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DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

14 CFR Part 71

[Airspace Docket No. 00–ACE–26]

Amendment to Class E Airspace; Pella, IA

AGENCY: Federal Aviation Administration, DOT.

ACTION: Direct final rule; confirmation of effective date.

SUMMARY: This document confirms the effective date of a direct final rule which revises Class E airspace at Pella, IA.

DATE: The direct final rule published at 65 FR 46240 is effective on 0901 UTC, January 25, 2001.

FOR FURTHER INFORMATION CONTACT: Kathy Randolph, Air Traffic Division, Airspace Branch, ACE–520C, DOT Regional Headquarters Building, Federal Aviation Administration, 901 Locust, Kansas City, MO 64106; telephone: (816) 329–2525.

SUPPLEMENTARY INFORMATION: The FAA published this direct final rule with a request for comments in the **Federal Register** on September 18, 2000 (65 FR 56240). The FAA uses the direct final rulemaking procedure for a non-controversial rule where the FAA believes that there will be no adverse public comment. This direct final rule advised the public that no adverse comments were anticipated, and that unless a written adverse comment, or a written notice of intent to submit such an adverse comment, were received within the comment period, the regulation would become effective on January 25, 2001. No adverse comments were received, and thus this notice confirms that this direct final rule will become effective on that date.

Issued in Kansas City, MO, on November 30, 2000.

N.J. Lyons, Jr.,

Manager, Air Traffic Division, Central Region.

[FR Doc. 00–31645 Filed 12–11–00; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 660

[Docket No. 00N–1586]

Revision to Requirements for Licensed Anti-Human Globulin and Blood Grouping Reagents

AGENCY: Food and Drug Administration, HHS.

ACTION: Direct final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the biologics regulations applicable to microbiological controls for licensed Anti-Human Globulin (AHG) and Blood Grouping Reagents (BGR). FDA is amending the regulations to remove the requirements that the products be sterile. FDA is publishing this direct final rule because the requirement that these products be sterile is not necessary for the products to be safe, pure, and potent. FDA is issuing these amendments directly as a final rule because they are noncontroversial and there is little likelihood that FDA will receive any significant comments opposing the rule. Elsewhere in this issue of the **Federal Register**, FDA is publishing a proposed rule under FDA's usual procedures for notice and comment in the event the agency receives any significant adverse comments. If FDA receives any significant adverse comment that warrants terminating the direct final rule, FDA will consider such comments on the proposed rule in developing the final rule.

DATES: This rule is effective June 11, 2001. Submit written comments on or before February 26, 2001. If FDA receives no significant adverse comments during the specified comment period, the agency intends to publish a confirmation document on or before the effective date of this direct final rule confirming that the direct final rule will go into effect on June 11, 2001. If the agency receives any significant adverse comment during the comment period, FDA intends to withdraw this direct final rule by publication in the **Federal Register** before the effective date of this direct final rule.

ADDRESSES: Submit written comments on the direct final rule to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Stephen M. Ripley, Center for Biologics Evaluation and Research (HFM–17), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–6210.

SUPPLEMENTARY INFORMATION:

I. Background

AHG and BGR are used primarily for testing human blood for the detection of red cell antigens and antibodies. As defined in 21 CFR 660.20, BGR is a product that comes from blood, plasma, serum, or protein-rich fluids and consists of an antibody-containing fluid containing one or more of the blood grouping antibodies listed in 21 CFR 660.28(d).

Under 21 CFR 660.50, AHG is a serum or protein-rich fluid that consists of one or more antiglobulin antibodies identified in 21 CFR 660.55(d). AHG and BGR are biological products as defined in section 351 of the Public Health Service Act (PHS ACT) (42 U.S.C 262). These products are also devices, as defined in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321), and fall within the definition of in vitro diagnostic (IVD's) products in § 809.3(a) (21 CFR 809.3(a)).

AHG and BGR must meet the licensing requirements of section 351 of the PHS Act and the regulations in parts 600 through 660 (21 CFR parts 600 through 660). Section 351 of the PHS Act, requires that a license applicant demonstrate that the biological product that is the subject of the application is safe, pure, and potent, and that the manufacturing facilities are designed to assure that the biological product continues to be safe, pure, and potent.

AHG and BGR are also medical devices and in vitro diagnostic products as defined in § 809.3(a) and therefore are subject under the act and 21 CFR 809.20(b) to the requirements in the quality system regulation (QSR) in part

820 (21 CFR part 820). The QSR requires that a manufacturer establish appropriate manufacturing controls. A manufacturer must validate the manufacturing process in accordance with § 820.75 and establish production and process controls (§ 820.70). See also the ''Guideline for the Manufacture of In Vitro Diagnostic Products'' published in the **Federal Register** of January 10, 1994 (59 FR 1402).

The standards for AHG and BGR were established by final rules published in the **Federal Register** of February 11, 1985, and April 19, 1988, respectively (50 FR 5574 and 53 FR 12760). The standards in §§ 660.20(a) and 660.50(a) require BGR and AHG to be manufactured by a ''method demonstrated to consistently yield a sterile product.'' In addition, the requirements for processing methods of BGR and AHG under §§ 660.21(a)(2) and 660.51(a)(3) state that ''[o]nly that material that has been fully processed, thoroughly mixed in a single vessel, and sterile filtered shall constitute a lot,'' and under §§ 660.21(a)(3) and 660.51(a)(4) that ''[a] lot may be subdivided into clean sterile vessels''.

When the regulations were codified, the agency expected that AHG and BGR would be manufactured as sterile under the conditions understood at that time. The agency also considered that the process of sterile filtration and a sterile container and closure system, e.g., vessels, would be sufficient to yield consistently a sterile product (50 FR 5574 at 5575; 53 FR 12760 at 12761). However, current good manufacturing practices require aseptic processing controls to be in place in order to ensure a sterile product. The agency considers AHG and BGR to be microbiologically controlled IVD's, which are IVD's that are capable of supporting microorganism life and growth and may contain certain levels of microorganisms. Microbiologically controlled IVD's do not need to be manufactured under aseptic conditions; however, they should be manufactured under conditions such that the microbial level will not adversely impact product performance. Manufacturers must establish specifications for these products through testing and validation. FDA's revision of the regulations would in no way undermine the safety, potency, or purity of the products. The revisions would also not prevent a manufacturer from implementing aseptic processing controls for manufacturing AHG and BGR, if the manufacturer determines such controls are appropriate for its product. Therefore, the agency is revising the standards for AHG and BGR to remove the requirement that these products be sterile.

II. Highlights of the Direct Final Rule

FDA is amending the biologics regulations by revising §§ 660.20, 660.21, 660.50, and 660.51 to clarify the agency's requirements with regard to microbiological control in manufacturing AHG and BGR. FDA is amending the regulations by deleting all references to sterile processing techniques such as sterile filtration and sterile container and closure systems. FDA is amending §§ 660.20(a) and 660.50(a) by deleting the phrase regarding preparation ''by a method demonstrated to yield consistently a sterile product'' because FDA recognizes that controls to ensure a sterile product, i.e., aseptic processing controls, are not necessary to ensure that AHG and BGR meet their performance specifications. In addition, § 660.21(a)(1) and 660.51(a)(1) include requirements regarding the adequacy of the processing method. FDA is amending §§ 660.21(a)(2) and 660.51(a)(3) by deleting the term ''sterile'' because the manufacturer must establish those controls appropriate for its product, and it may not be necessary for microbiologically controlled IVD's to undergo sterile filtration. FDA is amending §§ 660.21(a)(3) and 660.51(a)(4) by deleting the reference to ''clean, sterile vessels'' because FDA believes that manufacturers are in the best position to determine the appropriate level of microbial control for container and closure systems. Appropriate process specifications must be established by the manufacturer to ensure that microbiologically controlled IVD's are manufactured under appropriate conditions and controls resulting in a product that consistently meets all of its specifications. The manufacturer must demonstrate in the license application that the appropriate level of control of microbial contamination ensures that the biological product continues to meet the licensing requirements. The change to the regulation in no way affects the testing and validation a manufacturer must perform in order to establish that the manufacturing specifications are appropriate to ensure the product will perform as intended. In addition, under the current good manufacturing practice regulations for blood and blood components, end users of AHG and BGR, such as blood banks, are required under § 606.65(c) to perform daily checks for potency and specificity of supplies and reagents used in the collection and testing of blood and blood components.

The agency also believes the change is consistent with other requirements in the biologics regulations, such as the sterility testing requirements set forth in § 610.12. This section requires sterility testing for most biological products; however, BGR and AHG are specifically exempted from the sterility testing requirements for bulk and final container material (§ 610.12(g)(4)).

The direct final rule will also remove the requirement in § 660.51(a)(4) that a manufacturer who subdivides a lot shall include this information on the protocol. FDA is making this change to reflect current agency practice. Manufacturers will still be required to submit this information in the license application. See § 601.2 regarding requirements for the submission of samples and protocols to FDA.

III. Rulemaking Action

In the **Federal Register** of November 21, 1997 (62 FR 62466), FDA described its procedures on when and how FDA will employ direct final rulemaking. FDA has determined that this rule is appropriate for direct final rulemaking because FDA views this rule as including only noncontroversial amendments and anticipates no significant adverse comments. Consistent with FDA's procedures on direct final rulemaking, FDA is publishing elsewhere in this issue of the **Federal Register**, a companion proposed rule to amend the biologics regulations by amending the existing regulations to be more consistent with current accepted practices. The companion proposed rule provides a procedural framework within which the rule may be finalized in the event the direct final rule is withdrawn because of any significant adverse comment. The comment period for the direct final rule runs concurrently with the companion proposed rule. Any comment received under the companion proposed rule will be considered as comments regarding the direct final rule.

FDA has provided a comment period on the direct final rule of 75 days after December 12, 2000. If the agency receives any significant adverse comment, FDA intends to withdraw this direct final rule action by publication of a document in the **Federal Register** before the effective date of the direct final rule. A significant adverse comment is defined as a comment that explains why the rule would be inappropriate, including challenges to the rule's underlying premise or approach, or would be ineffective or unacceptable without a change. In determining whether an adverse comment is significant and warrants

terminating a direct final rulemaking, FDA will consider whether the comment raises an issue serious enough to warrant a substantive response in a notice and comment process. Comments that are frivolous, insubstantial, or outside the scope of the rule will not be considered significant or adverse under this procedure. A comment recommending a rule change in addition to the rule would not be considered a significant adverse comment, unless the comment states why the rule would be ineffective without additional change. In addition, if a significant adverse comment applies to an amendment, paragraph, or section of this rule and that provision can be severed from the remainder of the rule, FDA may adopt as final those provisions of the rule that are not subjects of a significant adverse comment.

If any significant adverse comment is received during the comment period, FDA will publish, before the effective date of this direct final rule, a document withdrawing the direct final rule. If FDA withdraws the direct final rule, any comments received will be applied to the proposed rule and will be considered in developing a final rule using the usual Administrative Procedure Act notice-and-comment procedures.

If FDA receives no significant adverse comments during the specified comment period, FDA intends to publish a confirmation document, before the effective date of the direct final rule, confirming the effective date.

IV. Analysis of Impacts

A. Review Under Executive Order 12866 and the Regulatory Flexibility Act and the Unfunded Mandates Act of 1995

FDA has examined the impact of the direct final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distribute impact; and equity). The agency believes that this direct final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. This direct final rule is not a significant regulatory action as defined by the Executive Order and therefore is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small business entities. Because the direct final rule amendments have no compliance costs and do not result in any new requirements, the agency certifies that the direct final rule will not have a significant negative economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required. This direct final rule also does not trigger the requirement for a written statement under section 202(a) of the Unfunded Mandates Reform Act of 1995 because it does not impose a mandate that results in an expenditure of $100 million or more by State, local, and tribal governments in the aggregate, or by the private sector in any one year.

B. Environmental Impact

The agency has determined under 21 CFR 25.31(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

C. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the order and, consequently, a federalism summary impact statement is not required.

V. The Paperwork Reduction Act of 1995

This direct final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520) is not required.

VI. Request for Comments

Interested persons may submit to the Dockets Management Branch (address above) written comments regarding this direct final rule by February 26, 2001. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 660

Biologics, Labeling, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 660 is amended as follows:

PART 660—ADDITIONAL STANDARDS FOR DIAGNOSTIC SUBSTANCES FOR LABORATORY TESTS

1. The authority citation for 21 CFR part 660 is revised to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360c, 360d, 360h, 360i, 371, 372; 42 U.S.C. 216, 262, 263, 263a, 264.

§ 660.20 [Amended]

2. Section 660.20 *Blood Grouping Reagent* is amended in paragraph (a) by removing the words ''prepared by a method demonstrated to yield consistently a sterile product and''.

§ 660.21 [Amended]

3. Section 660.21 *Processing* is amended in paragraph (a)(2) by removing the word ''sterile''; and in paragraph (a)(3) by removing the words ''clean, sterile vessels. Each subdivision shall constitute a sublot.'' and adding in its place the word ''sublots.''

§ 660.50 [Amended]

4. Section 660.50 *Anti-Human Globulin* is amended in paragraph (a) by removing the words ''and be prepared by a method demonstrated to yield consistently a sterile product''.

§ 660.51 [Amended]

5. Section 660.51 *Processing* is amended in the first sentence of paragraph (a)(3) by removing the word ''sterile'', and in paragraph (a)(4) by removing the words ''clean, sterile vessels. Each subdivision shall constitute a sublot'' and adding in its the word ''sublots'', and in the third sentence by removing the words ''and on the protocol''.

Dated: December 3, 2000.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 00–31586 Filed 12–11–00; 8:45 am]

BILLING CODE 4160–01–F