YOUR VITAMINS
FROM ANDREW LESSMAN

August 11, 2003

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

Docket No. 96N-0417
Good Manufacturing Practices for Dietary Supplements

These comments are submitted by Andrew M. Lessman, founder and CEO of Your Vitamins Inc. ("YVI"), a dietary supplement manufacturer in Henderson, Nevada.

I am the owner of YVI and I have been creating, formulating, and manufacturing dietary supplements for 25 years. As a former food and drug attorney, I am also intimately aware of the cGMPs and regulatory issues that the industry has faced and is now currently facing. I am taking this opportunity to issue my comments as to the economic impact of the proposed regulations. I believe that while the intent of the proposed regulations is to ensure safer, higher quality products, the methods described therein do not represent either a sensible or cost effective way to reach this goal. My own experience indicates that the costs involved with meeting these new cGMPs will be multiples of what the FDA has currently estimated.

1996 N - 0417

C243

430 Parkson Road, Henderson, Nevada 89015 • Tel 702.564 9000 • Fax 702 564.7829 • www YourVitamins.com

1. Legal Authority to Issue this Proposed Regulation.

With respect to FDA's request for comments on the agency's legal authority to issue this regulation, we fully endorse the need for rigorous and adequate dietary supplement GMPs modeled on cGMPs for conventional foods. We wish to affirm its full support for the issuance of final GMP regulations, which will serve both the industry and its consumers.

We do not, however, believe that the agency has either a Congressional mandate or legal authority to propose or issue dietary supplement GMPs that deviate in material respects from food GMPs. Section 403(g)(2) of DSHEA states that GMP regulations "shall be modeled after current good manufacturing practice regulations for foods..." FDA defines "modeled" as meaning "a preliminary pattern" for DS GMPs and also has created a new working concept/definition for "dietary supplement" that would treat dietary supplements and ingredients as a "hybrid" regulatory category which combines aspects of both food and drug regulation due to the "characteristics and hazards" of dietary supplements. Using this new concept, the agency argues that Congress intended to grant the agency authority to establish regulations in this rule that do not have parallel provisions under food cGMPs. The basis for this theory is the agency's reliance on a single dictionary definition of

"modeled" as a "preliminary pattern" to justify inclusion of drug GMPs. The agency also clearly states in this proposed rule that the detection and avoidance of adulteration is a principal feature in the construction of this proposed rule.

There are 51 dictionaries with English definitions for the word "model" and 15 dictionaries with English definitions for "modeled" (OneLook.com). Of these definitions, the principal definitions are:

- A plan or form after a pattern.
- To produce a representation or simulation.
- To construct or fashion in imitation of a particular model.

We believes that the clear language of DSHEA, coupled with the general definitions of model/modeled lead to one conclusion: that FDA's authority to issue this regulation must follow the pattern and intent of food GMPs to the exclusion of any other type of GMPs which FDA has or may issue. We also believe that the concerns expressed by the agency with respect to the safety of dietary supplements can all be addressed within the construct of food GMPs, as will be noted later. In summary, the We do not believe that the agency has the legal authority to issue a final regulation for dietary supplement good manufacturing practices that include in material or significant ways provisions from drug, medical device or other GMPs.

2. Economic Impact on the DS Industry and Small Business in Particular.

We believe that the agency has profoundly miscalculated the cost of compliance with this proposed regulation. Our preliminary analysis suggests that the costs to industry to comply with this proposed rule will be at least 50 times greater than that projected by FDA. We recognize that the agency noted in this proposed rule that it lacks adequate data to accurately calculate costs associated with compliance to small business in particular and other DS businesses generally. Our continuing research suggests that the costs associated with finished product testing alone are at least 100 times greater than that estimated by FDA. We have consulted with the owner and principal of Plant BioActives, Inc., which is cited by FDA as reference No. E51 as one of two references to calculate testing costs. FDA estimates the average cost of an analytical test to be $60. Our data indicates testing costs will range between $180-360 per test (see attachment No. 1). This does not include testing costs associated with finished raw materials or the cost to develop finished product testing methods, which would range from $50,000 to $100,000 per product if, in fact, it is possible to create a finished product test for complex multi-ingredient finished product. We are actively collecting additional data to assess, more accurately, costs associated with raw material and finished product

testing, and again request the opportunity to present additional data within 30 days after the comment period closes. We underscore our view that finished product testing is not appropriate. Rather, we propose that rigorous raw material testing be developed, together with statistical sampling of finished raw materials, and be implemented as the appropriate means to assure product quality, purity and safety.

3. FDA's Explanation and Rationale for this Proposed Rule – Protection of Public Health.

We wished to express our surprise and concern with respect to the reasons stated by the agency for dietary supplement cGMPs. Shortly after passage of DSHEA in late 1994, the four major dietary supplement trade associations met with FDA to discuss the need for good manufacturing practices. It was agreed that the DS industry would jointly prepare a framework for GMPs, which was shared with FDA. FDA published this framework on February 6, 1997 as an ANPR with additional questions raised by the agency to obtain comment on related issues. Nearly six years later, FDA published this rule, which virtually ignores the prior ANPR framework but rather stresses public health concerns based on several examples of adulterated, misbranded or mislabeled dietary supplements. The language of the preamble implies that dietary supplements are not subject to regulation by FDA, and that the stated examples of

adulteration are a result of the agency's apparent inability to inspect, regulate or enforce current cGMPs for food, to which all dietary supplement products are subject. At the April 29, 2003 public meeting at FDA's offices in College Park, Maryland, one FDA official stated that conventional food GMPs are based on the principle of sanitation, whereas this proposed dietary supplement GMP regulation is based on a principle of prevention and avoidance of adulteration. We object to the pejorative characterization of dietary supplements as a public health risk and that the need for this regulation is based on the avoidance of adulteration of dietary supplements by imposing manufacturing practices which far exceed food GMPs.

4. <u>Subset GMPs for Dietary Supplements</u>.

The definition of dietary supplement includes a broad array of substances such as vitamins, minerals, botanicals and other agricultural materials, animal tissues, marine products, probiotics and other substances. These materials also range from synthetic fine bulk chemicals to complex plant extracts. The expertise, available analytical methods and production requirements and associated expenses to assure consistent quality and safety for these various materials are profoundly different. We believe the agency should take these differences into account by developing, in cooperation with industry, subset

support having more specific guidance that

GMPs for those dietary supplement categories (principally vitamins and minerals, botanicals, fermented or live culture products) in order to minimize unnecessary expense while providing sufficient regulatory guidance on key issues such as testing needs and requirements, microbiological management, animal tissue handling and processing, temperature and humidity controls, performance testing (as appropriate).

We envision general dietary supplement GMPs which apply to all DS manufacturers together with any subset GMPs relevant to the products being produced and/or manufactured by individual companies. We note there is precedent within food GMPs to provide specific guidance of this type including low acid canned foods, bottled water and infant formula. We do not believe it is advisable or practical for the agency to propose or implement DS GMPs that are so broad as to fail in giving adequate notice and guidance for specific GMPs in areas as described above. We do believe that industry would value and support having more specific guidance that would help provide both a clear GMP standard for manufacturers and FDA inspectors who have the responsibility to assure compliance with this regulation. We strongly urge the agency to establish dietary supplement GMPs under the framework of food GMPs together with additional requirements that serve to assure the safety, potency and purity of DS products.

5. **All Dietary and Other Ingredients Must be Lawfully Sold.**

FDA's proposed 21 CFR 111.35(d) would require that all non-dietary ingredient components be either:

- Authorized for use as a food additive;
- Authorized by prior sanction;
- If used as a color additive, used in accordance with a listing the includes use in dietary supplements; or
- GRAS.

FDA states in the preamble that any claim that a substance is GRAS "must 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 a dietary supplement. Further, you could not use our (FDA) response to your GRAS notification as your basis for asserting compliance with the requirements in Section 111.35(d), because an FDA response letter to a GRAS notification is not the same as your explanation for why an ingredient is GRAS."

We note and agree with the comments filed by the International Food Additives Council and the Calorie Control Council that also express concerns with respect to the agency's position on reliance of a supplier's determination that a substance is GRAS.

We are also deeply concerned that this proposed requirement not only contradicts the general practice and purpose of GRAS affirmation/notification but also would create deep confusion and uncertainty as to when a substance is indeed GRAS affirmed or otherwise lawfully sold in dietary supplements. Moreover, a number of substances with a well-known history of use in foods as well as drugs, and which are currently used in dietary supplements, would be left in a state of regulatory uncertainty. This matter is of particular importance for dietary ingredients, which are recognized as "grandfathered" or old dietary ingredients but which do not, in many cases, enjoy GRAS affirmed status. We believe the agency should clarify and correct its proposed language to confirm that GRAS affirmation/notification is both appropriate and encouraged. We also believe there is an urgent need to harmonize international excipient standards with respect to safety and use to avoid major economic disruption and burdens on companies that have developed and are using safe and well tested substances which may be present in dietary supplement formulations.

6. <u>Consumer Complaints</u>.

The agency proposes a confusing and difficult scheme to review, investigate and resolve customer complaints that would require extensive human resources, record keeping and decision-making as to what is a consumer

complaint versus an adverse event report. There is no precedent for this requirement under cGMPs for foods. (See comment under Section I above.) Moreover, We believe that the issue of consumer complaints and adverse event reporting are important and relevant to all conventional foods (as well as dietary supplements) and cosmetics.

We support the development of a comprehensive system to track and analyze adverse event reports now under development within CFSAN. This new CFSAN Adverse Event Reporting System (CAERS) should replace the current patchwork of existing adverse event reporting systems. We are concerned that the agency's proposal to develop a consumer complaint adverse event reporting system, specific for dietary supplements, contradicts the overall objective of CAERS, which is to develop a harmonized system for foods, cosmetics and dietary supplements.

We therefore suggest that this section be removed from this GMP proposal and be dealt with under the developing CAERS system.

7. <u>Testing of Raw Materials and Finished Products</u>.

FDA proposes that all finished product be tested to confirm that specifications for identity, purity, quality, strength and composition are met, provided there are scientifically valid analytical methods available to conduct

such testing. Where this cannot be done, each shipment lot of components, dietary ingredients or dietary supplements must be tested to confirm identity, purity, quality, strength and composition of such materials. We object to this proposal on three grounds:

- In many cases, there are not yet scientifically valid analytical methods to test finished products, especially botanicals. Accordingly, companies would be subjected to the enormous burden of developing finished product testing methods for hundreds, if not thousands, of products at an estimated cost of $25,000-50,000 per finished product validation method. We have received advice from a number of analytical laboratories that for complex multi-ingredient products, this price could easily double, if it is even possible to develop a multi-ingredient finished product test.

- FDA places great reliance on finished product testing on the apparent belief that it is possible to test-in quality to a dietary supplement product. It is our view that quality should be built into and not tested into products, and the heavy emphasis on finished product testing places the emphasis at the wrong stage of manufacturing and production.

- The cost burden to test finished product is economically unfeasible for both large and small companies. The majority of dietary supplement products contain multiple ingredients, which makes finished product testing exceptionally difficult and expensive. Two of our member companies have developed economic models assuming they tested every ingredient in all finished products for conformance to this provision.

CASE STUDY

Assumptions: Based on third party laboratory costs of testing, with experience and trained staff in dietary supplement. This cost is for the final good and raw material testing only, with methods that have not been validated. The batches are small in order to provide maximum freshness to the consumer.

Average number of ingredients per product:	30
Required finished product tests per batch	$3,600
Required raw material tests per batch	$13,200
Average test cost per ingredient	$440
Batch per year	18
Additional cost of finished product testing (per year):	$302,400
Increase to cost of goods:	300%

FDA estimates the average analytical test will cost $60. Our research indicates the average cost of an analytical test to be between $165-300. Heavy metal testing ranges from $45-180 per test for lead (depending on the technique and method used). Microbiological testing using AOAC methods for aerobic plate count, E. coli, yeast and mold, Staph a., Salmonella, Listeria: $200. Pesticide testing – multi-residue screen: $550.

We believe that FDA has underestimated the cost of testing for finished and raw materials by a multiple of at least 3 to 6 times. We also believe the economic impact and burden imposed by FDA's proposed finished product testing requirements to be so significant as to cause more than 50% of all small businesses to cease operations and render a significant number of medium and

large businesses economically crippled. We therefore believe FDA's economic analysis is deeply flawed and must be comprehensively reevaluated.

We are seeking additional economic data used by FDA to develop its economic model for this regulation, which we have not yet received. We are also working with the State of Utah's Department of Community and Economic Development to further develop an economic impact assessment of this provision on Utah industry and therefore respectfully request additional time to submit our updated economic analysis and effect on small business when it is completed.

8. Certified Vendor Programs.

We strongly believe that the most effective means to assure that DS/DI conform to specifications for identity, purity, quality, strength and composition are to develop rigorous certified vendor programs, which require vendors of both DI/DS to demonstrate, by a certificate of analysis and a vendor screening and management program, conformance to specifications. This would include vendor audits, inspections and verification and acceptance procedures. The general food GMPs in 21 CFR 110 specifically allow the use of certificates of analysis to verify that ingredients meet their requirements for safety, microorganism content and conformity to toxin, pests and extraneous materials

levels. We also support in-bound raw material testing be a requirement, together with any necessary in-process testing requirements as appropriate.

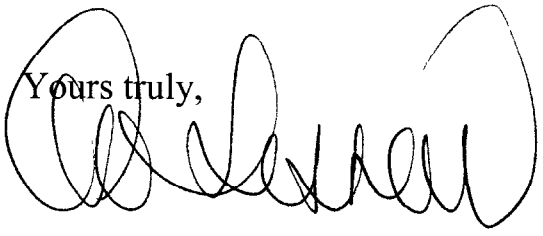
We further believe that industry should, as a matter of GMP best practices, develop harmonized certificates of analysis that would include all necessary information to provide the purchaser of the dietary ingredient or supplement to confirm conformance to specifications.

We note that FDA requested comment on whether this proposed regulation should apply to foreign manufacturers of dietary ingredients and dietary supplements (DI/DS). UNPA believes that all companies, domestic and foreign, should be held to the same standard of GMP requirements. However, given lack of FDA's jurisdiction over many foreign manufacturers and suppliers of dietary ingredients and supplements, it is essential that the principal obligation to assure conformity to specifications rest with the purchaser of DI/DS, which is best accomplished by a rigorous vendor certification program.

SUMMARY

We appreciate this opportunity to provide comments on this regulation for dietary supplements good manufacturing practices. We offer our continued support and willingness to cooperate with FDA to develop final regulations that reflect economic realities and a high common standard for the manufacture and sale of high quality dietary supplements.

Yours truly,



Andrew M. Lessman

President and CEO
Founder and Creator of Your Vitamins Inc.