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AMERICAN HOME PRODUCTS CORPORATION

June 6, 1997

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive
Room 1-23
Rockville, MD 20857

RE: Docket 96N-0417 Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Dietary Supplements

Reference is made to the Advance Notice of Proposed Rulemaking (ANPR) relative to Current Good Manufacturing Practice (cGMP) in Manufacturing, Packing, or Holding Dietary Supplements which was published in the Federal Register on February 6, 1997 [62(25):5700-5709]. American Home Products Corporation has an interest to participate in this rulemaking for dietary supplements as our Lederle Consumer Health and Wyeth-Ayerst Laboratories divisions are manufacturers and distributors of major brands of vitamin and mineral products.

We are commenting on the ANPR in order to convey our support of the industry-proposed cGMP document with a few minor modifications and clarifications. In addition, the enclosed comments respond to the Agency's request for industry opinion on specific issues delineated in the ANPR. American Home Products appreciates the opportunity to provide comments to the Agency as it considers whether to develop a proposed rule to establish cGMP for dietary supplements.

Sincerely,

AMERICAN HOME PRODUCTS CORPORATION

Rich Cuprys
Assistant Vice President
Regulatory Affairs

96N-0417

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1. **The Agency requested comments on whether there is a need for separate dietary supplement cGMP regulation or whether the food cGMP regulation (21 CFR part 110) continues to be adequate.**
   American Home Products believes that there is a need for a separate dietary supplement cGMP regulation which incorporates various critical quality, production and process control aspects not currently contained in the cGMP for food. It is our opinion that these aspects (which include, but are not limited to, requirements for written procedures, laboratory records, and batch production and control records) are necessary to ensure that dietary supplements are produced under conditions that will result in properly labeled product that is not adulterated or misbranded.

2. **The Agency requested comments on the regulatory framework presented in the industry-proposed cGMP for dietary supplements .**
   American Home Products supports the industry-proposed cGMP document with a few minor modifications and clarifications as follows:

- We believe the cGMP regulation should identify specific requirements without dictating how firms should comply with such requirements. Any non-binding examples of how to comply with stated requirements should be identified as such. Acceptable approaches to complying with requirements in a regulation can be delineated by the Agency in a guidance document.
- Under Definitions (62 FR 5701) Section (b) should be clarified to indicate whether the definition allows material manufactured in the same campaign to be designated as a batch or lot.
- Under Definitions (62 FR 5703) Section (s) should be clarified to define "clean" in the context of the definition for rework.
- Under Sanitation of Buildings and Facilities (62 FR 5703), Section (d) states that **potable** water be provided in specified areas where required. It is suggested that that this section be revised to reflect that **potable is the minimum quality standard for water** that is to be provided in such areas.
- Under Equipment and Utensils (62 FR 5703), Section (a)(5) should state that "equipment that **is used in**" rather than "equipment that **is in**" the manufacturing or product handling area and that does not come in contact with a dietary product shall be constructed that it can be kept in a clean condition.
- Under Quality Control and Laboratory Operations (62 FR 5704), Section (c)(1) reflects optional expiration dating for dietary supplements. It is our opinion that dietary supplements should be required to bear an expiration date.
- Under Production and Process Controls (62 FR 5704), Section (a)(2)(vii) should be clarified to indicate whether "all labeling" refers to only finished packaging components or to in-process materials as well.
- Under Warehousing, Distribution and Post-Distribution Procedures (62 FR 5706), Sections (a)(2), (b), (c)(1) and (c)(2) reflect optional expiration dating for dietary supplements. As stated previously, it is our opinion that dietary supplements should be required to bear an expiration date.

3. **The Agency requested comments from both large and small businesses on how closely the current practices of firms manufacturing dietary supplements conform to this industry cGMP submission.**
   The current operations in place at Lederle Consumer Health and Wyeth-Ayerst Laboratories' are representative of and in substantial compliance with the industry-proposed cGMP for dietary supplements. Although we represent a large business, it is our opinion that the industry-proposed cGMP for dietary supplements can be applied to any size business without imposing any undue burden.

4. **The Agency requested comments on whether cGMP for dietary supplements should be mandatory or voluntary.**
   American Home Products believes that cGMP should be mandatory to assure a consistent quality standard for dietary supplement products made available to the consumer in the marketplace.

5. **The Agency requested comments on whether there is a need to develop specific defect action levels (DAL's) for dietary ingredients since the Agency has tentatively concluded that it would be inappropriate to apply the current DAL's which have been established for food ingredients to dietary supplements.**
   American Home Products agrees with the Agency's tentative conclusion that it would not be appropriate to apply the current DAL's which have been established for food ingredients to dietary supplements. We would also agree that consideration should be given to developing DAL's for non-synthetic dietary ingredients, although this subject should be evaluated as a special issue outside of the cGMP rulemaking.

6. **The Agency requested comments on the appropriate testing requirements to provide positive identification of dietary ingredients, particularly plant materials, used in dietary supplements. More specifically, the Agency has requested comments on what constitutes adequate testing from a technical and scientific feasibility standpoint for identity of different types of dietary ingredients and in the absence of testing, what types of practices would be effective alternatives to testing to ensure the identity of different types of dietary ingredients.**
   In cases where a standard compendial (i.e. USP/NF) or published (i.e. AOAC, FCC) identification method(s) exist for a dietary ingredient, these method(s), or alternate identification method(s) which have been shown to be scientifically sound, should be considered adequate. In cases where no generally recognized identification methods exist, it should be the responsibility of individual manufacturers on a case-by-case basis to develop adequate and effective identification testing procedures, requirements or practices to ensure the identity of the dietary ingredients used in their processes.

7. **The Agency has requested comments on standards that should be met in certifying that a dietary ingredient or dietary supplement is not contaminated with filth; that it is free of harmful contaminants, pesticide residues, or other impurities; that it is microbiologically safe; and that it meets specified quality and identity standards.**
   American Home Products believes that it should be the responsibility of the manufacturer to determine on a case-by-case basis whether a certification by a supplier provides adequate assurance that a dietary ingredient is what is purports to be and that it is not adulterated.

8. **The Agency has requested comments on whether cGMP should include requirements for manufacturers to establish a mechanism to document that the procedures prescribed for the manufacture of a dietary supplement are followed on continuing or day-to-day basis.**
   American Home Products does not believe that it is necessary or of any added value for cGMP to include requirements for manufacturers to establish a mechanism to document that the procedures prescribed for the manufacture of a dietary supplement are followed on continuing or day-to-day basis. Rather, it should be the manufacturer's constant responsibility to assure, through employee training, self-audit programs and batch records, that quality control and other procedures prescribed for the manufacture of a dietary supplement are properly and diligently executed.

9. **The Agency has requested 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. The Agency has also requested comments on whether dietary supplement cGMP should require firms to establish procedures for determining whether a reported injury constitutes a serious problem, and what actions are to be taken when serious problems are identified.**
   It is American Home Products opinion that any rulemaking pertaining to adverse event evaluation for dietary supplements should be handled as a separate issue outside of the cGMP rulemaking. Dietary supplements have historically demonstrated a consistent safety profile. This fact is recognized in Section 2 the Dietary Supplement and Education Act of 1994 (DSHEA) which states that "dietary supplements are safe within a broad range of intake, and safety problems with the supplements are relatively rare...". As such, American Home Products does not believe that dietary supplements pose any threat to public health when used as recommended in their labeling. American Home Products believes that it is unnecessary and inappropriate to incorporate aspects pertaining to adverse event evaluation into dietary supplement cGMP.

10. **The Agency has requested comments on whether dietary supplement cGMP should require that manufacturers establish procedures to identify, evaluate, and respond to potential safety concerns with dietary ingredients.**
It is American Home Products opinion that any rulemaking pertaining to the safety of dietary ingredients as used in dietary supplements should be handled as a separate issue outside of the cGMP rulemaking. The safety of dietary ingredients which <u>are not new</u> is evidenced by the favorable historical safety profile of dietary supplements. The safety of dietary ingredients which <u>are new</u> is effectively facilitated under DSHEA through the premarket notification process (*which requires the manufacturer or distributor to provide the Agency with the history of use or other evidence of safety, including any citation to published articles, which is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such dietary ingredient will reasonably be expected to be safe under labeled conditions of use*), or alternatively, the petition process (*which requests that the Secretary prescribe conditions under which a new dietary ingredient can be marketed such that it is reasonably expected to be safe*). American Home Products believes that it is unnecessary and inappropriate to incorporate aspects pertaining to the safety of dietary ingredients into cGMP for dietary supplements.

11. **The Agency has requested comments on whether specific controls are necessary for computer controlled or assisted operations which are used in the production of dietary supplements.**
American Home Products believes that it would be appropriate to include a requirement in dietary supplement cGMP to properly *design, test, qualify, and periodically evaluate* software programs and computerized equipment. Specific approaches to comply with this requirement should be identified by the manufacturer based on knowledge of the process. Please also note our opinion that it is unnecessary and inappropriate to impose *validation* requirements on dietary supplements since such requirements exceed what is necessary to assure consistent quality for these types of products without adding any value over qualification, evaluation and verification requirements.

12. **The Agency has requested 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.**

American Home Products does not believe that HACCP programs would suffice in place of cGMP since HACCP addresses safety concerns but does not necessarily product quality concerns. We also believe that HACCP programs administered in conjunction with cGMP would provide an added assurance of safety in only a very limited segment of the dietary supplement and dietary ingredient industry. As such, we would not support *mandatory* implementation of HACCP plans for the dietary supplement and/or dietary ingredient industry in general. However, we would not oppose *voluntary* implementation of HACCP plans by those segments of the industry where such programs might have some meaningful application (i.e. botanicals, herbals, etc.).

13. **The Agency has requested comments on whether broad cGMP regulations can address the diversity of operations in various segments of the dietary supplement industry based on the observation that the dietary supplement industry includes a broad spectrum of firms that conduct one or more distinct operations (such as the manufacture or distribution of raw dietary ingredients, the manufacture of finished products, or solely the distribution and sale of finished products manufactured by a separate firm) at the wholesale or retail level.**

It is American Home Products opinion that broad cGMP regulations proposed by the industry can address the diversity of operations in various segments of the dietary supplement industry since manufacturers and distributors need only apply cGMPs to the extent that it is appropriate and applicable to their processes.