



American Academy of  
Orthopaedic Surgeons®

AAOS

American Association of  
Orthopaedic Surgeons®

August 11, 2003

Mark B. McClellan, M.D., Ph.D.  
Commissioner  
Food and Drug Administration  
5630 Fishers Lane  
Dockets Management Branch  
HFA-305 Room 1061  
Rockville, Maryland 20852

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Dear Dr. McClellan:

The American Academy of Orthopaedic Surgeons (AAOS/Academy), representing over 19,000 Board-certified orthopaedic surgeons, welcomes the opportunity to comment on the Food and Drug Administration's (FDA) proposed rule on Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Dietary Ingredients and Dietary Supplements. [Docket No. 96N-0417; Federal Register, March 13, 2003]. As advocates for our patients, the AAOS recommends the highest standards for patient care and safety.

The need for more stringent regulation of dietary supplements has grown in concert with the increased use of dietary supplements by the American public. The current absence of minimum manufacturing standards has contributed to the adulteration of dietary ingredients and supplements. Incidents of super- and sub-potency, undeclared ingredients, and ingredient content that varied from its declared content have been documented in dietary supplements through the FDA Health Hazard Evaluations<sup>1</sup>. The AAOS is committed to improving the quality and safety of dietary supplements available to all patients.

In general, the Academy commends the FDA's proposed rule on good manufacturing practices (GMPs) as the primary impetus in improving the quality and safety of dietary supplements brought to market. The proposed rule allows both consumers and medical professionals to utilize dietary supplements with reasonable assurance that they are unadulterated. The Academy has eagerly anticipated the release of this proposed rule, and submits the following specific recommendations on its finalization and implementation:

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- The AAOS supports personnel, physical plant, equipment and utensils, and holding and distributing practices as proposed;
- The AAOS urges appropriate testing of dietary ingredients and dietary supplements for identity, purity, quality, strength, and composition;
- The AAOS encourages the FDA to require manufactures to report adverse events;
- The AAOS emphasizes the importance of maintaining accurate and written records documenting compliance with good manufacturing practices as well as with consumer complaint follow-up and investigation practices;
- The AAOS suggests the FDA extend to small manufacturers no more than one additional year to comply with the final rule.

**The AAOS supports personnel, physical plant, equipment and utensils, and holding and distributing practices as proposed.**

The AAOS recognizes that the manufacturing process is fraught with the opportunity for contamination or adulteration to occur. The protections offered in the proposed rule aim to safeguard the public from inadvertent conditions that may cause the dietary supplement to become contaminated at any point in the manufacturing process.

The Academy supports FDA's personnel requirements for dietary ingredient or supplement manufacturers, and contends that enforcement of these regulations will impart upon employees their significance and utility in relation to producing an unadulterated final product. The AAOS recognizes the necessity for a sanitary, well-maintained physical environment in which supplements are produced in order to prevent contamination of ingredients or supplements. Appropriate separation and storage of components, ingredients, and supplements also protects against contamination and adulteration. Equipment and utensils should be properly maintained and calibrated to ensure accuracy and precision.

**The AAOS urges appropriate testing of dietary ingredients and dietary supplements for identity, purity, quality, strength, and composition.**

The AAOS is aware that contamination can occur at any stage in the production process. Testing ingredients and supplements for identity, purity, quality, strength, and composition at critical control points, including the points of receipt, in processing, and at the finished product stage, will reduce the likelihood of adulteration and cross-contamination. Multiple-point sample testing will allow manufacturers to pinpoint possible sources of contamination within the production sequence, should a tested sample show contamination. Properly recorded quality control measures such as the batch production and master manufacturing records will aid manufacturers in producing dietary

supplements in a consistent and uniform manner, as well as serving as tools to assess possible sources of contamination and flaws in the production process.

The Academy agrees with the FDA that manufacturers of final product batches that cannot be tested by valid analytical methods for identity, purity, quality, strength, and composition should not rely upon suppliers' certification or guarantee in lieu of performing testing on each shipment or lot of components or ingredients received. It is imperative that a dietary supplement contain what it purports on its label. Establishing ingredient identity, purity, quality, strength, and composition upon receipt, in cases where testing cannot be performed on the finished product, will provide an additional safeguard to prevent the possibility of adulterated or misbranded supplements coming to market.

The AAOS commends the FDA for acknowledging the existence of various valid analytical methods and standards for manufacturers to utilize in ingredient and supplement testing. This flexibility will allow the manufacturers to employ more sensitive and sophisticated testing methodologies as they are developed and validated.

**The AAOS encourages the FDA to require manufacturers to report adverse events.**

The 2003 RAND Corporation<sup>2</sup> study commissioned by the NIH compiled approximately 17,000 case reports of adverse events attributed to dietary supplements containing ephedra or ephedrine alkaloids. Historically, the number of adverse events reported to health professionals or MedWatch is a minute fraction of the actual number of events occurring in the general population. In addition, numerous reports in the popular media have called the public's attention to the possible health hazards of dietary supplements.

The AAOS contends that the FDA should enforce its general rule making authority under 701(A) of the Federal Food, Drug, and Cosmetic Act to demand that manufacturers of dietary supplements report all adverse events to the FDA. The Academy supports the collection of adverse events into a well-designed comprehensive database that could prove useful as an early-warning system to identify problems with dietary ingredients or supplements.

**The AAOS emphasizes the importance of maintaining accurate and written records documenting compliance with good manufacturing practices as well as with consumer complaint follow-up and investigation practices.**

The Academy insists that the ability of the dietary ingredient and supplement manufacturer to keep and maintain written, accurate records is an important protection for the public's health. Access to documentation of a manufacturer's process through its batch production and master manufacturing records is integral to facility inspectors, and will allow the FDA to assess the adequacy of the manufacturer's practices.

The AAOS endorses the proposed requirements for documenting the practices of manufacturers who receive a consumer complaint. As defined in the proposed rule, consumer complaints express dissatisfaction with the quality of a dietary ingredient or a

dietary supplement related to good manufacturing practices and may or may not include concerns about a possible hazard to health. Again, proper record keeping will prove valuable in the FDA's assessment of manufacturer practices, and may well serve to assist in an epidemiological investigation in cases where the consumer complaint may include a particular concern about a hazard to health.

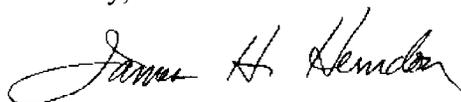
**The AAOS suggests the FDA extend to small manufacturers no more than one additional year to comply with the final rule.**

The AAOS holds patient safety as its highest priority. The possibility of a manufacturer releasing adulterated products into the marketplace for several years following the implementation of the final rule is an unacceptable public health risk. The time period between the advanced notice of proposed rule making (February 1997) and the proposed rule (March 2003) served to put manufacturers on notice of impending regulation. The AAOS recommends the FDA allow no more than one year for smaller companies to come into compliance with the final rule.

**Conclusion**

In conclusion, the Academy urges the FDA to take appropriate steps to safeguard the health of the American public. We appreciate the FDA's willingness to seek perspectives from interested parties on regulatory considerations on good manufacturing practice in manufacturing, packing, or holding dietary ingredients and supplements. The AAOS shares the concerns of the FDA in ensuring that safe and effective products are available to all patients. We look forward to working with the FDA on future initiatives to increase patient safety.

Sincerely,

A handwritten signature in cursive script that reads "James H. Herndon". The signature is written in black ink and is positioned below the word "Sincerely,".

James. H. Herndon, M.D.  
President

## References

1. FDA Health Hazard Evaluation, Classification, and FDA-Enforcement Report for Firm-Initiated Recalls:  
Super Potent Vitamin A, US FDA Recall #F-157/158-5, 1994.  
Super Potent Vitamin D, US FDA Recall #F0610-3, 1993.  
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Lactose, US FDA Recall #F-271-6, 1995.  
Sulfites, US FDA Recall #F538/539-9, 1999.  
  
Gurley BJ, Gardner SF, Hubbard MA, Content versus Label claims in Ephedra-Containing Dietary Supplements, *American Journal Health Systems Pharmacy*, 57, pp. 963-969, 2000.
2. Shekelle P, Morton, S., Maglione M, et al. Ephedra and Ephedrine for Weight Loss and Athletic Performance Enhancement: Clinical Efficacy and Side Effects. Evidence Report/Technology Assessment No. 76 (Prepared by Southern California Evidence-based Practice Center, RAND, under Contract No. 290-97-0001, Task Order No. 9). AHRQ Publication No. 03-E022. Rockville, MD: Agency for Healthcare Research and Quality. February 2003.