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AMERICAN BOTANICAL COUNCIL

HERBALGRAM

August 11, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Docket No. 1996N-0417 -- Good Manufacturing Practices for Dietary Supplements

Dear Sir or Madam:

The American Botanical Council (ABC) is herewith providing comments on the proposed regulations for Good Manufacturing Practices for Dietary Supplements, as published by the Agency in the *Federal Register* on March 13, 2003.

ABC is an independent nonprofit research and education organization under section 501c3 of the IRS code. ABC is not directly involved in the importation, manufacture, distribution, or marketing of any dietary supplements. However, as a publisher of the quarterly peer-reviewed journal *HerbalGram* and other publications that deal with the regulation, quality, safety, and efficacy of herbs and various herbal preparations, we consider the issue of GMPs for botanical dietary supplements to fall within the scope of the subject matter about which ABC researches and educates. Accordingly, we offer the comments below.

ABC is aware that numerous trade associations, industry members, and other interested parties are providing detailed comments on specific aspects of the proposed rules. ABC's comments are being offered independently of other groups and, in general, will not deal in detail with issues regarding specific technical areas of manufacturing, testing and related processing matters.

1. Regarding Dietary Supplement GMPs "modeled" after Food GMPs and Enforcement of Existing cGMPs

Up to the present and until the Agency determines its final rules for GMPs for dietary supplements, the GMPs governing the manufacture of all herbal dietary supplements are those current GMPs that apply to the manufacture of conventional food products. ABC supports the development of reasonable and appropriate GMPs for the manufacture of herbal dietary supplements and appreciates the FDA's extensive work in developing the propose rules. ABC believes that although new, more strict GMPs may be reasonable and appropriate, that full implementation and enforcement of the currently existing GMPs governing conventional foods can adequately deal with many of the issues that the Agency has given as examples of adulteration and poor quality. For example, the problem several years ago where a shipment of plantain leaves (*Plantago major* and other spp.) from Europe was accidentally adulterated with yellow foxglove leaves (*Digitalis lanata*) could have been adequately obviated with the implementation of quality control measures that are part of current GMPs for conventional food ingredients (per CFR Title 21, Part 110, Subpart E, Section 110.80(a); available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=110.80.)

1996N-0417 C240

Section 9 of the Dietary Supplement Health and Education Act of 1994 (DSHEA) authorized the FDA to promulgate GMPs modeled after those GMPs already in existence for conventional foods ("shall be modeled after current good manufacturing practice regulations for foods...") or that the Agency's definition of "model" to mean "a preliminary pattern" is consistent with the intent of Congress in this matter, especially considering that the Agency appears to have chosen a relatively narrow definition of "model" from many that are available in various dictionaries. While we are supportive in general of the idea that manufacturers should adequately test raw materials used in the production of high quality herbal dietary supplements, in reviewing the Agency's proposed rules for GMPs published in March, we are not convinced that the proposal reflects processes and techniques that are consistent with GMPs required for conventional foods, and it appears that the Agency has gone outside of the domain of such GMPs to include specific GMP requirements that seem to be drawn from those required of drugs (i.e., finished pharmaceuticals) and medical devices.

Furthermore, we are aware that the basic premise for GMPs for foods is based on principles related to *sanitation*, while GMPs for drugs are based on principles of protecting the public from *adulteration* and related problems, based on the premise that drugs may be inherently unsafe. We do not believe that it is appropriate for the Agency to presume the general lack of safety of dietary supplements in general, and herbal dietary supplements in particular. We believe that the market experience related to the vast majority of herbal dietary supplements sold in the United States confirms the strong evidence supporting the relative safety of most herbal dietary supplement products, notwithstanding a few notable exceptions (e.g., ephedra).

We are also concerned about some of the language in the preamble to the proposed rules in which the Agency suggests that dietary supplements are not subject to the Agency's regulatory overview, and that the Agency is unable to adequately inspect or enforce current GMPs for conventional foods.

2. Consumer Complaints and Adverse Event Reporting

The Agency has proposed that consumer complaints about dietary supplements be incorporated into record-keeping procedures as a part of the proposed GMPs. As an educational nonprofit organization concerned with educating the public about the benefits and potential risks of herbal dietary supplements, ABC considers such information that can be gained from such reporting to be valuable. However, we are not aware of any such requirement in current food GMPs. Further, we are aware that the Agency is currently revising and improving its adverse event reporting system (CFSAN Adverse Event Reporting System, CAERS) and we believe that this and other appropriate mechanisms should be developed outside the framework of GMPs to gather and evaluate consumer comments, complaints and adverse event reports on foods, dietary supplements, cosmetics and other consumer products that fall within the scope of the Agency's regulatory authority.

3. Recognition of Compendial Standards

In section 111.35 of the proposed rules, the Agency discusses numerous laboratory methods that can be utilized for the identification and quality assessment of botanical ingredients. These methods include macroscopic, microscopic, and chemical analytical methods of various types. The analytical methods developed and validated by AOAC International and the methods included in United States Pharmacopeia (USP) monographs have been acknowledged as valid by FDA. ABC believes them to be authoritative sources for such methods. In addition, ABC believes that there are other reliable sources of appropriate analytical methods that the Agency should acknowledge, including the botanical monographs of the American Herbal Pharmacopoeia (AHP), the European Pharmacopeia (Ph Eur), and other EU national pharmacopeias, e.g., the German Pharmacopeia (DAB), among numerous others. These botanical monographs are among the most useful and scientifically credible source of identification testing and quality control information for botanical ingredients. For example, the AHP monographs contain methods of identification for authentic materials as well as potential adulterants, plus guidance information regarding the sourcing of botanical material materials of acceptable quality. Taken together, these sources (including two volumes of monographs produced by the World Health Organization, WHO) provide guidance and testing methods for over 100 botanical materials. ABC believes that FDA should recognize and explicitly acknowledge the authoritativeness of these monographs (i.e., AHP, Ph. Eur., DAB et al.) as authoritative sources of scientifically valid analytical methods, and quality standards for botanical dietary supplements and botanical ingredients.

4. Exemption for Clinicians and Compounding Pharmacists

ABC believes there should be an exemption in the GMPs for practitioners. Other nations, notably Australia and Canada, have developed GMPs and related guidance for botanicals that recognize that there are various types of practitioners who dispense herbs and herbal preparations in a clinical setting. This includes some licensed acupuncturists as well as compounding pharmacists, who operate in an appropriately licensed retail establishment that is designed for pharmacy dispensing and compounding. Such practitioners dispense small quantities of herbal preparations directly to patients and consumers, often providing a unique service of blending custom formulations that are specific for each patient/consumer and which may not be available in a pre-prepared retail supplement product. For example, the Therapeutic Goods Act of Australia makes such an exemption from GMP requirements for such practitioners.* Further, the newly developed Canadian Natural Health Products Directorate (NHPD) has also published guidelines that exempt practitioners.** We believe that such an exemption from the Agency's GMP regulations is reasonable and appropriate and is in the public's interest.

*The actual wording of the Australian exemption is shown in a table at the end of this letter.

** The wording of the Canadian exemption is a follows: "These Regulations place requirements on persons who sell NHPs, namely manufacturers, distributors, importers, packagers and labellers. The NHPD considers that growers, who handle and/or treat a product in order to

preserve the integrity of the raw material, are not considered manufacturers. Health care practitioners (for example, pharmacists, Traditional Chinese Medicine (TCM) practitioners, herbalists, naturopathic doctors, etc.) who compound products at the request of a patient are not included within the manufacturer definition. The NHP Regulations are not aimed at regulating the practice of complementary and alternative health care practitioners or the practice of traditional Aboriginal medicine. The NHPD intends to adopt a guidance document regarding the distinction between manufacture and sale of NHPs and compounding and distribution of compounded products by complementary and alternative health care practitioners and Aboriginal healers." [Canadian Natural Health Products Directorate (NHPD) Regulatory Impact Analysis Statement concerning the Natural Health Product (NHP) Regulations; available at: http://canadagazette.gc.ca/partII/2003/20030618/html/sor196-e.html]

5. Recognition of Benefits of Dietary Supplements and Impact on Consumers

The FDA writes in its proposal that GMP regulations "will help to ensure that the potential health benefits that Congress identified as the basis for DSHEA are obtained and that consumers receive the dietary ingredients that are stated on the product label." We concur with the Agency that adherence to appropriate GMPs is important to help ensure that "potential health benefits" of dietary supplements are delivered to consumers and that consumers are receiving what they are paying for. We believe that in the interests of greater public health that it would be appropriate for the Agency to begin to publicly recognize some of the scientifically documented "potential health benefits" of dietary supplements and that the agency become more proactive in educating the public in this area.

Further, ABC believes that implementation of the currently proposed GMP regulations will create financial burdens that are not attainable by many small manufacturers of herbal dietary supplements, some of whom produce high quality unique products that are unavailable elsewhere in the marketplace. Thus, implementation of the currently proposed GMPs could be counterproductive to consumer choices in natural healthcare.

The American Botanical Council is grateful for the opportunity to present its views on this important issue and is willing to work with the Agency in any appropriate manner to produce rational, meaningful, and appropriate rules to govern the manufacture of high quality herbal supplements.

Sincerely,

Mark Blumenthal
Founder, Executive Director
American Botanical Council
Editor, *HerbalGram*

Cc: ABC Board of Trustees

*Schedule 8 Persons exempt from the operation of Part 3-3 of the Act

(regulation 18)

[Format of schedule in TGA is slightly modified for inclusion herein; text is verbatim.]

1. medical practitioners, dentists and other health care workers registered under a law of a State or Territory:

the manufacture of:

(a) a medicine by a medical practitioner or a dentist specifically for a patient under his or her care; or

(b) a therapeutic device by a health care worker specifically for a patient under his or her care;

2. pharmacists the manufacture of therapeutic goods produced by the pharmacist:

(a) in a pharmacy where the pharmacist practices and the pharmacy is open to the public; or

(b) on the premises of a dispensary conducted by a Friendly Society; or

(c) on the premises of a private hospital;

for supply (other than by wholesale) on or from those premises;

3. biomedical engineers, radiochemists and pharmacists in public hospitals:
the manufacture of therapeutic goods by the person when employed by a public hospital or a public institution and produced by that person for supply in hospitals or public institutions in the same State or Territory:

4. herbalists, nutritionists, naturopaths, practitioners of traditional Chinese medicine or homoeopathic practitioners engaged in the manufacture of any herbal, homoeopathic or nutritional supplement preparation where the preparation is for use in the course of his or her business and:

(a) the preparations are manufactured on premises that the person carrying on the business occupies and that he or she is able to close so as to exclude the public; and

(b) the person carrying on the business:

(i) supplies the preparation for administration to a particular person after consulting with that person; and

(ii) uses his or her own judgment as to the treatment required.

5. a person who applies supplementary labelling to a manufactured product the application of supplementary labelling, where the supplementary label contains only a name and address or the registration or listing number of goods.

Source: Australian Therapeutic Goods Regulations 1990, Statutory Rules 1990 No. 394 as amended, made under the Therapeutic Goods Act of 1989, as revised July 1, 2003, the exemption [Schedule 8: Persons exempt from the operation of Part 3-3 of the Act (regulation 18) (p. 220-1)].