

CONTAIN-TECH

10329 Vandergriff Road
Indianapolis, IN 46239
Phone: (317) 862-4552
Fax: (317) 862-9135



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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Rm 10761
Rockville, MD 20852

RE: Docket Number 00N-1357
(Concept Paper: Drug Products That Present Demonstrable Difficulties for
Compounding Because of Reasons of Safety or Effectiveness)

Dear Sir or Madam,

The focus of my comments is sterile *products compounded under procedures other than those described in Chapter 1206 of USP*. I agree that there is a need for a consistent minimum standard for compounding sterile products. Most state requirements for preparation of sterile products do not adequately address facilities, training and quality assurance issues.

My experience during more than thirty years in the pharmaceutical industry has given me an appreciation for the complexities involved in the preparation and handling of sterile products. My involvement includes; Past President, International Society of Pharmaceutical Engineering, Technical committee and monthly columnist on contamination control for CleanRooms magazine, PDA committee member, contributor to the ASHP Guidelines on Quality Assurance for Pharmacy- Prepared Sterile Products.

I perceive that members of State Boards of Pharmacy are hard working, dedicated individuals who volunteer their time. Pharmacy education addresses many theoretical and technical issues valuable in pharmacy practice, but most university programs do not emphasize sterile processing. Facility, equipment, training and quality assurance expertise are usually not adequately stressed in academic programs.

In the work place, most pharmacists do not have technical engineering support available. They must deal with facilities, training and quality assurance issues based on information gathered from technical journals and training programs. Much of the information contained in these sources addresses only the technical product issues.

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The American Society of Health-System Pharmacists has recognized this problem and has expanded its attention to facility, training and quality issues in both its journal and educational programs. This is an important step in the path toward improving awareness in those areas.

As you are well aware, pharmaceutical industry expertise has been used to develop guidance consistent with the FDA's goal of assuring safety and effectiveness of drug products. The pharmaceutical industry has benefited immeasurably from the availability of clearly defined guidelines. The partnership formed between the FDA and The International Society of Pharmaceutical Engineering in developing the *ISPE Baseline Guide* is an example of the optimization of co-operative efforts.

USP1206 and the *ASHP Guidelines on Quality Assurance of Pharmacy Prepared Sterile Products* are both open to interpretation by individuals who may not be totally familiar with the requirements, in terms of facilities, training and quality assurance necessary to produce safe and effective sterile products. Both are, therefore, in need of improvement. Since the FDA has indicated an initial preference for the *USP1206* document, I would like to point out some critical shortcomings of this document. Similar examples can also be cited in the *ASHP* document.

Specific examples of deficiencies are:

USP1206 – Facilities

P817 – calls for separation of controlled workspaces and sites using partitions, plastic curtains or solid walls. Two of the three choices, partitions and plastic curtains, are incapable of controlling the critical parameters of temperature, humidity and pressure differential. Later in the document (P818) materials of construction are described in terms of surfaces, which contradicts the use of plastic curtains and partitions. This adds to the confusion of the statements.

P818 – the reference to 10 air changes per hour for temperature control in the paragraph discussing particulate control levels of Class 10000 and Class 100000 is very confusing. Good clean room design requires a greater number of air changes to maintain the particulate control. The reference to 10-air changes could be interpreted as meeting the classification requirement. Experience with the implementation of clean room regulations in New Jersey hospitals has shown that we cannot assume qualified engineering support is available to those who would be expected to meet the standard.

P818-819 – describes the need for an anteroom but sets no air quality requirements nor does it describe the use of a pass thru as an alternative to reduce traffic in the processing clean room. The proposed use of carts without tack mats (which are not mentioned) would result in tracking contaminants from the anteroom into the processing clean room.

General comments

USP1206 does not define critical environmental factors for clean rooms (i.e. temperature, humidity and pressure differential). It does not define conditions under which particulate count is to be measured (i.e. static or dynamic conditions).

USP1206 does not mention the use of isolators, which the FDA has recognized as having advantages in aseptic processing.

USP1206 does not mention materials of construction or the differences in control capability of Class 100 environments. It uses the general statement of laminar flow.

This is not a complete list of omissions!!

USP1206 Personnel and Gowning

Comments: To my knowledge, clean room gowning requirements consistent with those in the pharmaceutical industry, do not exist anywhere in the hospital and home health care field. Gowning procedures in the sterile product preparation areas of hospital and home health care, usually consist of donning a lab coat and hair covering. The use of gloves does not meet the standard of "aseptic technique" in gloving used in the pharmaceutical industry. When gloves are used in pharmacy compounding of sterile products, it is not common practice to use sterile gloves. When gloves are used they are sometimes sanitized by spraying with 70% isopropyl alcohol before entering the "hood".

The suggestion that it is unnecessary to have an anteroom for Class 100000 is confusing and leaves much open to interpretation in terms of classification and gowning requirements for the area adjacent to the clean room.

The guideline leaves the impression that clean rooms are the only alternative to providing an aseptic environment and does not include advanced technologies, such as isolators.

USP1206 Training

The document references the need for a formal written training program and for individual competency evaluation but lacks details regarding critical parameters, which the training should address. For example, training in gowning technique, which is critical in maintaining the quality of the environment in clean rooms is not mentioned.

USP1206 Validation, Testing and Quality Assurance

The section on validation presents good examples and introduces a concept not widely understood in most pharmacy practice settings.

Summary of comments

1. The need for common guidance is necessary but must be presented in such a way that pharmacists will understand and implement the changes, which will insure compliance. The use of USP1206 does not meet this need.
2. USP1206 does not address the use of isolation technology as a means of providing the environment necessary to perform aseptic manipulations although the FDA has recognized and encouraged the use of isolators in pharmaceutical operations.
3. The specific critical parameters for clean rooms are not addressed in adequate detail. Some parameters, such as pressure differential between classified environments, are not addressed at all.
4. The concept of gowning is not defined to a level that is meaningful.

Guidance provided in USP1206 is inadequate to assure compliance with FDA goals of providing safe and effective compounding of sterile products in hospital, home care, outpatient clinics, or physicians' offices. To achieve this goal, specific minimum requirements in terms of facilities, personnel gowning, training and quality assurance programs, for the settings where sterile products are compounded must be written in such a manner as to be easily understood by those expected to implement the necessary changes. Equally important is the communication and training aspects of the new requirements. With proper support, the American Society of Health-System Pharmacists is the ideal organization to meet this need.

The FDA has set a precedent of partnering with those industries that it regulates. The partnering has resulted in producing workable guidance documents that communicate expectations in clear and complete terms. The agency and industry both will benefit from continuing to follow this successful model by allowing such a partnership to take place. ASHP is in the best position to coordinate the preparation of such a document by utilizing the expertise of its membership as well as the USP and pharmaceutical industry resources. This document could be ready for FDA review in less than six months.

Respectfully,



Hank Rahe
Director Technology
ContainTech, Inc.