

DEPARTMENT OF HEALTH AND HUMAN SERVICES

[Docket No. 2003D-0382]

Food and Drug Administration

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Display Date 9-29-04 2:14 pm
Publication Date 10-4-04
Certifier R. LEESMA

Guidance for Industry on Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled “Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice.” This guidance explains FDA’s current thinking on manufacturing of sterile drug products produced by aseptic processing in the context of complying with certain sections of the current good manufacturing practice (CGMP) regulations for drug and biological products. This guidance is issued with the goal of providing clear and consistent communication of regulatory expectations to promote voluntary compliance with current FDA requirements.

DATES: General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the guidance to the Division of Drug Information (HFD-240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857; or the Office of Communication, Training and Manufacturers Assistance (HFM-40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448. Send one

self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT:

Richard Friedman, Center for Drug Evaluation and Research (HFD-320), Food and Drug Administration, 11919 Rockville Pike, Rockville, MD 20852, 301-827-9031; or

Robert Sausville, Center for Biologics Evaluations and Research (HFM-624), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448, 301-827-6201; or

Robert Coleman, Office of Regulatory Affairs (HFC-240), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 404-253-1295.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled “Sterile Drug Products Produced by Aseptic Processing— Current Good Manufacturing Practice.” This guidance explains FDA’s current thinking on manufacturing of sterile drug products produced by aseptic processing in the context of complying with certain sections of the CGMP regulations for drug and biological products (21 CFR parts 210, 211, and 600 through 680, respectively).

In the **Federal Register** of September 5, 2003 (68 FR 52782), FDA announced the availability of a draft guidance entitled “Sterile Drug Products Produced by Aseptic Processing— Current Good Manufacturing Practice.” The draft guidance was finalized after consideration of received public comments. Consistent with the objectives of FDA’s CGMPs for the 21st Century initiative, this guidance provides updated information regarding CGMP expectations for aseptic processing facilities, reflects the latest science in the area of sterile drug quality, and promotes innovations in manufacturing that achieve increased sterility assurance. Through this guidance, FDA hopes to facilitate a higher assurance of process consistency and promote better contamination prevention practices.

Sterile drug products are a high priority in FDA’s risk-based inspectional program. These drug products are generally of high therapeutic significance. Clarifying relevant regulatory standards for sterile drug products will help reduce the incidence of manufacturing problems with this class of pharmaceuticals, thus facilitating the ready availability of these therapeutically significant pharmaceuticals and avoiding drug shortages.

This guidance document is the product of extensive public input. FDA first published a preview of its current thinking in the form of a concept paper on September 23, 2003. We presented our CGMP approach for aseptic processing at the Advisory Committee for Pharmaceutical Science on October 22, 2002. At this meeting, the concept paper was discussed in a public forum and critiqued by the advisory committee’s members as well as a panel of invited aseptic processing experts. The advisory committee meeting yielded a number of issues that provided impetus for further discussion. In December 2002, an aseptic processing working group was formed under Product Quality

Research Institute (PQRI) to address these issues. The working group, composed of 41 prominent aseptic processing experts from industry, academia, and FDA, prepared technical recommendations on the guidance document. The PQRI Steering Committee forwarded the working group's final report to FDA on March 19, 2003, and it was subsequently posted on PQRI's Web site (www.pqri.org).¹ The draft guidance was published on September 3, 2003.

The advisory committee and PQRI Working Group recommendations provided valuable contributions and many of these recommendations have been adopted in the guidance.

II. Comments Received on the Draft Guidance

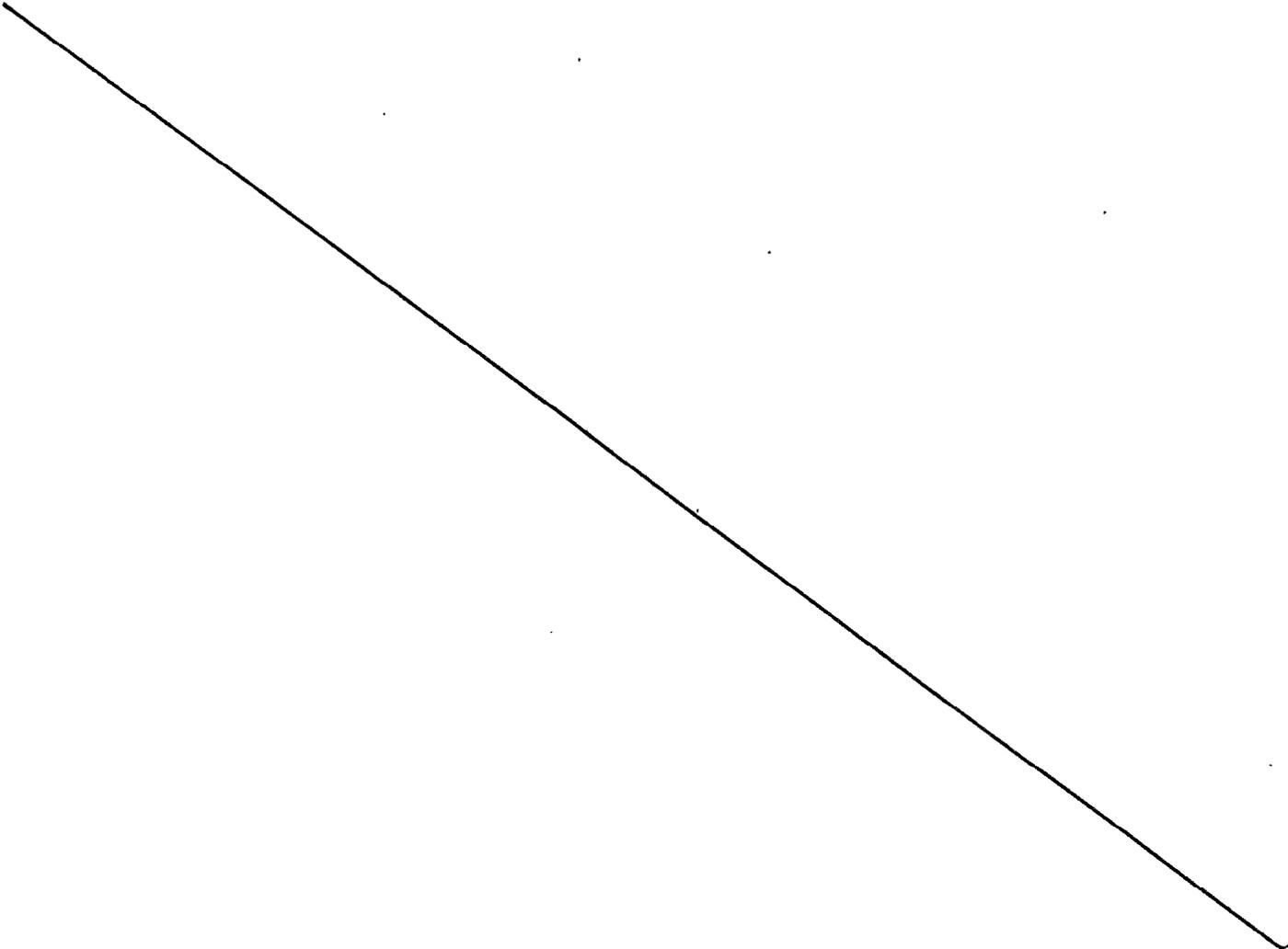
A number of comments were received on the draft guidance, most of which concerned the need to further enhance the precision of guidance provided on certain topics. As a result, many clarifying changes were made. Major changes include the revision of the Sterility Testing section of the guidance to clearly emphasize and reference the United States Pharmacopeial Sterility Test <71>. In the guidance, table 1 entitled "Air Classifications," which summarizes clean area air classifications and recommended microbiological action levels, has been modified to acknowledge that alternate action levels can be justified depending on the method of analysis used. Further clarifications have been made regarding process simulations. In addition, the guidance recommends "building quality into products" through science-based facility, equipment, and systems design for sterile drug manufacture. We underscore our encouragement of alternate approaches and innovations to achieve increased sterility assurance.

¹ FDA has verified the Web site address, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.

This level 1 guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the agency's current thinking. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if the approach satisfies the requirements of the applicable statute and regulations.

III. Paperwork Reduction Act of 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3520). The collection of information in this guidance was approved under OMB control number 0910–0139, until August 31, 2005.



IV. Electronic Access

Persons with access to the Internet may obtain the guidance at either *http://www.fda.gov/cder/guidance/index.htm* or *http://www.fda.gov/ohrms/dockets/default.htm*.

Dated: 9/28/04
September 28, 2004



Jeffrey Shuren
Assistant Commissioner for Policy

[FR Doc. 04-????? Filed ??-??-04; 8:45 am]

BILLING CODE 4160-01-S

