

**Comments to the Federal Food and Drug Administration  
Docket #99N-1174**

**Prepared by**

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**Introduction to the American Herbal Pharmacopoeia™**

The American Herbal Pharmacopoeia™ (AHP) is a non-profit educational organization dedicated to the development of quality control and therapeutic monographs for botanical products in the United States. The AHP was formed to address deficiencies in the current manufacture and use of botanicals whether as dietary supplements or as medicines. This includes confusion regarding the analysis of botanical products or accurate information regarding their use.

We commend the Agency for addressing issues regarding consumer safety, labeling regulation for health related products, and streamlining the process by which such issues are addressed and resolved. The AHP welcomes the opportunity to work with the Agency in developing rational guidelines for the regulation of herbal products. Following are our comments to the questions posed by the Agency.

1. Are there any safety issues, labeling, or marketplace issues that the agency should address quickly through enforcement efforts in order to ensure that products on the market are safe and not misleadingly labeled?

**Safety Issues:** There are two primary areas to be focused on regarding safety issues. The first is regarding adulterations and contaminations; the second is regarding the reporting of adverse events and interactions with conventional medications. Adulterations and

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contaminations can be minimized through education. The primary focus of the AHP is to provide the information needed by manufacturers to eliminate the use of unintentional adulterants in the marketplace. Our work provides complete botanical, macroscopic, and microscopic descriptions for identification purposes, and additionally provides a thin layer chromatography fingerprint. Each monograph also identifies the most common adulterants used for a particular botanical so that manufacturers can be informed of potential substitutions in the marketplace. The AHP encourages FDA to work cooperatively with other government and non-governmental organizations in facilitating this type of work. One area where FDA could have assisted in improving the safety of botanicals was regarding the relatively recent adulteration of plantain with digitalis leaves. FDA did a significant amount of work on this issue which increased the awareness of this potential problem in the industry. The Agency should go one step further in making all of the identification information including microscopic identification known to the industry so that future problems could be avoided. To the best of my knowledge this information was never forwarded to any of the trade associations for dissemination to member companies. Several requests from AHP to obtain this information for inclusion in a Botanical Microscopy Identification Handbook we are developing were not responded to.

Contamination is a significant issue that needs to be addressed. FDA should provide clear guidelines on ways that microbial contamination of botanicals can be minimized through proper treatment methods. Currently, ethylene oxide, autoclaving,  $\gamma$ -irradiation and microwaving are the primary means of sterilization. Each has their inherent problems regarding safety, preservation of constituent profile, relative cost, availability, and environmental impact. Guidance from the Agency would assist the industry greatly.

Regarding reporting of adverse events, it is clear that the current MedWatch adverse reporting system of FDA is inadequate for generating meaningful data that can be used to increase the level of safety of dietary supplements by consumers. MedWatch is a passive system with no critical review of the data that are submitted. This we believe is its greatest flaw and has led to findings being misrepresented in the media. In order to be a meaningful reporting system, raw data must be critically reviewed to determine whether the adverse event reported is in fact associated with the botanical(s). We understand the enormity and difficulties of such a task but believe it is achievable by employing a multi-

disciplinary committee of health professionals consisting at least of: herbalist, physician, pharmacist, pharmacologist and an industry representative. The data and findings generated from such a committee would provide a significant service to the industry, the Agency, and to consumers.

The AHP developed an active reporting system for botanicals. The system included specially trained nurses who would do an adverse event intake from a variety of sources including consumers, health professionals, and manufacturers. The reporting form was designed to garner enough information so as to be able to make an educated decision about the relative validity of the report and direct association with the botanical. If further information was required the system was designed to track it down by directly contacting the individual making the report until all pertinent information that could be obtained was obtained. Data collection would be facilitated through the dissemination and publication of adverse events reporting forms and through a toll free number.

This adverse reporting system had two basic arms: the first was an Immediate Response mechanism by which those conducting the intakes would immediately inform the contracting organization (AHP) of potential health hazards that have been observed. The contracting organization (AHP) would then initiate an immediate review with the appropriate personnel in order to quickly generate an appropriate response. This response would then be disseminated through a variety of channels including the trade organizations and the FDA, as well as other organizations as appropriate. The second arm included a review of the accumulated data collected. The information would be reviewed by a multidisciplinary committee of botanical medicine experts and annual or bi-annual reports would be generated. The findings represented from these reports could then form the basis for appropriate warnings on labels regarding short term and long term toxicity, dosages, interactions with conventional medications, and other such information. The AHP had arranged to conduct a small pilot study to test the system. Confirmed data collection centers included two herbal supplement manufacturers (one of whom currently has adverse event reporting systems in 8 countries), two hospital pharmacies, two naturopathic dispensaries, and two medical doctors who utilize botanical medicines in their practices.

This pilot study was never conducted due to the inability to obtain funding from the herbal products industry. The information was turned over to FDA who also expressed that lack of funding would prevent such a system from being implemented. We believe such a system is a necessity not a luxury. Increased use of botanicals will lead to increased reporting of adverse events and drug interactions. The industry, health professionals and consumers need accurate, critically reviewed information about the safe use of this product category. The current MedWatch system, due to its uncritical structure, does a great disservice to the public who requires and desires an accurate assessment of botanical safety.

One immediate step FDA could take in increasing public safety regarding botanical product use is by acknowledging the value and importance of already existing national and international monographs such as those produced by American Herbal Pharmacopoeia, European Scientific Cooperative of Phytomedicine, German Commission E, United States Pharmacopoeia, and World Health Organization. These resources contain a tremendous amount of information that should be considered as authoritative, and their use for qualitative and therapeutic purposes be encouraged by the Agency.

2. What type or area of research on dietary supplements should FDA direct its resources.

The comments included here mimic testimony provided previously by the American Herbalists Guild. There are a number of different areas we feel are important for the Agency to invest in. First and foremost is education of manufacturers in quality control issues, especially among the smaller and relatively new companies. FDA has made strides in this area through the sponsorship of botanical microscopy workshops which have been well received. Additional classes and workshops in botanical identification, raw material sourcing, macroscopic, microscopic, and chemical fingerprinting, record keeping, good manufacturing practices, etc. are needed and would go a long way in improving the quality control of the industry. This would require the Agency take a proactive participatory role rather than a regulatory and adversarial role as has been the case historically.

Other areas to focus on would be the review, development, and/or acceptance of validated analytical methods used for the qualitative and quantitative evaluation of raw botanicals and botanical products. Works are underway by other organizations such as United States Pharmacopoeia, American Herbal Pharmacopoeia, and the Institute for Nutraceutical Advancement. Efforts should be made to work cooperatively avoiding the duplication of efforts.

Lastly, we believe it is important for FDA to take a proactive role in investigating the potential benefit of botanical supplements. It is not a mistake that botanicals have remained the oldest form of medicine known to humans. It is for good reasons, many of which defy normal pharmacological investigation, but which none-the-less have value. The Agency has historically primarily reacted to problems in the marketplace rather than taking a proactive role in partnering with industry to minimize problems. Perhaps this is inherent in the Agency's mandate. We would like to suggest that it does not have to be this way. If the political will was there, FDA could assume a leadership role in determining the role dietary supplements have to play in American health care. FDA's role in this capacity should be well defined and limited so as not to be duplicating the efforts of others such as the Office of Dietary Supplements.

3. In light of limited resources, how can FDA leverage more resources to implement its strategies

Based on the goals as stated above, partnering with industry on specific initiatives such as an improved adverse reporting system, enhanced good manufacturing practices (GMPs), and identification of known adulterants would be the most efficient means for improving the quality control of dietary supplements for consumers.

4. What tasks should be included under each separate program area listed in the priorities document?

No comments.

5. What factors, such as regulations and guidances, should FDA consider as it determines how to best implement each program area?

We do not believe FDA has tapped into the expertise necessary for making an informed decision about how botanicals should be regulated and feel that FDA should focus on the development of guidelines rather than regulations. Too many times such policy statements are made by so-called experts who possess no, or little, knowledge about the practical use of botanicals. While able to provide valuable input, these typically-relied-upon botanical experts lack the skill and experience needed to make informed decisions about herb safety policy. Similarly, the professional herbalists community has been all but completely ignored in such discussions both within the Agency and the herbal products industry. We oppose the Agency's attempt to impose regulations that we feel it lacks the expertise to address adequately. We encourage the Agency to actively seek cooperation from members of the industry and the professional herbal medicine community in addressing these various issues.

Regarding adverse reporting systems, many herb companies currently have such systems in place. Similarly, pharmacovigilance programs are available worldwide. This information need only be collected and reviewed to provide a good basis of knowledge from which to work from. We believe it would be appropriate to encourage the primary herbal products trade associations to create an annual assessment (based on sales volume) to members in order to fund an adequate adverse reporting system.

6. In addition to ensuring consumer access to safe dietary supplements that are truthful and not misleadingly labeled, what other objectives should the overall strategy include?

FDA should assist consumers in understanding the benefits of dietary supplements. The Agency appears to continue to operate from the mind set that dietary supplements are of questionable safety and negligible benefit. It is time this attitude be changed to embrace that fact that an ever increasing body of scientific knowledge and consumer satisfaction demonstrates there is significant value in the use of dietary supplements.

7. Are the criteria for prioritizing each task appropriate? Which tasks should the agency undertake first?

No Comments

This concludes our comments. We appreciate the Agency accepting these comments and the AHP will support all rational efforts to develop appropriate guidelines that assure botanical products, whether used as supplements or medicines, are used with the highest degree of safety and efficacy.