Compliance Policy Guide
CPG Sec. 280.110: Microbiological Control Requirements - Licensed Anti-Human Globulin & Blood Grouping Reagents

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Guidance for FDA Staff

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(4)(i). Submit one set of either electronic or written comments on this guidance at any time. Submit electronic comments to https://www.regulations.gov/. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with docket number FDA-2014-D-0428.

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
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Contains Nonbinding Recommendations

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This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION:

The purpose of this Compliance Policy Guide (CPG) is to provide guidance to FDA staff on the microbiological control requirements for Anti-Human Globulin (AHG) and Blood Grouping Reagents (BGR) licensed by the Center for Biologics Evaluation and Research (CBER).

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA's current thinking on a topic and should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. The use of the word "should" in FDA's guidances means that something is suggested or recommended but not required.

II. BACKGROUND:

The Quality System Regulation found at Title 21 of the Code of Federal Regulations Part 820 (21 CFR Part 820) applies to the manufacturing process for in vitro diagnostic products (IVDs). IVD products regulated by CBER, including AHG and BGR, may have additional manufacturing requirements as a condition of licensure based on the biologics regulations found in 21 CFR Parts 600-660.

IVDs are classified into three major categories based on microbiological control: (1) IVDs labeled as sterile; (2) IVDs that are microbiologically controlled but are not labeled as sterile; and (3) IVDs that are not microbiologically controlled. The level of microbiological control necessary for the manufacture of a specific IVD is established by the manufacturer's design controls (21 CFR 820.30) and process validation studies in accordance with 21 CFR 820.75. Most, if not all, IVDs regulated by CBER fall into the category of microbiologically controlled products, including BGR and AHG.

III. POLICY:

The requirement for sterility for biological products is found in 21 CFR 610.12; however, there is a specific exception to the test for sterility for AHG and BGR (21 CFR 610.12(h)(1)). The biologics regulations describe additional standards for licensed BGR (21 CFR 660.20) and AHG (21 CFR 660.50). CBER amended the regulations for BGR and AHG on December 12, 2000 (65 FR 77497), to remove the requirements that these products be sterile or aseptically processed because: (1) the manufacturers do not claim these products as sterile on the product labels; (2) quality checks are required for the end users of licensed IVDs (21 CFR 606.65(c)); (3) all BGR and AHG contain preservatives; and (4) historically, CBER has not requested sterility requirements during the license application review of these products. Therefore, unless specified in the license application, CBER does not expect AHG and BGR to be manufactured under aseptic conditions; however, they should be manufactured under conditions such that the microbial level will not adversely impact product performance.

IV. REGULATORY ACTION GUIDANCE:

Investigators should not cite a manufacturer of BGR or AHG on the Form FDA 483 for not following aseptic processing procedures unless: (1) the product is labeled as sterile; (2) aseptic processing is required as part of its license; or (3) the firm is not following its own manufacturing standard operating procedures (SOPs) (e.g., 21 CFR 820.70 (production and process control); 21 CFR 820.30 (design control)). Manufacturers should develop the process control procedures necessary to ensure the product meets its specifications. Investigators should verify that the manufacturer has established appropriate specifications and validated the process control procedures, including control of those environmental conditions that could have an adverse effect on product quality. If investigators have any questions regarding the requirements for a particular product, they should consult with CBER's Office of Compliance and Biologics Quality using the email CBERInspections@fda.hhs.gov.

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