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Statement by Norman R. Farnsworth, Ph.D., College of Pharmacy,
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August 18, 1999, 1999

(Docket Number 99N-1174)

I would first like to thank the FDA for giving me this opportunity to provide comments that may assist the Agency in developing an overall strategy for achieving effective regulation of dietary supplements under DSHEA. My remarks will be concerned only with those products generally referred to as "botanical dietary supplements", but they may also apply to other categories of DSHEA products.

My name is Norman R. Farnsworth, Ph.D. and I am a Research Professor of Pharmacognosy at the College of Pharmacy, University of Illinois at Chicago. In addition, I serve as Director of the Program for Collaborative Research in the Pharmaceutical Sciences in the College of Pharmacy and as Director of Research for the Functional Foods for Health Program (UIC and UIUC). The College of Pharmacy has been designated as a World Health Organization Collaborating Centre for Traditional Medicine since 1983 and I also serve as Director of this Centre. Most recently I served as a member of the "Commission on Dietary Supplement Labels". I was initially trained as a Pharmacist. Although I do not officially represent any organization, I believe that my experiences in the aforementioned capacities and my continuous research experiences in the field of natural products, all me to express opinions that I feel would be consistent with the research community in natural products.

I believe that a high priority by the Agency should be directed, either by regulation, or by recommendations for changes in the Act, that every company manufacturing finished products for sale must have a substantiation file for each product that presents evidence of safety and efficacy for the structure-function claim being made and that this file should be made available to the FDA on request for products that FDA has found necessary to question based on "courtesy letters" to the manufacturer. FDA has already accepted the guidance concerning the content of the substantiation file made by the Commission on Dietary Supplement Labels (CDSL). The CDSL debated this issue in depth but felt for confidentiality reasons, if FDA received a copy of the substantiation file, it

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would no longer be a "confidential" document and could be requested under a Freedom of Information request by competitors. There can be nothing in a Substantiation File that is not already in the public record, i.e. references to safety and efficacy studies from published scientific papers. My personal opinion is that the public good will be better served, as will legitimate manufacturers of botanical dietary supplements, if FDA could request a copy of this file to better enable them to assess questionable products.

Further, I strongly believe that a section of the Substantiation File should include the methods and results for each batch of manufactured product to show that the product was "standardized". This is the only way that consumers can be assured that each batch of product is consistent with previous batches. The "standardization" could be as simple as a thin-layer chromatography profile (fingerprint), or other chromatographic profile. Whether or not individual peaks would have to be identified is less important than showing that essentially the same number and magnitude of "peaks" are present in the product from batch-to-batch. Some manufacturers might elect to quantify individual components of a mixture. When previously unseen major "peaks" appear in a "fingerprint", this would be cause for concern. There are very few botanical dietary supplements in which a single "active" component can be identified and thus the overall picture of the components would be most important.

Also, in "standardized" products, when a "percentage" of active material is given, this is a very deceptive procedure. Standardization should be in terms of the weight (mg.) of material in each dosage form being claimed. A good example is that most St. John's Wort products claim standardization as 0.3% of hypericin (or a mixture of similar compounds). If 10 mg of extract containing 0.3% hypericin is put into a table or capsule with a filler, the dosage form no longer contains 0.3% hypericin.

As you are probably aware, most of the promotion of botanical supplements as seen by the public on national television is reasonably truthful, but advertisements in magazines, newspapers and sent through the mail to consumers, to me contain false and misleading claims that could eventually be detrimental to human health, and could never be substantiated based on science. Also, I have recently seen bottled water containing various botanical extracts, i.e. St. John's Wort, Echinacea, etc. that bear DSHEA labels. There is no way that these products with a DSHEA label could be backed up with a Substantiation File that shows EFFICACY in support of the structure-function claim. If the Substantiation File in such cases were available to FDA, these products could then be removed from the market place.

Assessment by the FDA of the substantiation file on questionable products to me is a high priority item for the agency to address.

Second, I am quite concerned that in their proposed rules, the

Agency has found it necessary to redefine "disease" in order to allow tighter regulations concerning allowable structure-function claims. This makes me wonder whether "constipation" or "hangover" or any number of short term, transient or occasional syndromes are "diseases". To quote from DSHEA the CDSL was to "...evaluate how best to provide truthful, scientifically valid, and not misleading information to consumers so that such consumers may make informed and appropriate health care choices for themselves and their families...". If the CDSL had known that the FDA was to recommend a change in the definition of "disease", the recommendations might have been different. In FDA's proposed rules, they have recommended allowing such structure-function claims as "for men over 50" and others that surely do not fulfil the mandate of "not misleading". The FDA should utilize the age-old definition of disease and allow a greater degree of flexibility in claims based on the science that exists in support of the claims, i.e. claims allowable under OTC monographs (with expansion of these types of claims).

Third, I would like to address the issue of safety of botanical supplements. It has generally been my opinion that if the ingredient stated on the label of a supplement represents what is in the container, and if the recommended dosages are not exceeded, that botanical supplements are quite safe. The literature attests to this. The problem lies in assuring that an extract or whole plant material is consistent from batch to batch and from year to year. There are ways to do this in a cost-effective and efficient manner, but when I think of the recent problem of a "plantain" product being allowed to enter the USA and then distributed to many sources and being put in many products and then finding out that it contained Digitalis after several consumers were hospitalized, I am appalled. A simple five minute examination of this product under light microscopy would have told the trained observer that Digitalis was in the product! I am therefore hopeful that when the final rules are put forth by FDA on GMP that issues such as this will be addressed.

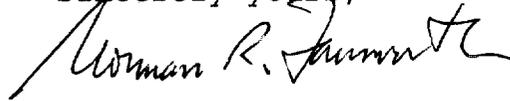
Fourth, Although the Agency is in the process of developing guidelines for the OTC review of botanical dietary supplements, I would strongly recommend that this activity should be expedited and be given a very high priority, as also stated in the CDLS report. If there is an even playing field, and botanical dietary supplements are reviewed according to the guidelines of the previous OTC review panels, perhaps as many as 80 per cent of the 25 most frequently used botanical supplements would receive OTC status. If this should occur, most of the problems facing the Agency with regard to regulations being promulgated for this area of supplements would disappear.

Fifth, as you are aware, the Agency has been criticized in making regulations without appropriate input by scientists and others who are qualified by education, training and experience in the field of botanical research. The CDSL was aware of this when it made the guidance recommendation that "an expert advisory committee

on dietary supplements be established to provide scientific review of label statements and claims and to provide guidance to the industry regarding safety, benefit and appropriate labeling of specific products". The Agency should indicate whether or not they feel that such an expert advisory committee would be useful to their short term and long term deliberations on dietary supplements. It is my recommendation that such an advisory group, outside of the agency, would be useful to FDA.

Finally, each of the issues that FDA identified in the May 13, 1999 Federal Register announcement, were discussed in the Report of the Commission on Dietary Supplement Labels, published November 24, 1997 in accord with Section 12 of DSHEA. The comments by FDA on this report (Fed.Reg.63(82):23633-23637) in early 1998 were less than substantive and I would strongly recommend that FDA conduct a reassessment of the guidance and recommendations of the CDSL, including the available public record of testimony before the Commission, in formulating its final rules.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Norman R. Farnsworth". The signature is written in a cursive style with a large, stylized initial 'N'.

Norman R. Farnsworth, Ph.D.
Research Professor of Pharmacognosy

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