottle and/or label finished dosage forms need to be held responsible for potency, identity, and purity, but not be required to do batch testing.

Supplement cGMPs should be more flexible

The proposed rule lacks appropriate flexibility in areas where general direction would suffice to produce safe and accurately labeled products. In most instances, more reasonable and effective alternatives are already being used by industry. The following examples illustrate the type of flexibility we are requesting.

- Companies need flexibility to design appropriate and effective testing regimes. For instance if a raw ingredient is tested upon receipt, it likely does not need to be re-tested for those same specifications when it is incorporated into multiple products.

- Companies need the flexibility to incorporate a statistical approach to finished product testing. Statistical testing provides necessary control as the consistency of test results and manufacturing processes are verified. First, through initial tests for conformity; and then once conformity is established, manufacturers then have the option to reduce the amount and frequency of testing based on the attributes of both the product and manufacturing process.

- Companies need flexibility to design manufacturing facilities to suit their operation. We believe, for instance, that ceiling surface is irrelevant to manufacturing processes which are completely enclosed. Moreover, manufacturers that are working with ingredients that are not hygroscopic, such as calcium, or in areas with low humidity, may not need to install equipment to control humidity.

- Section 111.65 is a good model as to an appropriate level of flexibility. This section, which covers requirements that apply to manufacturing operations, clearly states the requirements and presents relevant factors that must be considered when determining how to best meet the mandate of the rule. It is not overly prescriptive.

Written procedures and documentation should be required in key areas

FDA has excluded the use of written procedures and documentation from its proposal in some key areas where existing industry standards require them. Written procedures and documentation are key in-process controls. We suggest they are necessary in the following areas: 1) cleaning and maintaining equipment; 2) individual equipment logs; 3) responsibilities and procedures applicable to the quality control unit; 4) lab records; 5) raw material handling and testing; 6) reprocessing of batches; 7) packaging and labeling; and 8) handling complaints. Written procedures are vital to ensure uniform process control, and that employees are properly trained and supervised. They also provide an effective basis for FDA to assess the adequacy of a manufacturer's cGMP program. FDA should modify their proposal accordingly.

Unnecessary, duplicative and burdensome re-checking by Quality Control of receiving and testing records against finished batch records should not be required

Proposed Section 111.37 appears to require that in order for Quality Control to approve and release a batch for distribution, QC must *re-review all of the receiving documents for each material* (including Certificates of Analysis, test results and lot numbers assigned to dietary components) after production of a batch. This is completely redundant and imposes a prohibitive expense upon manufacturers.

Each lot of each material received in our facility is tracked by part I.D. and by lot number. Each lot must be inspected, tested and approved by QC prior to its release from quarantine status to ensure that it is the correct part and that the part meets all specifications. Verification includes review of all documentation and test results prior to releasing the material from quarantine. Each batch record and all work orders issued to the Production Unit are reviewed by QC prior to release of the batch record and work orders for use in Production, and QC verifies part IDs against the formula and master manufacturing record as part of this review. QC further verifies that the warehouse has selected the correct part ID for use in the batch record prior to releasing the material to Production. Production tracks each part ID and lot number, and the

quantity used in manufacturing as part of the batch record, and compares theoretical yield of each step of the manufacturing process against actual yield plus verifiable waste. Inventory controls track the quantity of material for each part ID and lot issued to Production and the quantity used as well as the quantity of any remaining material returned to the warehouse from Production. All material is accounted for as part of the documentation associated with each batch record. Therefore the existing controls and documentation provide thorough security to ensure that the proper part ID and lot number of a material is used in each batch record, and that the batch is manufactured according to meet all specifications.

To require a *second review* of receiving documents that were already reviewed and approved by QC serves no purpose other than to force the manufacturer to pay for more QC personnel to pull documents and records that were previously reviewed and approved. There is no justification for this redundant requirement and we urge FDA to delete it from the final rule.

Expiration dating/shelf-life dating

FDA has declined to require expiration or shelf life dating on dietary supplement ingredients. We disagree, however, and believe that the final rule should require expiration or shelf life dating to appear on product labels. Consumers have come to expect an expiration or "best before" date on food products and we believe this can be accomplished without unduly burdening manufacturers. We recommend that FDA include the following paragraph, which is based on a requirement from the NNFA GMP program, within the final rule:

> (a) All products must bear an expiration date or a statement of product shelf life. Expiration dates or a statement of product shelf life must be supported by data to assure that the product meets established specifications throughout the product shelf life. Such data may include, but is not limited to:
>
> > (1) A written assessment of stability based at least on testing or examination of the product for compatibility of the ingredients, and based on marketing experience with the product to indicate that there is no degradation of the product; or,
> > (2) Real time studies, accelerated stability studies or data from similar product formulations.
>
> (b) Evaluation of stability shall be based on the same container-closure system in which the product is being marketed.

Economic Impact

The economic costs outlined by FDA are grossly underestimated. The economic and financial impact of the proposed rule will have a significant and detrimental impact on the dietary supplement industry. Most adversely affected will be very small and small (as defined by the FDA) establishments. FDA officials stated during a public meeting to explain their proposed rule, held in Oakland, California on May 6, 2003, that the rule would put approximately 250 companies out of business. We have been informed by NNFA, however, that based on their research this number is probably much higher. Many products, especially multi-ingredient products, will no longer be economical to manufacture and will disappear from retailers' shelves. We understand that prices of the products that remain will increase considerably.

Responsible companies in the industry have effective testing programs in place. But we are concerned that even responsible companies will be faced with costs beyond FDA's estimate. FDA has miscalculated costs most significantly by underestimating the (a) the number of batches produced by companies per year; (b) the cost to perform specific analytical tests; and (c) the number of tests that would need to be required under the proposal.

Adopting a more reasonable economic burden on companies, especially by decreasing the testing burden on the bottler, packager and distributor, would give companies more flexibility to develop testing programs

around established specifications. Allowing companies to rely on verified certificates of analysis reduces the testing burden on companies. Allowing a statistical approach to finished product testing, along will allowing more flexibility in general, will also reduce costs.

Implementation of the Rule

FDA proposes allowing large companies one year and very small and small firms three years to comply with the final rule. We support the compliance periods that FDA has proposed as they will provide regulatory relief for small entities and allow them the necessary time to modify their systems in accordance with the final rule.

We agree that a longer compliance period will reduce the significant economic impact on very small and small companies because they will have additional time to set up recordkeeping systems, make capital improvements to the physical plant, purchase new or replacement equipment, and other one-time expenditures.

Further, products supplied by small companies are vital to the diversity, quality and price of products in a health food store, where most of these brands are carried. Consumers want these quality products, which are familiar to them and essential to retailers in the natural products industry, to remain available.

Conclusion

Finally, our company fully supports cGMP rules for dietary ingredients and dietary supplements. We recommend that FDA modify the proposed rule so that an appropriate testing regime is adopted and to require written procedures and documentation in some critical areas. Companies also need more flexibility to meet the mandates of the rule. These recommendations, coupled with the framework of manufacturing and quality controls that FDA has proposed, will lower the economic burden of this rule to a level which responsible companies in the supplement industry are able to bear, without compromising the legitimate goals of cGMPs. Consumer can also be assured that safe and affordable dietary supplement products from a variety of manufacturers remain available.

We urge FDA to give full consideration to our comments while also acting swiftly to issue a final rule that is not overly burdensome and will allow the industry to continue to provide consumers with a wide variety of safe, affordable, and high-quality dietary supplements.

Sincerely,

Susan Ulery
Quality Assurance Director
The Synergy Company of Utah, L.L.C.