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

**RE: DOCKET NO. 96N-0417, GMPs FOR DIETARY SUPPLEMENTS, REQUEST FOR EXTENSION OF 120 DAYS IN COMMENT PERIOD**

The Council for Responsible Nutrition, representing mainstream manufacturers of dietary ingredients and finished dietary supplement products, hereby urgently requests an extension of 120 days in the time permitted for submission of comments on the above-noted docket concerning Good Manufacturing Practices (GMPs) for dietary supplements. This would extend the comment period to early October. The 90-day comment period is currently scheduled to close on June 11, 2003. For the reasons outlined below, this is not sufficient time to fully develop a meaningful response, including workable alternatives to resolve some of the serious issues raised by the current proposal, which differs markedly and importantly from the ANPR in key respects.

CRN's Regulatory Affairs Committee is intimately familiar with the issues involved in the development and implementation of GMPs. In the 1980s, it was our committee that wrote the guidelines that formed the basis of the current USP manufacturing guidelines for nutritional supplements. In 1995, it was our committee that took the leadership in preparing the industry draft modeled after food GMPs, which was submitted to FDA by CRN and an industry-wide coalition of other associations in November of 1995 and which was published verbatim in the ANPR of 1997.

Since FDA published the proposed GMP rule on March 13 of this year, CRN members have invested substantial time in analyzing the proposal individually and have participated in several long conference calls and two full-day committee meetings on the subject – one on March 26 and one on April 30. Numerous assignments have been made to subgroups on specific topics that require additional study. Members of our Regulatory Affairs Committee, as well as CRN staff, have participated fully in the FDA briefings made available so far and will participate in those planned in the near future, in order to better understand the agency's views on the correct interpretation and scope of the proposal now before us.

At our most recent full-day meeting on April 30, CRN members regretfully determined that we could not avoid the need to request additional time for comment, due to the

magnitude of the challenges that remain to be resolved. As mentioned above, this rule is critical to the future of the industry, and we take seriously our responsibility to prepare a comprehensive response that provides meaningful assistance to FDA in preparing a final rule.

CRN shares the concerns expressed by three other industry trade associations in their April 21 request for a 60-day extension, but we also believe there are additional issues that must be addressed, beyond those already articulated.

This GMP rule is essential to the ability of the industry to function effectively in the future and to continue to supply consumers with high quality dietary supplement products that deliver meaningful health benefits, and it is critical for FDA and the industry to work together to ensure that the regulation is appropriately crafted to accomplish that outcome. CRN and its member companies have already invested considerable time and resources into this effort, and we will continue to devote the resources necessary to help the agency finalize and implement a sound regulation.

CRN believes the current proposal needs substantial amendment, in order to achieve its objectives in a manner that is consistent with well-established principles of quality assurance, which focus on the integrity and control of the entire production process, and we will be bringing some expert consultants with long FDA experience to assist us in making appropriate recommendations. The current proposal focuses to an inappropriate degree on exhaustive testing as its major tool for guaranteeing quality. This approach imposes major and unnecessary costs on companies that already have well-controlled processes in place. It also fails to provide the appropriate model for improving control in companies that need better procedures. Related to this point, the USP general notices recognize that "data derived from manufacturing *process validation* studies and from *in-process controls* may provide greater assurance that a batch meets a particular monograph requirement than analytical data derived from an examination of finished units drawn from that batch. On the basis of such assurances, the analytical procedures in the monograph may be omitted by the manufacturer in judging compliance of the batch with the Pharmacopeial standards."

FDA rightly emphasizes a number of small business concerns, and CRN is giving serious thought to an alternative implementation plan for very small businesses that will provide immediate improvement in their process control, perhaps through a stepwise approach. We do not believe merely providing additional time for compliance will meet the critical needs of very small businesses in this industry. The possible alternatives will require substantial discussion and elaboration within the business community, in order to ensure that all concerns are fairly addressed.

It must be recognized, however, that being small or even "very small" does not relieve a company of its obligation to be competent in its operation in order to protect the public health. These firms, regardless of their size, should already be subject to food GMPs, and those requirements should have been vigorously enforced all along. There is no excuse for any company in this industry <u>not</u> to be in compliance with basic food GMPs. Yet the

FDA survey indicates that a surprisingly large percentage of "very small" businesses say they are operating without reference to any GMPs. CRN does not believe inadequately controlled operations of any size should be allowed to continue to operate today, let alone to continue for three years after the new GMPs are finalized before enforcement would occur.

One of the keys to a well-controlled production process is for companies to prepare and adhere to written procedures (standard operating procedures, or SOPs) for various aspects of the manufacturing process. The industry draft submitted in 1995 put a heavy emphasis on the need for such written procedures. FDA's proposal omits most of these requirements, apparently in the belief that they merely add to the paperwork. In actuality, written procedures are essential to any company's ability to maintain control over the production process. Written procedures permit a complex operation to be broken down into its component parts and therefore managed effectively. For small businesses, improvements in recordkeeping, including the development of SOPs, are probably the single most effective as well as economical means of improving manufacturing practices. CRN will be revisiting these aspects of the proposal with regard to their content as well as their economic impact.

It is essential that further consideration be given to the GMP provisions that may be applicable to ingredient suppliers in the industry. CRN's member companies include a number of diverse ingredient manufacturers, including major agricultural processors, large vitamin manufacturers, and botanical ingredient suppliers. These companies supply ingredients that may be used globally in dietary supplements, in conventional foods, or in animal feeds, cosmetics, or pharmaceuticals. In many cases, only a small fraction of their production of these ingredients goes into dietary supplement products marketed in the United States. It may not be feasible for some of these producers to institute unique procedures applicable only to that portion of its production that goes into the U.S. dietary supplement industry. We are carefully considering the provisions that may be most appropriate for these diverse ingredient manufacturers, in order to ensure production of quality ingredients for use in our industry. As in the regulations applicable to GMPs for pharmaceutical finished products and the guidelines for pharmaceutical bulk active ingredients, a distinction may be required between ingredient manufacturers and companies that produce finished products. A related question exists regarding the point in processing at which a "raw agricultural product" may become a "dietary ingredient." Such questions have been addressed in the drug GMPs and in industry manufacturing guidelines for pharmaceutical excipients, and we are in the process of evaluating these precedents in order to make specific recommendations to the agency. However, some time will be required to obtain agreement within the industry on the types of distinctions that may be necessary. CRN is committed to devote the time necessary to obtaining such agreement, in order to provide FDA with concrete and feasible solutions.

CRN has a number of concerns about the economic analysis provided in the proposed rule. Since DSHEA specifically emphasized the benefits of dietary supplements in improving health and helping protect against disease, we are surprised and disappointed that projected savings in health care costs were not included among the benefits of this

rule. We believe that by improving consumer confidence in the product category, this rule can be expected to result in increased health benefits by increasing the usage of dietary supplements. Our comments will provide data that can be used in calculating some of these expected benefits.

Our member companies are only now beginning to develop a sufficient depth of understanding of the proposal to prepare their own cost estimates. The estimates that have been shared with us so far are greatly in excess of the FDA estimates. Naturally, these require further study and evaluation to be sure they are appropriately calculated. We believe it is our obligation to help the agency correctly evaluate the likely costs of any proposed rule, and, as mentioned above, we are also committed to be helpful in proposing some additional benefits that can be balanced against such costs.

CRN's member companies have a long history of providing consumers with safe and beneficial dietary supplements, made to high quality standards. We believe the purpose of GMPs is to support and help ensure product quality, for the benefit of the public health. We are dismayed by language in the preamble to the proposed rule suggesting that, in the absence of mandatory regulations, dietary supplement companies lack incentives to produce quality products. For CRN's member companies, nothing could be further from the truth. A company's reputation and good will are priceless, and our members are proud of their high standing with consumers and with the health professionals who often recommend dietary supplements to consumers.

We remain committed to the need for a GMP rule, and we hereby reaffirm our intent to be of assistance to FDA in finalizing and implementing an appropriate GMP regulation that will raise the bar for the entire dietary supplement industry, increase consumer confidence in our products, and ultimately contribute toward improving the public health – without creating new and unnecessary costs for companies that already have well controlled manufacturing practices. In order to provide that assistance to the agency, we urgently need an additional 120 days to fully evaluate some alternatives and to secure industry wide support for the most appropriate solutions.

Respectfully,

A Dickinson

Annette Dickinson, Ph.D.
President

cc: Lester Crawford, Dan Troy, Joe Levitt, Christine Taylor, Karen Strauss