PHARMACEUTICAL PRINTED LITERATURE ASSOCIATION

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August 8, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852
Attn: Dockets Manager

RE: 21 CFR Parts 111 and 112, Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Dietary Ingredients and Dietary Supplements [Docket No. 96N-0417]

Dear Dockets Manager:

I am writing on behalf of the Pharmaceutical Printed Literature Association (PPLA) with regard to the request for comments on 21 CFR Parts 111 and 112, Current Good Manufacturing Practice (CGMP) in Manufacturing, Packing, or Holding Dietary Ingredients and Dietary Supplements, published as Docket No. 96N-0417 in the March 13, 2003, edition of the *Federal Register*.

The PPLA joins with the dietary supplements industry, and related consumer groups, in applauding the United States Food and Drug Administration (FDA) for taking aggressive steps in establishing quality assurance for dietary supplements by implementing rigorous standard practices in manufacturing. The PPLA particularly supports the imposition of accountability to manufacturers for delivering consumers full disclosure of product contents and potency via new labeling and packaging standards. As the agency has requested in the proposed rule, the PPLA offers in these comments information and suggestions regarding labeling content, manufacture and cost.

As the world's only trade group exclusively representing printers and manufacturers of pharmaceutical inserts, labels and cartons, the PPLA is uniquely qualified to speak to labeling requirements, particularly because the Agency's proposed CGMPs are appropriately more akin to those for over-the-counter (OTC) drug products than for other products that are regulated as food. We have therefore limited our comments to Proposed Subpart E relative to labeling. The PPLA specifically suggests, as will be detailed in these comments, that the following additions and amendments be made before the rule is finalized by the Agency:

- Establish specific label content for dietary supplements to include, among other things, batch, lot or carton number;
- Stipulate that the label be the manufacturer's responsibility and that it be included in the manufacturer's Master Manufacturing Report (MMR);
- Require a "use by" or similar date that indicates shelf life to be printed on dietary supplement packaging;
- Allow a year for labeling compliance for all manufacturers regardless of their size.

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PPLA Background

The PPLA is a not-for-profit trade association chartered in 2001 to serve as the voice of pharmaceutical printed package information manufacturers, and provides a forum for members to promote and improve delivery of information for protection of patients and consumers in general. The PPLA is comprised of member companies that print package inserts, outserts, folding cartons, labels and other components for the pharmaceutical industry, as well as companies that manufacture machinery and raw materials used to produce pharmaceutical printed literature. For more information on our association I invite you to visit our Web site at www.pplaonline.org.

Printed packaging and literature supplied by PPLA members typically contain FDA-approved copy that is intended to help make drugs safe and effective for end users. Printed packaging and labeling also supports health care professionals in their duties caring for patients and preventing health problems. PPLA members put enormous effort – and take extreme care – to manage their product and information flows so that the correct label copy accompanies drugs from the time they are manufactured through the time when they are ingested. Our trade group's mission is to improve safety and risk communication, and we see the labeling provisions of the proposed rule as no less central to public health than those in place for OTC medications.

PPLA Comments

1. Establish specific label content for dietary supplements to include, among other things, batch, lot or carton number.

FDA requested comment on label content and specifications. As labeling is a core expertise of our trade group, the PPLA maintains it is well qualified to respond on this point. Members of the PPLA have extensive experience producing labels and packages for multiple product formats including capsules, liquids and powders. Our member printing companies produce labels that accommodate a wide variety of content. The technology and mechanical tools exist to produce expanded labeling for dietary supplements efficiently and cost-effectively. Therefore, the PPLA respectfully requests that FDA incorporate into its final rule guidance for specific label content. The content should include a complete listing of ingredients, their relative percentages, batch or lot number, intended use, safety information, directions and product information.

Specifically, the PPLA supports the labeling recommendations of the U.S. Department of Health and Human Services' (HHS) Office of the Inspector General (March 2003, "Dietary Supplement Labels: Key Elements," publication no. OEI-01-01-00120, http://oig.hhs.gove/oei/reports/oei-01-01-00120.pdf). This framework follows a model similar to that of OTC drugs, which is an established tool in limiting consumer adverse events. The Office of the Inspector General (OIG) states in the guidance document that Congress has recognized in the Dietary Supplement Health and Education Act (DSHEA) the importance of labels and their role in helping consumers make informed and appropriate health care choices for themselves and their families. Moreover, "Labels can be particularly significant, given that dietary supplements are often used as self-care products, and labels are an easily accessible source of information...label oversight is a key regulatory tool for FDA to promote the safe use of dietary supplements among consumers." (Executive Summary, OEI-01-01-00120, page i).

The PPLA endorses the HHS recommendations, with the addition of batch or lot number on the label, and emphatically appeals for their adoption in the forthcoming rule. We further endorse the OIG's proposed label presentation, which calls for: 1) a standardized format with similar types of information in a similar order across supplements; 2) distinct product features to assist consumers in distinguishing supplements from other healthcare products; 3) readability, with language and visual cues that are easily understood by consumers; 4) balance to present information in a fair and balanced format that omits marketing and sales pitches; and 5) constructive use of space whereby innovative packaging is employed to expand label space.

2. Stipulate that the label be the manufacturer's responsibility and that it be included in the manufacturer's Master Manufacturing Report (MMR).

The proposed rule calls for the creation and use of a Master Manufacturing Report (MMR) by all producers of dietary supplements. The PPLA supports this directive and further requests that the final rule stipulate that the MMR be the responsibility of the manufacturer, and that it include the specific label to be applied to each dietary supplement package or container.

This is a requirement in place for pharmaceutical drug products that is effective as the manufacturer is accountable for product integrity, and is best positioned to provide guidance on safe use. It seems appropriate and correct to apply the same standard to manufacturers of dietary supplements because consumers use them as medicinal products, rather than as a food. Supplements also have been shown to result in adverse events when not taken properly, or when ingredients and potency are not as stated on the label.

3. Require a "use by" or similar date that indicates shelf life to be printed on dietary supplement packaging.

The proposed rule does not call for inclusion of an expiration date on dietary supplement packages, and the Agency requested comment on whether expiration dates should be required. The PPLA maintains that the final rule should require a use-by date in the interest of consumer information relative to effectiveness.

We recognize the Agency's reasoning for not requiring expiration dates in the proposal, particularly with regard to botanicals and unclear information regarding active ingredient. However, our experience with manufacturers of products marketed for health benefit informs our view that accountability is appropriately required for efficacy, a critical value feature that directly impacts benefit and ingredient integrity. If the Agency intends to oblige dietary supplement producers to deliver a sounder product to consumers, it should require producers to be familiar enough with products' active ingredients to know their "freshness window" and thereby make a determination of shelf life for those ingredients. To enable an informed public through full disclosure relative to freshness, shelf life or expiration information must be conveyed to consumers, and it is the manufacturer's responsibility to do so on the product label.

4. Allow a year for labeling compliance for all manufacturers regardless of their size.

It is the position of the PPLA that the higher labeling standard be applied uniformly across manufacturers because consumers are unlikely to differentiate between small companies and large ones when selecting their supplements. For this reason, the PPLA asks FDA to allow one year for labeling compliance for all

manufacturers regardless of their size.

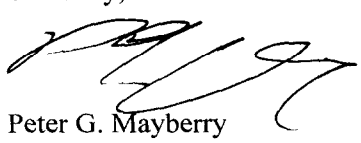
We further maintain that small manufacturers are more likely to suffer competitively if their labels lack important ingredient and other information relative to labeling employed by their larger competitors. As we will show later in these comments, enhanced labeling is a cost-effective packaging feature and should not represent a significant cost burden when outsourced to a qualified print-packaging vendor. Moreover, labels already represent a budgeted cost item for dietary supplement producers. Labels with additional content would add little to manufacturer overhead.

Supplemental Cost Information and Conclusions

FDA has asked for comment from manufacturers regarding costs related to the proposal. While the PPLA represents printers and manufacturers of pharmaceutical labels, packages and inserts, and not dietary supplements, we wish to note for the record that our experience could be of use to the Agency and industry. Our members represent the majority of U.S. printers and manufacturers of pharmaceutical printed literature whose customers primarily are drug manufacturers. Member companies employ the latest technology and equipment to assure the very best cost-to-value ratios to manufacturers. Economies of scale enable PPLA members to offer manufacturer customers a highly cost effective end product, produced on time and on budget, with great sensitivity to the customer's bottom line. The PPLA would be pleased to provide the Agency, if useful, with production cost estimates and information for any new labels and other printed information that may be called for in the final rule.

The PPLA again asserts support for the FDA proposal to establish CGMPs for dietary supplements, especially with regard to expanded and improved labeling. If we can provide any information on the technical aspects of printing-related applications, please do not hesitate to call upon us.

Sincerely,



Peter G. Mayberry
Executive Director