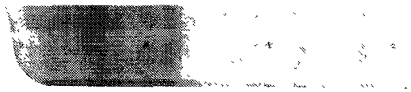
SUMMARY



I. SUMMARY OF NNFA'S RECOMMENDATIONS

A. The Requirements for Effective Process Control, Including Written Procedures and Documentation in Key Operations, Should be Enhanced

The key to a more cost efficient and effective framework for ensuring quality of dietary supplements is to strike a more appropriate balance between an effective process control system and a testing scheme that confirms that the ingredients in the product meet specifications and that the process results in consistent quality products. This proper balance must start with a greater emphasis on an effective process control system, including written procedures and documentation for all key processing operations. FDA's proposal excluded the use of written procedures and documentation for some key areas in an effort to reduce the economic burden of the proposal. Written procedures and documentation are important aspects of an effective process control system. Such controls play a vital role in the proper training and supervision of employees as well as providing an effective enforcement mechanism. An effective process control system reduces the need for the type of exhaustive and duplicative finished product testing scheme set forth in the proposal and justifies the use of a more flexible testing scheme as discussed herein. Such process controls are necessary in the following areas: 1) cleaning and maintaining equipment; 2) individual equipment logs; 3) 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.

B. The Testing Approach Should be Re-Oriented to be More Flexible and Cost-Efficient

The proposed rule appears to rely on an unnecessarily exhaustive and rigid testing scheme. The proposed rule would require analytical testing of every ingredient of every batch at the finished product stage if possible. NNFA recommends FDA modify its approach to product testing to recognize the more cost-efficient and effective approach of using reliable certificates of analysis, then relying on an effective process control system and reasonable tests necessary to assure the identity, purity, quality, strength and composition of individual dietary ingredients and dietary supplements.

1. Verified Certificates of Analysis

NNFA recommends that the final rule permit the use of verified certificates of analysis to confirm testing has been conducted and shows that the ingredients meet the manufacturer's specifications. There is no economically feasible alternative to using certificates of analysis, which play a key role in the GMP frameworks for foods and drugs. The final rule should permit use of such certifications if: (a) specific and appropriate test results are provided on the certificate; (b) the manufacturer confirms the reliability of the certificates of analysis, and that their supplier has an adequate cGMP program in place, at appropriate intervals; and (c) the manufacturer tests or examines the raw ingredients to confirm the identity of the ingredient specified on the certificate of analysis.

2. Frequency and Feasibility of Testing

While NNFA supports reasonable testing, it is only necessary to test dietary ingredients and supplements for conformity with specifications based on a frequency established under a statistically valid method to ensure in-process controls are adequate to assure the identity, purity, quality, strength 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. We discuss these issues in detail under section 111.35(g) and section 111.35(h) of our section-by-section comments.

3. Testing Responsibilities of Different Entities in the Supply Chain Should Be Clearly Demarcated

The proposed regulation should clarify the different testing obligations that should be imposed upon different companies with different roles in the supply chain. NNFA recommends that the final regulation make it clear that testing obligations fall primarily upon the raw material supplier and the manufacturer of the finished product, and that only one company in the chain has to perform the appropriate testing. For instance, companies that merely bottle and/or label finished dosage forms should be held responsible for testing that is commensurate with their role in the supply chain – testing to ensure that the manner in which such entities hold the dietary supplement does not adversely impact the potency, identity, purity or stability of the product -- but should not be required to perform the majority of laboratory requirements.

C. Dietary Supplement cGMPs Should Apply to the Entire Industry, Including Raw Material Suppliers and Foreign Firms

NNFA agrees with FDA's proposal and the industry's draft submitted in the ANPR that this rule should apply to the entire industry, including raw material suppliers and foreign firms. Broad application of the rule offers an additional layer of assurance that products have the identity, purity, quality, strength and composition they purport to have. Establishing that ingredients meet specifications in a reliable manner at the beginning of the process, and then maintaining quality through appropriate process control by manufacturers, is the most effective and efficient manner to assure quality.

Raw ingredient suppliers are the only entities in the supply chain in some instances (e.g., some botanicals or unique formulations) with the expertise to evaluate a raw material properly. NNFA understands that some suppliers are taking the position that the rule should not apply to them, arguing, in part, that as suppliers of food and dietary supplement ingredients around the world it may not be feasible to make significant changes in their process to supply to the dietary supplement industry in the U.S. NNFA believes that it will be more feasible for such suppliers to comply with the final rule without major changes to their processes or equipment if: (a) more flexibility were built into certain sections of the rule, as NNFA proposes; (b) FDA ensures a level playing field for responsible suppliers by enforcing the final rule against foreign suppliers, some of whom have a history of non-compliance and undercutting responsible suppliers; and (c) FDA works with regulators from other countries to implement standards and enforcement internationally.

D. The Final Rule, Which is Required to be "Modeled After" Food cGMPs, Should be More Flexible Where Possible

The proposed rule is rigid and overly specific in many areas where general direction would suffice to produce safe and accurately labeled products. NNFA recommends that the final rule be drafted with more consistent flexibility where possible. Appropriate flexibility means recognizing, where appropriate throughout the rule, that in many instances there may be several reasonable alternative means to achieve the legitimate mandate of the rule and, in those instances, permitting the different companies to use the most reasonable and effective means under their circumstances to achieve the legitimate GMP mandate. The following examples illustrate the type of flexibility NNFA recommends:

- 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.

- The definition of "sanitize" is more specific than food GMPs and the ANPR proposal in its requirement of a "reduction of 5 logs" of representative disease micro-organisms of public health significance. These other standards are more appropriate and flexible in that they require that sanitation be "effective in destroying vegetative cells of microorganisms of public health significance, and in substantially reducing numbers of other undesirable microorganisms", but are not overly specific.

E. Expiration or Shelf Life Dating is an Effective and Achievable Requirement When Companies are Given Appropriate Flexibility to Comply

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 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.

The NNFA GMP program includes and expiration or shelf life dating requirement, which our recommendation above is based upon. We believe and it has been our experience that expiration or shelf life dating is an effective and achievable requirement when companies are given appropriate flexibility to comply with the mandate.

F. NNFA Supports FDA's Timeline for Implementation of the Rule as long as the Final Rule Includes Appropriate Flexibility and a Balanced and Cost-Efficient Testing Regime

FDA proposes allowing very small and small firms three years to comply with the final rule. NNFA supports the compliance periods that FDA has proposed as long as the final rule includes appropriate flexibility and a balanced and achievable testing regime. In that case, we agree that the compliance framework FDA proposed will provide regulatory relief for small entities and allow them the necessary time to modify their systems in accordance with the final rule.

NNFA agrees 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. It would also delay the impact of the annual costs of compliance.

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.

G. Reasonable Enforcement Includes the Use of Third Party Inspectors

Proposing that this rule will totally eliminate recalls in the industry, as FDA does on page 12244 of the preamble, is not accurate. Recalls often times are the result of human error and are a fact of life in the food and heavily regulated drug industries; the supplement industry is no different. Our concern is that inaccurate expectations, such as totally eliminating recalls, will carry through the entire agency so that sound enforcement policies are not developed.

Supplement companies have always been held to food manufacturing standards, yet remarkably, FDA's own survey results indicate that a significant number of companies follow no formal GMP program at all. We are concerned that supplement GMPs will only hurt this industry to the detriment of public health if companies do not adhere to them as a result of lax FDA enforcement.

Further, the proposed rule does not shed light on how FDA will conduct inspections, the qualifications of those who will be conducting inspections, or enforce compliance with these new requirements. NNFA contends that while FDA could seek additional funding from Congress to actually implement inspection/enforcement activities, sufficient appropriations from Congress, especially in times like these when the federal government is running a huge deficit, will be difficult, if not nearly impossible to achieve.

The industry and members of Congress are all keenly aware of the fact that without a proper inspection/enforcement mechanism in place, maintaining consistent and widespread compliance with the regulations will be difficult. NNFA recommends that FDA seek and consider yet another already tested and successful method for inspecting manufacturing facilities, enforcing and implementing the final regulations: third-party entities that could and would be qualified to conduct inspections of entities that are subject to the final regulation.

Models for doing this can be found in the Medical Device User Fee and Modernization Act of 2002 (MDUFMA). Third party inspection is an alternative to seeking increased funding from Congress. NNFA believes that third-party certification inspections when conducted by "accredited" inspectors would not only help reduce the costs to the government, and result in quicker wide-spread compliance with the final rules but would also enable an industry to prepare for and come into compliance with these new regulatory mandates.

FDA should seek viable ways to establish an "inspection by accredited" program. At present there are several non-profit entities that presently perform similar functions and those groups could and would be helpful to FDA in developing such a third-party accreditation system.

H. It Would Assist Industry for FDA to Issue Guidance on the Type of Information that Should be Included in a Certificate of Analysis, Appropriate Test Methodology and Information to Consider When Establishing Specifications

FDA invited comment on the use of guidance documents, education, training, or other potential sources of education and training that would assist industry efforts to implement cGMP requirements. We have the following recommendations with regard to guidance documents:

- The type of information that should be included in a reliable certificate of analysis. The NNFA GMP Handbook provides an example on page 31 of the type of guidance it would be useful for the industry to have from FDA on this subject.

- How a company makes a proper determination as to the appropriateness of various test methods to show conformance to specifications, especially regarding appropriate identity testing.

- Provide an expanded description of what specifications are and the issues that must be considered when establishing appropriate specification. An example of what this guidance could look like is contained within the attached NNFA GMP Handbook, under appendix D and E.

I. NNFA's Recommendations are More Economical than FDA's Proposal Without Compromising the Legitimate Goals of cGMPs

NNFA fully supports current good manufacturing practices (cGMPs) rules for dietary supplements. The proposed rule, however, would implement a framework that is unnecessarily rigid and focuses heavily on exhaustive and expensive testing mandated and attempts to cut costs by easing certain necessary process control requirements.

FDA's assessment of the economic impact of the proposed rule grossly underestimates the cost to the industry. Most adversely affected will be very small and small (as defined by the FDA) establishments. FDA officials have stated during the course of the stakeholder meeting process that the rule would put approximately 250 companies out of business. Based on a survey we conducted of our members, NNFA believes this estimate should be much higher. Moreover, many multi-ingredient products, will no longer be economical to manufacture and will disappear from retailer's shelves. We estimate that prices of the products that remain on retail shelves will increase by approximately 35 to 50 percent.

NNFA's recommendations to improve the final rule will provide a more cost efficient and effective framework for ensuring quality of dietary supplements. The keys to such a framework will be (a) striking a more appropriate balance between an effective process control system and a reasonable testing scheme that is calculated to confirm the quality of dietary supplements; and (b) providing companies with greater flexibility in developing a specific cGMP program that meets the mandates of the rule. These changes will ease the economic impact and unnecessary burdens of the proposed rule to an acceptable level without compromising the legitimate goals of cGMPs.

While NNFA's recommendations ease the economic impact on the industry, they do so without compromising quality. Quality is built into the system by a greater emphasis on an effective process control system, including written procedures and documentation in key areas, that is still supported by reasonable testing.