American Herbalists Guild

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Food and Drug Administration
Docket Management Branch (HFA-305)
12420 Parklawn Dr. Rm. 1-23
Rockville, MD 20857

May 22, 1997

To Whom It May Concern,

Please find enclosed 2 copies of our comments regarding the Good Manufacturing Practices proposal (Docket 96N-0417) as published in the Federal Register. We hope these are helpful to the Agency, and appreciate the ability to provide these comments.

Sincerely,

Roy Upton, Herbalist
Vice-president
Director, Legislative Affairs

96N-0417

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American Herbalists Guild

Comments to

Advanced Notice of Proposed Rulemaking
May 18, 1997

Docket No. 96N-0417
RIN 0910-AA59

Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Dietary Supplements; Proposed Rule

Department of Health and Human Services
Food and Drug Administration

Docket Management Branch (HFA-305),
Food and Drug Administration
12420 Parklawn Dr. Rm. 1-23
Rockville, MD 20857

Prepared by

Roy Upton, Herbalist
Vice-president, Legislative Coordinator

Submitted
May 18, 1997

The American Herbalists Guild
The American Herbalists Guild (AHG) is the only peer-review organization in the United States representing herbalists who specialize in the medicinal use of plants. As such, the AHG predominantly represents health care practitioners utilizing herbal supplements, including herbalists, licensed acupuncturists and naturopathic physicians. Many practitioners compound their own herbal supplements specifically designed for the needs of their clients. A small percentage of our membership also are involved with small herbal cottage industries. We respectfully submit the following comments to represent the views and concerns of our membership.

Introduction
It has been estimated that there are approximately 15,000 practicing herbalists in the United States consisting of traditional herbalists, licensed acupuncturists and naturopathic physicians. These health professionals represent the most highly trained and most experienced herbalists in the United States. Many herbal health professionals maintain their own dispensing and compounding dispensatories.

One integral component of many traditional herbal practices is the need to develop an herbal combination that is specifically designed for the needs of the client. Often times, ready-made dietary supplements do not fit these needs. Such individual compounding can consist of the combining of powders or whole crude herbs or the mixing of various liquid extracts. In many cases, most specifically for traditional herbalists, the herbalists are gathering their own plants so as to maintain the highest degree of quality control, gathering plants at their optimal growing time and processing them in their fresh or freshly dried state to assure maximum potency, rather than be dependent upon commercially available supplies that often do not meet the herbalists, or client's need.

Initial Comments
Request for practitioner exemptions: The nature of manufacturing dietary supplements for commercial sale, is vastly different than the compounding or manufacture of individual herbal preparations by practitioners. The experience and training of herbalists allows for the ready identification of adulterants and visual contaminants. In the majority of cases, the herbs to be used are prepared as teas or alcohol:water extracts which minimizes the risk of microbial contamination. In addition, the practitioner is directly interfacing with the client and is able to readily determine if a problem exists with a botanical preparation. We therefore, respectfully request that should additional GMP's be put in place, that a specific exemption be established for practitioners individually manufacturing and compounding for their clients. Such exemptions have been established in various countries for herbal practitioners including in Australia, China, Japan, India and the United Kingdom.

I. Background
We feel it is important to emphasize that the Dietary Supplement Health and Education Act (DSHEA) does not require that the Agency develop additional good manufacturing practices (GMP's) for the manufacture of dietary supplements, but acknowledge that the Agency may propose such regulations. We strongly support the amendment as reflected in section 402(g) (21 U.S.C. 342(g)) which states that

"Such regulations shall be modeled after current good manufacturing practice regulations for food and may not impose standards for which there is no current and generally available analytical methodology."

We agree with the objectives as outlined in the industry submission that dietary supplements should be manufactured in a way that assures their safety, are unadulterated and not misbranded, and meet labeling declarations. In response to the Agency's initial inquiry of whether additional GMP's are needed, or if current food GMP's are adequate to assure the afore-mentioned objectives,we believe that current GMP's as mandated for food products are adequate to serve these purposes.

There appears to have been a long history of safe use of dietary supplements in the United States when manufactured according to food GMP's as is currently mandated. The majority of toxicity issues that have arisen with dietary supplements have been associated with improper or excessive use of potentially toxic botanicals such as ephedra as used in weight loss and "natural high" products. In other cases adverse effects have been associated with adulterants or contaminants which under current GMP's, should have been detected.

In the first cases, these toxicities have been a result of insufficient education on the part of the consumer, or insufficient labeling guidelines. Prior to DSHEA the Agency would not allow specific warnings on dietary supplement labeling, or such a product could be branded as a "drug". Therefore, manufacturers were limited in their ability to provide sufficient labeling guidelines to consumers. DSHEA has amended this deficiency, and now manufacturers have the ability to provide such information. This change has already resulted in more appropriate labeling on dietary supplements. In the latter cases, current food GMP's require that appropriate manufacturing and handling procedures be established that prevent adulteration and contamination. If a manufacturer is not processing their products in a manner that assures a product is not contaminated or adulterated then they are already out of compliance with current GMP's which is predominantly an enforcement issue.

Therefore, we believe that the current GMP's as established for food products, are sufficient to assure that dietary supplements are manufactured in a way that assures they are safe, unadulterated and adhere to the label declaration, and do not support the establishment of additional GMP's at this time. We further have a concern that certain elements of the industry-proposed GMP's are similar or identical to pharmaceutical GMP's. These may be impossible for small businesses to meet, and will surely be impossible for practitioners who compound their own preparations to meet, thus significantly and negatively impacting their livelihoods and practices.

II. The Industry Submission
B. The Industry Draft

In the second paragraph of section B "dietary ingredient product forms" are defined as "tablets, capsules, soft-gels, gel caps, liquids and other forms including--under some conditions--conventional food forms." This definition would encompass the majority of preparations prepared by individual practitioners. It could also include conventional herbal teas which are largely classified as foods. We believe a clearer distinction needs to be made to avoid confusion as to what GMP's the manufacture of a particular product needs to adhere to. If a product is marketed as a conventional food, it should be clear that food GMP's are mandated. If marketed for therapeutic purposes, then appropriate GMP's must be in place.

IV. Summary and Request for Comments
1. Is there a need to establish defect action levels (DALs) for dietary supplements?

In the discussion of whether or not defect action levels (DALS) should be established for dietary supplements, the Agency states that consumption of botanicals as dietary supplements may result in a much greater exposure to the botanical ingredient for consumers "because the dietary supplement will be consumed in greater amounts than if the ingredient was in a food as a spice or flavoring agent."

While we agree that DALS should be established for botanicals, based on recommended consumption patterns, we do not feel consumption of botanical dietary supplements will result in greater exposure than if used as a food. Just the opposite is true. The largest

percentage of botanical dietary supplements are meant to be taken for limited periods of time, whereas the same botanical included in foods as a spice are ingested, oftentimes in relatively large amounts, for long periods of time. Botanical supplements, by the very nature of their being "supplements", are used in conjunction with an overall health promoting lifestyle that incorporates dietary modifications, exercise, stress reduction techniques, etc. However, regulatory restraints have prevented the inclusion of appropriate use instructions on dietary supplement labels. It is our hope that the provisions of DSHEA will result in more appropriate labeling and use information for dietary supplements.

The American Herbal Products Association has begun the process of collecting data points as a means for identifying DAL baselines as presently reflected in industry supplies. These data points will provide the guidelines necessary for developing meaningful DALS. We strongly support these efforts, but at this time, until the necessary data is collected, do not feel it should be mandated under GMP's.

2. Testing requirements for positive identification of dietary ingredients, particularly plant materials.

There are numerous procedures for ascertaining the identification of botanical materials. These include gross organoleptic, macroscopic and microscopic analyses, thin layered chromatography (TLC), high performance liquid chromatography (HPLC), gas chromatography-mass spectral analysis, UV—RI spectography, etc. There is an abundant amount of information regarding the macroscopic and microscopic analyses of plant materials. This data is widely available in the primary literature, as well as in compendial texts worldwide. For qualitative purposes, TLC fingerprinting is very reliable and relatively inexpensive. Though there is an abundance of available HPLC methods available for botanicals, there is a limited amount of methods that have been independently verified. However, efforts are underway to develop and validate analytical methods by various organizations including the American Herbal Pharmacopoeia and the United States Pharmacopoeia.

The methods of analysis necessary for qualitatively or quantitatively determining herb identification and relative strength will be determined by the form of raw material that is used. When crude botanicals in their whole form are utilized, gross organoleptic analysis, in most cases, will be sufficient for ascertaining, with a large degree of confidence, the identity of botanical materials with strict adherence to gross anatomical characteristics. Organoleptic analysis requires specialized training in traditional herb processing or pharmacognosy. If crude powdered materials are used, microscopic analysis is a minimum requirement for proper identification. When standardized extracts are utilized, accurate certificates of analyses, or independent HPLC validation, or other quantitative procedures, are required. In the area of analytical testing, we feel it is important to develop methods that are subjected to peer review and institute a certification program for testing facilities as the analysis of natural products requires specialized training in natural product chemistry.

3. Standards for Contamination with Filth

The industry efforts to establish DAL baselines will provide the basis for establishing meaningful limits for filth. In addition, such limits have already been established and are cited in numerous pharmacopoeial compendia, including past and current editions of the United States Pharmacopoeia, current pharmacopeias in the international community, and standards as established in the American Herbal Pharmacopoeia.

4. The Agency asks for comments on whether there is a need for CGMP to include requirements for manufacturers to establish procedures to document that the procedures prescribed for the manufacture of a dietary supplement are followed on a continuing or day-to-day basis.

We support the rational documentation that GMP's have been adhered to, and that such requirements should be similar to those required for foods.

5. The agency asks for comments on whether dietary supplement CGMP should require that reports of injuries or illnesses to a firm be evaluated by competent medical authorities to determine whether follow-up action is necessary to protect the public health.

We feel that some type of evaluatory procedure is necessary for determining the seriousness of reported adverse effects, but are not sure as to the best means for establishing such a reporting mechanism. Most manufacturers and distributors do not have trained medical personnel to serve this function adequately. Minimally, we believe that procedures should be established by which consumers could be informed to seek medical assistance in the event of a potentially serious adverse event, and be advised to seek the assistance of a qualified health professional if the need arises. However, we also acknowledge that this category of products has been among the least problematic from a toxicological point of view.

Long-term we feel it is important to establish a meaningful herbal adverse reporting mechanism. We feel the Agency's Medwatch program is insufficient due to its lack of criticalness. The American Herbalists Guild has developed an adverse reporting form but lacks the funding to implement a reporting system.

6. FDA asks for comments on whether CGMP for dietary supplements should require that manufacturers establish procedures to identify, evaluate, and respond to potential safety concerns with dietary ingredients.

We feel that every manufacturer has the responsibility to determine if the ingredient they are to use has the potential to pose a safety hazard. However, we disagree with the assertion that dietary ingredients as used in dietary supplements have little history of use as foods, in the amounts used in dietary supplements. Until DSHEA, nutritional and botanical supplements were regulatorily classified as foods. The majority of botanicals used have a considerable amount of traditional and scientific data regarding their use, including more than 100 years of use in the United States for many of them, regulatorily as foods. The majority of nutritional supplements, most specifically, the conventional vitamins, minerals and amino acids, have been consumed for decades. A large percentage of herbs used in traditional Chinese and Ayurvedic herbalism have a literal history of thousands of years, including food use in soups, teas and syrups.

While acknowledging that manufacturers have a responsibility to use safe ingredients, we feel that the self affirmation of GRAS process, as established for food substances, and previously in place for supplements, has historically proved to be sufficient to assure the safety of ingredients used in dietary supplements. We also feel the Agency has the authority to challenge a manufacturer of its assertion, and that the manufacturer has the obligation to provide substantive documentation that they believe the ingredient is safe. However, we strongly support the provision outlined in DSHEA that establishes that the Agency may not act arbitrarily, but must establish that there is a factual basis for asserting that a dietary ingredient is unsafe.

For the overwhelming majority of dietary supplements, particularly for botanicals used in dietary supplements, authoritative historical data of the botanical's use should form the basis for using the herb. This should also be supported by a collection of modern studies supporting the use of the plant, or other authoritative sources of information such is contained in pharmacopoeial compendia. Should new information bring the safety of an ingredient into question this would require appropriate evaluation and a benefit-risk assessment.

7. The agency asks for comments on whether specific controls are necessary for computer controlled or assisted operations.

No comments.

8. The agency asks for comments on whether certain, or all, of the requirements for manufacturing and handling dietary ingredients and dietary supplements may be more effectively addressed by a regulation based on the principles of Hazard Analysis and Critical Control Points (HACCP), rather than the system outlined in the industry submission.

While HACCP provisions may be necessary for foods with a high propensity for microbial contamination that can pose a significant public health risk, we do not feel they are necessary for the manufacture of dietary supplements, and strongly oppose HACCP requirements. Botanicals, and other dietary ingredients used in the manufacture of dietary supplements. We also strongly disagree with the Agency's assertion that HACCP requirements may provide a more flexible and less burdensome regulatory framework for manufacturers. HACCP was specifically designed to minimize potential problems within a high risk industry, and are very burdensome to adhere to. Historically such risks have not been associated with the dietary supplement industry, and therefore this class of products should not require HACCP procedures.

9. The agency asks for comments on whether broad CGMP regulations will be adequate, or whether it will be necessary to address the operations of particular segments of the dietary supplement industry.

We believe that some differentiation between various segments of the industry needs to be made, most specifically between manufacturers and raw material suppliers. Broad GMP's should be applicable to the manufacturing industry if consideration is given to the procedures necessary for testing various types of products as included in our comments under #2. However, procedures specific to raw botanical suppliers may be warranted. A raw material paper trail should be generated by which manufacturers can determine with a high degree of accuracy the source of their raw materials. Ideally, affidavits should be required as to the source of the material, who provided the botanical identification, when the material was harvested, location of harvest, drying and handling procedures, etc. While valuable, and in some cases necessary, such requirements will be difficult to implement and enforce, especially for imported botanicals. Alternatively, such affidavits would not be necessary if manufacturers adhere to their own internal standards for identification of raw materials.

Conclusion

While we have provided comments to the industry's proposal, at this time, we do not feel that additional GMP's are necessary for the manufacture of dietary supplements. We hope these comments will be helpful to the Agency, and we would be happy to provide additional assistance if it would be of help.