EnzymaticTherapy
NATURAL MEDICINES®

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April 1, 2003

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

Re: Comments to Information Collection pertaining to Docket No. 96N-0417

Dear Sirs:

This letter is in reference to Docket No. 96N-0417, proposed 21CFR Parts 111 and 112, "Current Good Manufacturing Practice in Manufacturing, Packing, or Hold Dietary Ingredients and Dietary Supplements". Comments provided here address Information Collection for which the comment period ends April 14, 2003.

Recordkeeping Burden Dramatically Understated

Simply stated, it is our studied opinion that your estimate of annual recordkeeping burden of the proposed regulation at **500,587** hours (68 Federal Register 12219, Table 1) is not only astounding but even more troubling is **likely low, possibly by several orders of magnitude**. The time spent creating records that then must be maintained for at least three years and must always be available for FDA inspection and copying will be daunting for the dietary supplement industry.

The reason we believe the estimate is low has to do with the assumptions used in generating it. You state in section V of the proposed regulations that the estimated 1,566 firms representing the dietary supplement industry will expend the 500,587 hours of time involved in the recordkeeping burden of the proposed regulation. This amounts to an average of 320 annual hours per firm assuming your estimate of 1,566 firms involved in manufacture of dietary supplements. The 320 annual hours per firm is derived at least partially from the estimated annual batch production you assumed of 260 batches per year per firm.

> **During the annual period between March 1, 2002 and February 28, 2003 Enzymatic Therapy processed 1,337 production batches. Using your relationship between batch numbers and hours, this would translate to a burden of 1636 hours in recordkeeping only for our firm.**

This number of batches is 5-fold higher than the estimated annual batch number assumed in your calculations. While there could be some efficiencies to be realized as batch numbers hit certain count plateaus, Enzymatic Therapy's recordkeeping burden will be at least several orders of magnitude greater than the 320 hours per firm your assumptions make. We suspect that many firms like us who are categorized as small by your size criteria will face a similar circumstance.

We believe the assumptions you have used are flawed and need to be redone once you have better data which you will certainly get from industry comments. Since

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this is such an important point, why not consider simply asking industry to provide you with their most recent number of annual batches as you have defined it in this proposed statute before you finalize it?

A further reason for challenging the validity of your data comes from the fact it was determined from Research Triangle Institute (RTI) survey results obtained by sampling only 238 of your estimated 1,566 firms that manufacture, repackage, supply, hold, import or export dietary supplements (data from §VII.B.4.b, 68 Federal Register 12226 of the proposed regulations). In addition to that point, the request for survey information was preceded by a "lead letter on FDA letterhead and a one page brochure to explain the purpose of the survey, the value of the establishment's participation, and the agency's confidentiality procedures" (quotation from 68 Federal Register 12226). We believe the survey responses represent biased input due to fear of reprisals if responses had the potential to put respondents in bad light with FDA. It is also possible that industry participants who did not respond to the survey are those operating most outside the requirements of current law. We at least hope you can see the plausibility of this hypothesis given the low response rate of your survey.

Cost Implications Dramatically Understated

It naturally follows that the cost assumptions you have made in the proposed regulations would also be flawed since these are derived from the same data from which the batch assumptions were derived. We will provide you a complete analysis of cost impact to our company in the comments we will be sending you on this subject prior to the end of the June 11, 2003 comment period. It should be noted, however, that we believe the costs will be very significant to our company and like sized companies throughout the industry.

Related Considerations

Your analysis is predicated upon the assumption that recordkeeping activities will center predominantly on the processing of specific batch numbers during the year. Batches can vary greatly in complexity as a function of the number of active ingredients and excipients used. Some formulas contain a single active ingredient while others have active ingredient numbers in the 30-45 range. Our firm has many products with comprehensive vitamin and mineral supplementation including trace mineral blends. Under the proposed regulations these products would be highly intensive with regard to analysis and recordkeeping. You propose strict recordkeeping requirements in §111.40(c)(1) on components, ingredients, supplements, packaging, and labels received by manufacturers. A company that produces batches of single ingredient products (e.g., vitamin A, C, E, etc.) in one packaging configuration would have much lower recordkeeping burden than a company that produces multiple ingredient products in several packaging configurations. Similarly the influence of the number of ingredients in a product will also be impacted by §111.35(d)(4) which deals with the documentation of GRAS status. This will add to the recordkeeping burden making it onerous as well as highly costly. It is not clear whether your analysis has taken these influencing factors into account.

We have not attempted to make specific recommendations about the individual hours by tasks in Table 1 (68 Federal Register 12219) because it is too confusing and provides insufficient background for us to substantiate it. For example, you state the annual need for 367 recordkeepers pertaining to the recordkeeping intensive section §111.35(c). This implies that the vast majority of companies will

not even have a recordkeeper. This makes little sense to us unless you project that only a small percentage of current companies will be in business once the proposed regulation is fully implemented, a conclusion not quantified in any of your assumptions. There are numerous other examples in this table which are difficult for us to understand how they were derived.

Agreement with Principle, Object to Proposed Execution

While we wholeheartedly agree with the intent of the proposed regulation...to ensure the identity, purity, quality, strength and composition of dietary supplements, we feel the basis for recordkeeping requirements to support this proposed regulation is seriously flawed. It dramatically underestimates the recordkeeping burden and cost to be placed upon the dietary supplement industry.

Suggested FDA Action Steps

1. We suggest one step you could take which is actually rather simple would be to ask industry manufacturers to state and provide support for the number of production batches that would need to be analyzed on an annual basis.
2. Similarly you should ask the industry to dimensionalize other influencing factors such as the number of analytes in those production batches manufactured.
3. Once you have these pieces of information, you could more confidently provide the recordkeeping analysis as well as cost and cost/benefit analysis.

We are hopeful you will find this insight helpful as we are supportive of the principle and intent of the proposed initiative. We do also hope you will not implement these proposed regulations in their current form, as they will add a very significant burden to companies our size and to the industry in total. There are ways to provide the assurances we all seek in relation to product identity, purity, quality, strength and composition without making the recordkeeping burden so onerous. We will provide you additional insights on these alternatives in our comments pertaining to the June 11 comment period.

Sincerely,

Robert C. Doster, Ph.D.
Sr. V.P., Scientific and Regulatory Affairs