CHPA

founded 1881

January 11, 2011

Sandy Benton
Center for Drug Evaluation and Research
U. S. Food and Drug Administration
10903 New Hampshire Ave., Bldg. 22, Rm. 4204
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Re: Draft Guidance for Industry on Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an Investigational New Drug Application; 75 *Fed. Reg*. 63189-63191 (October 14, 2010). Docket No. FDA-2010-D-0503

Dear Ms. Benton:

Founded in 1881, Consumer Healthcare Products Association (CHPA) is the national trade association that represents manufacturers and distributors of over-the-counter (OTC) medicines and dietary supplement products. Members from the CHPA Dietary Supplements Committee (DSC) are submitting comments on the FDA draft guidance for industry entitled "Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an Investigational New Drug Application[1,2]." These comments are focused on issues related to dietary supplements as referenced in the draft guidance (Section VI. C.).

VI. C. Dietary Supplements

As outlined on page 10 of the draft guidance, CHPA DSC members agree that when the intent of the clinical investigation is to support a claim of a dietary supplement's ability to diagnosis, cure, mitigate, treat, or prevent a disease (*i.e.*, a drug claim), an investigational new drug application (IND) is needed.

[1] Draft Guidance for Industry on Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an Investigational New Drug Application (October 2010). Accessed November 14, 2010, at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM229175.pdf.
[2] 75 *Federal Register* 63189-63191 (October 14, 2010). Accessed December 10, 2010, at http://edocket.access.gpo.gov/2010/pdf/2010-25851.pdf.

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Furthermore we agree that an IND is not needed for studies intended only to investigate the effect of a dietary supplement on the structure or function of the body.

CHPA DSC members understand the intention of the examples used in the draft guidance to demonstrate the subtle differences for when an IND is needed. However, we recommend the agency include additional clarity as to when an IND is required for dietary supplement research. The final document will be more beneficial if more definitive examples are used (see line numbers 376-383 of the draft guidance). For example, the draft guidance states that clinical studies to evaluate a dietary supplement's ability to treat constipation would need to be conducted under an IND. However, clinical studies could also be conducted to evaluate a dietary supplement used for relief of *occasional* (emphasis added) constipation, an allowed claim under the Dietary Supplement Health and Education Act of 1994 (DSHEA)[3]. In the January 6, 2000, Final Rule[4] (Final Rule) published by the agency, it is stated in the preamble that claims "for relief of occasional constipation" would not be considered as disease claims so long as the product is not labeled for the treatment of chronic constipation, and thus we would expect this type of research to be permitted without an IND.

There are other examples of physiological conditions that, depending on the claim made, could be elements of a drug or dietary supplement claim. These distinctions should be considered when incorporating examples of when an IND is, and is not, needed in the final guidance. One illustration of these differences is in the preamble of the 2000 Final Rule[4]. In this rule, FDA notes that "…some minor pain relief claims may be appropriate structure/function claims for dietary supplements" if there are no references to any other conditions, symptoms, or parts of the body that would imply treatment or prevention of disease[4]. We would expect a clinical study on this type of structure/function claim to be conducted without an IND. Clinical studies to support statements made regarding treatment or prevention of disease related to relief of minor pain (drug claims) would require an IND. Another instance where a claim could be either a drug or dietary supplement claim, depending on the language used, involves cholesterol levels. The agency has stated that a dietary supplement claim of maintaining cholesterol levels that are already within a normal range would not necessarily imply a disease claim[4]. Claims regarding "lowering cholesterol" are interpreted as implied disease claims[4]. Hopefully the examples cited in this submission demonstrate the subtle differences between the language of a disease claim and a dietary supplement claim that help determine when an IND would be required. Because the guidance document should be written for industry personnel of all experience levels, the examples used in the final guidance should be as clear and concise as possible.

Additionally the CHPA DSC recommends that the final guidance clarify that studies to substantiate qualified health claims (QHCs) or Significant Scientific Agreement (SSA) health claims would not necessarily require a sponsor to conduct the clinical evaluation under an IND. Consistent with FDA regulations[5] and guidance[6] on QHCs, support for a QHC may be based on the totality of the publicly available evidence for the claim, which may include data from well-designed studies conducted using generally recognized scientific procedures and principles. Furthermore, we believe studies should be exempt from INDs if they are conducted on dietary supplements for target endpoints associated with an

[3] Dietary Supplement Health and Education Act of 1994. Accessed November 30, 2010, from http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/ucm148003.htm.
[4] Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body; Final Rule (January 6, 2000). Accessed January 6, 2011, from http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=2000_register&docid=00-53-filed.pdf.
[5] 21 CFR 101.70. Accessed January 7, 2011, from http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm.
[6] Qualified Health Claims. Accessed December 6, 2010, from http://www.fda.gov/food/labelingnutrition/labelclaims/qualifiedhealthclaims/default.htm.

approved health claim. In our opinion the final guidance should reflect that the need for an IND for studies to substantiate dietary supplement health claims should be determined based on the intent of the study.

Other Points to Consider

CHPA DSC members request that any industry guidance that is ultimately issued be reconciled with the agency's interpretation of Section 912 of the Food and Drug Administration Amendments Act of 2007 or FDAAA (US Public Law 110-85[7]). Specifically, Section 912 of FDAAA prohibits introduction into interstate commerce any food to which has been added certain drugs or biological products, unless these products meet certain requirements. Under Section 912, a food (dietary supplements are regulated as a subset of foods) cannot be marketed if a drug or biological product has been added to the food unless such product was marketed in food prior to FDA approval and before substantial clinical investigations have been instituted. Therefore, depending on the use and claims made for the finished product, a substance used as either a drug or as a dietary ingredient could no longer be used as a dietary ingredient once an IND is filed as the application would connote initiation of a substantial clinical investigation. Under this circumstance, the substance would have to be marketed in a food product prior to filing of the IND to continue its use as both a drug and dietary ingredient. To the best of our knowledge, FDA has yet to issue a formal response to its request for comments on Section 912 of FDAAA as noted in the July 29, 2008, *Federal Register* notice[8]. Therefore we recommend that the agency consider this point as it finalizes this draft guidance.

There are other factors that FDA should consider when finalizing this guidance. A great deal of research on dietary supplements is conducted by academic researchers independent of industry funding or support. Academic researchers may not have access to information needed (*e.g.*, chemistry, manufacturing, and controls (CMC) information) to complete an IND. If independent investigators are required to submit INDs to conduct their studies, valuable research on dietary ingredients and products could potentially be stifled. Although the document is entitled as "Guidance for Industry," other stakeholders beyond industry may in fact use the information contained in the document. Therefore, we recommend that FDA be mindful of other users of this guidance as the agency finalizes the document.

Summary

Members of the CHPA Dietary Supplements Committee thank FDA for the opportunity to provide comments on the draft guidance on IND applications[1]. In summary, for the final guidance, we ask the FDA to:

- provide greater clarity as to when an IND is needed for dietary supplement research,
- use clear and concise examples to demonstrate the differences for when an IND is needed for dietary supplement research and when it is not,

[7] Food and Drug Administration Amendments Act of 2007 (US Public Law 110-85). Accessed November 22, 2010, from http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf.

[8] Food and Drug Administration Amendments Act of 2007; Prohibition Against Food to Which Drugs or Biological Products Have Been Added; Request for Comments. *Federal Register* vol. 73, No. 146 (43937-49340). Accessed November 22, 2010, from http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=2008_register&docid=fr29jy08-61.pdf.

- ensure the final guidance on the need for an IND for dietary supplement research is reconciled with Section 912 of FDAAA, and
- consider the potential implications of the guidance beyond users of the document from the industry sector.

We look forward to your thoughtful consideration of our recommendations and are happy to answer any questions.

Sincerely,

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Director, Regulatory & Scientific Affairs

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