96N-0417

Mineral Resources International
1990 w. 3300 s.
Ogden, Utah 84401

Mineral Resources International in conjunction with Trace Minerals Research worked with the NNFA to help develop the NNFA comments that were submitted to you on August 7, 2003. We support the NNFA with their comments.
In addition to these we would like to add some clarifications and additional comments that we feel help the overall meaning for the benefit of our industry as well as for the FDA and NNFA.

Regarding Expiration dating pg 4 Section E of NNFA:

We should eliminate the use of the word "expiration" and be very careful with the use of the word "date." Expiration carries a "drug like" connotation, also a connotation of a hazard if the product is used beyond that date. That connotation simply does not apply to most dietary supplements. In most cases, it is simply a potency issue, where the product is still fully safe, and even maintains most of its original effectiveness, but may not still be at full label claim potency. In other cases, a product may, over time, lose some "delivery system" effectiveness, such as a product not disintegrating as fast, or the like. Anytime a product becomes essentially ineffective after a certain date, or especially if it becomes unsafe to consume after a time, an expiration date is appropriate. Most of the time, however, terms like "best used by," "best sold by," "potency guaranteed through . . ." or similar terms are more appropriate. In some cases, a statement that a product does not have an expiration date because the product does not lose its quality over time, may also be appropriate, if such a statement works from a perspective of marketplace needs, systems management, etc. In any case, the regulation must allow the manufacturer the flexibility to determine the best way to meet the requirement.
I propose the following wording:

Dietary Supplement finished products should contain an appropriate statement of shelf life. Manufacturers shall establish these dates and/or statements, and maintain appropriate supportive data to support them.

*Requirement to have two individuals involved in measuring and adding of ingredients: I am OK with requiring or not requiring. I would prefer not to require it. However, I believe that most of the time it is a very good idea. I would recommend something like the following:
It is recommended to have two individuals involved in measuring and adding of ingredients: one to measure and one to verify the accuracy of the measurement, similarly, one to add and one to verify the accurate addition of the ingredients. In the absence of this, you must have and follow a written procedure that is sufficient to ensure and verify the accuracy of both measurement and addition of all ingredients listed on the master and batch production records.

96N-0417

C 225

Re: 111.50(f), the part that says: **You must not reprocess a dietary ingredient or dietary supplement if it is rejected because of contamination with microorganisms of public health significance or other contaminants, such as heavy metals;**
Several points:
Sterilization is allowed. Sterilization of herbal materials by prior manufacturers/suppliers is common practice, including multiple sterilizations at the sterilization plant until the material meets the desired specification. This proposal would seem to only prohibit re-sterilization as a form of rework. However, sterilization can take place at a variety of times and places prior to final QC approval of finished product, and in a variety of ways. Sometimes a mild form of sterilization is applied more than once during processing, until the desired level is achieved. If a product reaches final form and a final test reveals that insufficient sterilization has been applied, that should not preclude any form of rework processing that would have been allowable if it had been applied earlier in the process, as long as that rework process can be shown to NOT damage other essential characteristics of the product in an irreparable way because of the process being applied at this later stage of manufacture.

For example, we purchase many herbal ingredients in an unsterilized state, and run plate count testing, as needed. The stage at which material is plate count tested varies according to need, which we have learned by our experience with the product. We believe it is more in keeping with the natural character of the ingredients to avoid sterilization when we can, to only sterilize where experience and testing have shown it is needed, and we only accept certain types of sterilization. Our proprietary process provides a partial, but quite effective sterilization. If the end product has a higher plate count than the standard we have set for ourselves, in some cases, and as determined by our QC unit, the product can be put through an additional sterilization phase, which would have also been allowed at an earlier stage, and end up with the same level of sterilization and purity that the product would have had, if the process had been applied at the earlier stage, and without any significant negative effect on the end product. We can see no legitimate consumer benefit from prohibiting this, as long as the proper steps are followed. Further, since appropriate training and or experience are required in a QC unit, we believe an appropriately trained or experienced individual would be able to recognize or figure out when this type of reprocessing would and would not be appropriate.

Regarding heavy metals: Most heavy metals that would be found in a dietary ingredient or dietary supplement are not present as a result of an act of contamination, but rather, are a naturally occurring component of the original raw material(s). Heavy metals that have been determined to be problematic have had various "maximum allowable level" standards set for them. Mere presence is not a problem, only presence above certain levels, or more accurately, consumption above certain levels. (See Recommended Dietary Allowances, 10th Edition, by National Research Council, National Academy Press, Washington DC, 1989. Among other things, the discussion in this book acknowledges the possibility that at least some of the heavy metals considered toxic may play a beneficial nutritional role at very low naturally occurring amounts, which presupposes that their mere natural presence in foods is not problematic.) (Additionally, the levels of those metals at which potential for harm is present, are also effected by the presence or absence of other substances. This has been researched and documented elsewhere.)

Remember, it was not that long ago that selenium was considered a toxic metal, and it still is, if consumed above certain levels. For naturally occurring substances that are allowed at all, whether they be heavy metals or important nutrients or other substances, blending to raise or lower the overall levels should NOT be a problem, if the appropriate levels can be achieved by such blending.

We would propose that such reprocessing (for both microorganisms and for other contaminants) should be allowed, as long as it can be determined, for each instance, that such reprocessing will eliminate or acceptably reduce such forms of contamination and that the reprocessing will not inappropriately adversely effect the component, dietary ingredient or dietary supplement.

One caveat: Perhaps a distinction should be made between naturally occurring or previously existing substances on the one hand, and contaminants that are introduced during processing on the other. Introduced contaminants would generally be of a nature that they shouldn't have been there in the first place, they may be indicative of a deeper problem, and in some cases it may be more difficult to remove them appropriately. EVEN SO, IF IT CAN BE DETERMINED, by one with appropriate training, that the contaminant is not an indication of a deeper problem, or that the deeper problem has also been appropriately addressed, AND that it can be properly and appropriately removed, it should be allowed.

DSHEA recognizes the admirable safety record of the dietary supplement industry. The industry existed prior to DSHEA. One of the purposes of DSHEA was to guarantee to the consuming public continued access to those products. This was based partly on the safety record of the products, the consumers' right and desire to continued freedom to choose in the marketplace and to continue to have a variety of products to choose from, and the consumers' strong desire for continued access to, and information regarding this industry's products in particular. This is evidenced by the overall strength of the response congress received from the public regarding DSHEA.

FDA's assessment does not adequately account for the impact of the proposed regulations on certain segments of the dietary industry which existed prior to DSHEA, and were included in the industry's safety record and the reasons for the existence of DSHEA. One of those segments includes small manufacturing companies making relatively small batches of products and products with multiple ingredients, often a large number of ingredients. The effect of the proposed GMPs, as we understand them, would likely eliminate this entire segment of the industry.

To be more specific, our company, Mineral Resources International, has been manufacturing dietary products for over 33 years. Our original products are still on the market. For over 20 years, we have manufactured formulated products with multiple ingredients, in relatively small batches. In order to maintain freshness, many of the ingredients are purchased in relatively small quantities just prior to manufacture of the batch. For many of the products, the cost of testing every testable nutritional ingredient in every batch for identity, purity, quality, strength and composition, is more than the total cost of raw materials for the entire batch. For many raw ingredients, the cost of testing every incoming lot for identity, purity, quality, strength and

composition is more than the purchase price of the incoming lot. For example, many of our ingredients are whole botanicals. The quantity of the botanical is listed on the label, but no claim is made for any specific active substance in the botanical, although in many cases, the known minimum level of some vitamin and mineral constituents of the botanical are included in the total calculations for the specific nutrients. The standard test for strength and composition of a botanical would use HPLC methodology, testing for specific chemical substances and compounds. We do not currently own an HPLC, as with the case for many companies of our size, so we must send these tests to an outside independent lab. The cost of a single test can be in the range of $100-300.00, sometimes more. The results of the test would not improve the information on any of the product labels, nor would they improve the quality of the product. The cost of the testing, if required, and especially if required on every incoming raw ingredient and/or on every finished batch, would make using the ingredient economically unfeasible. Removing beneficial botanical ingredients from formulations because of economics of required but not beneficial testing cannot possibly be an economic benefit to consumers. In some cases, the testing requirement, as proposed, would add such an economic burden to the cost of manufacturing the product that the entire formulation would become economically unfeasible to manufacture. I.e., the required selling price of the product would be too high to be feasible in the marketplace. We believe that over half the products we manufacture would fall into this category.

Other testing requirements create similar hardship, if required as proposed.

Allowing the use of verified Certificates of Analysis is a much more economical alternative, and is sufficient to accomplish the purposes of DSHEA. The GMP should establish reasonable *minimum* standards for certificates of analysis. Among these could be a requirement that the C of A truthfully disclose what tests were actually performed on the particular batch of ingredient. We believe it is also reasonable for a C of A to report other information as long as the document truthfully discloses the nature of that information. A requirement that manufacturers verify the validity of a C of A is a reasonable requirement, but the actual method of verification should be left to the manufacturer or the Quality Unit, based on the actual circumstances. Requiring the actual test data to be a part of the C of A would make the C of A too costly and cumbersome, and to someone who is not trained to understand the chemistry and method of calculation, would make the C of A impossible to understand correctly. However, a review of the actual test data from which finished numbers were derived, for of a number of Certificates of Analysis would be a valid method of verifying the validity of a particular supplier's C's of A.

Allowing skip lot testing, or other reasonable methods of testing "as needed" to verify product compliance with the label claim, potency, safety, etc., requirements, as those requirements exist for each individual product, and according to the nature of each individual product, is also a reasonable and satisfactorily economical alternative, and sufficient to accomplish the purposes of DSHEA.