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Dockets Management Branch (HFA-305)
Docket No. 96N-0417
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD. 20852

COMMENTS OF JARROW FORMULAS, INC.
RE GMP STANDARDS FOR THE DIETARY SUPPLEMENT INDUSTRY

1. *DSHEA standard of food for dietary supplements.* The dietary supplement industry specifically sought and achieved statutory limitations on any GMPs for the category. The language states, "Such regulations shall be modeled after current good manufacturing practice regulations for food. . . ." The agency's February 6, 1997 ANPR frankly states, "However, the agency recognizes that the first question that must be addressed is whether there is a need for such regulations or whether part 110 (21 CFR. . .) continues to be adequate." The ANPR does not attempt to answer this question, nor to my knowledge, has the agency done so to date in other documents. This is particularly disturbing in light of the potential for redundant testing requirements. More than any other issues, redundant testing – including shelf life stability if an expiration date is used – is a more pharmaceutical than food GMP procedure, and will be exorbitantly expensive. Threshold Distributors, parent company of Source Naturals and Planetary Formulas, has written the NNFA concerning the issues of shelf life testing and has received no response. The company, and many others, are very concerned about this issue because the NNFA's new regulations require expiration dating and will trigger the FDA stability testing requirement.

Any requirement to prevent "cross-contamination" seems hypothetical, OTC rather than food-oriented and excessive. The equipment and rigid separation may be desirable but it does not appear to be essential.

The agency should answer the following questions: Are GMPs necessary or are current regulations adequate? Many companies, including Jarrow Formulas, believe current regulations are, for the most part, adequate, but simply have not been

enforced. We questions whether failure to enforce a policy should become a self-justifying argument to inflict a more rigorous regime. Second, the agency needs to state whether each particular policy or procedure exceeds food GMPs and state the justification for doing so, including the cost versus the benefit.

2. *Statutory requirement for OMB review of economic impact.* (*Failure of NNFA to consider economic impact.*) The agency understands its responsibility to report to the Office of Management and Budget on the economic impact of its proposed rules. While the agency states that it had been "approached" by elements of the industry, the fact is that a very substantial portion – if not the majority – of the NNFA membership feels that the organization's leadership acted unilaterally and without proper consultation wit the affected membership. The views presented were those of large companies that run up the costs of smaller companies with superfluous testing. In July of 1998 I asked the late Michael Ford – and also a supplier member of the NNFA board from a large company – why a product, such as vitamin E from a GMO manufacturer such as Henkel – needs to be revalidated every time, why a periodic check to give a statistical result would not be appropriate as long as the manufacturer was GMP, that the chances of mislabeling a shipment were too rare to justify the ongoing, collective enormous expense of such redundant testing – including the finished product. Both made an ad hominem response – which obviously did not answer the question. The question of revalidating materials acquired from a GMP house appears to be an issue with NNFA standards and not FDA, but entities need to be addressed at this time given the parallel tracks.

   Again, the agency – with the cooperation of the industry – needs to survey the reliability of the industry's products before such an enormously expensive and time consuming project is undertaken. While we are currently building a new facility and intend to install an on-site analytical lab, I estimate that the GMPs will cause us to hire at least two persons in addition to the lab personnel already planned. Additional costs will ripple through the company as our suppliers are required to do the same thing. The end benefit to the consumer will be quite questionable. The persons who would supervise GMP adherence would tend to be expensive to hire – certainly in excess of $50,000 per year.

   There becomes a serious concern that many smaller, good quality tablet and capsule making facilities will be put of business.

3. *Time Frame: Phase in GMPs beginning with ISO 9000 standards. FDA allotting more time than NNFA.* Sometimes cliches are also common sense: Walk before you run applies here. The best approach to increasing quality control, and one that would save costs and give a sense of direction for the future, would be to implement ISO 9000-type standards first. Raise the quality of paper work, traceability, and reproducibility of procedures first. This will prepare an industry that is still growing and learning for the next stage.

In a sense, this industry is burdened by its own success. Since DSHEA, the industry has surged forward and is popular with the American people. Small, family-run businesses must now meet higher standards and compete with their newly-interested competitors: mass marketers and pharmaceutical houses. We have been a last-frontier industry in many ways: the self-taught, small entrepreneur with a passion for the subject. Now, we must compete against multi-billion dollar companies who are also playing favorites. BASF has given favorable treatment to two large players for its SAM-e product and the natural foods industry has been hit hard by the supplier's disregard for those who made this industry from the ground up. Now, to further burden us with a short time frame – particularly by the NNFA – to make further substantial changes and adjustments while we are being undercut by e-commerce and disloyal suppliers, is problematic timing. Accordingly, Jarrow Formulas thinks it wiser to start with ISO 9000 type procedures, and a phased approach, while the industry adjusts to the ongoing consolidation of our retail market and an uncertain future with our chemical suppliers.

4. *Over emphasis on manufacturing of capsules and tablets compared to raw materials.* Phil Vigeant, Vice President of Reliance Vitamin Company, has correctly pointed out that the real quality issue in our industry is the raw material supplier. He cites, for instance: L-tryptophan from Showa Denko containing Peak E because they failed to adhere to set procedures and completely altered their manufacturing (and possibly violated a Drug Master File, which issue has never been investigated): ginseng and quintozene; creatine monohydrate and dihydrotriazine; alpha lipoic acid and the EPI contaminant if not purified; and others. If a raw material is not coming in from a GMP-certified house, in a sealed drum from a GMP-certified distributor, then the tablet maker should be required to do more checking on the material, but there should not be an over-emphasis on the tabletting house. We are concerned that there will be a bottom-up rather than a top-down approach. (I asked the late Mr. Ford about this at the NNFA show in July and received an ad hominem response.) Accordingly, falsification of raw material certifications should carry appropriate penalties.

5. *Impact of expiration dating due to shelf study requirement, including cost and probable delays in product introduction.* This question might be better addressed to the NNFA which seems intent on not answering it, but the NNFA expiration dating requirement will trigger the FDA's shelf life study requirement. Other than the cost of these studies due to their complexity – periodic testing through the study period of each ingredient for which there is a test method – the resulting delay will destroy the competitive ability of most companies. Companies will not be able to introduce their products into a market that often has a short market life for peak sales. Also, this appears to be more pharmaceutical than food in nature: Food generally has product category expiration periods. This will require product-by-product testing rather than by category. An effort should be made to establish ingredient life expectancies depending on the delivery form an packaging.

6. *Need for industry-wide data on reliability of manufacturing tablets and capsules with micronutrients; need for data on stability of inherently oxidizable compounds such as vitamin A or carotenoids.* This impacts, clearly on expiration data, but also on best manufacturing methods. There probably should be industry-wide standards set for pre-mixing micronutrients and of oxidizable compounds. Currently, this is a matter of trade secrets. However, some sort of minimum industry processes should be set. Products presently on the shelf should be studied for these issues and then a study made of manufacturing issues.

7. *Analytical methodology problems.* The foremost problem of analyzing finished products is sample preparation. It is not uncommon to have virtually impossible sample preparation procedures. For instance, analyzing a finished ginkgo product versus the bulk material often yields very large differences. Accordingly, verification of manufacturing may often need to be done based upon input versus yield calculations.

8. *Need to develop reasonable statistically-based analytical requirements*: More reasonable cost is commensurate with low level of risk. The cost of analyzing difficult materials or multiple ingredients mitigates against universal testing, particularly considering the low risk to consumers and the low payoff in quality assurance. The agency and industry need to adopt a hazard analysis and critical point assessment approaoch. For instance, if a multi-vitamin/mineral formula is checked for its micro-nutrients, or a certain number of them with good results, then little or no testing should be required on the macro nutrients. Also in multi-nutrient products, higher priority should be given to RDI nutrients than to ingredients such as herbs where the cost of analysis is high and the benefit of such testing low. Also, potentially toxic ingredients, such as selenium if overdosed, should receive a higher priority.

9. *GMP standards should be set by the FDA, not the NNFA (and the NNFA should stay out of marketing and not promote an "NNFA GMP" logo).* For one, the logo of this health food retailer organization will be brought into the mass market by brand names that sells to both. That disserves the NNFA's health food retailers who are being seriously impacted by the mass market. Any GMPs are not a marketing issue for a trade organization particularly when there is no third party verification.

10. In conclusion, there is an industry-wide concern that the drive for GMPs is being driven by mass market and pharmaceutical companies who wish to drive out competition from smaller companies. In particular, Jarrow Formulas is concerned that GMPs will invite FDA inspections where companies simply get nit-picked. Many agents remain hostile to the industry and still they resent passage of DSHEA. I have noticed that five years after the fact, FDA field agents frequently still do not know the difference between a DSHEA-authorized Structure & Function claim and a drug claim. Opening the door to over-regulation of tabletting and encapsulating while

the greater issue is raw material integrity does less to protect the consumer than the cost warrants.

Respectfully submitted:

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