DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 610

[Docket No. FDA–2016–N–1170]

Standard Preparations, Limits of Potency, and Dating Period Limitations for Biological Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Direct final rule.

SUMMARY: The Food and Drug Administration (FDA or Agency or we) is amending the general biological products standards relating to dating periods and also removing certain standards relating to standard preparations and limits of potency. FDA is taking this action to update outdated requirements, and accommodate new and evolving technology and testing capabilities, without diminishing public health protections. This action is part of FDA's retrospective review of its regulations in response to an Executive order. FDA is issuing these amendments directly as a final rule because the Agency believes they are noncontroversial and FDA anticipates no significant adverse comments.

DATES: This rule is effective September 16, 2016. Submit either electronic or written comments on this direct final rule or its companion proposed rule by July 18, 2016. If FDA receives no significant adverse comments within the specified comment period, the Agency intends to publish a document confirming the effective date of the final rule in the **Federal Register** within 30 days after the comment period on this direct final rule ends. If timely significant adverse comments are received, the Agency will publish a document in the **Federal Register** withdrawing this direct final rule within 30 days after the comment period on this direct final rule ends.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *http://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *http://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand delivery/Courier (for written/paper submissions):* Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2016–N–1170 for ''Standard Preparations, Limits of Potency, and Dating Period Limitations for Biological Products.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *http://www.regulations.gov* or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *http://www.regulations.gov.* Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *http://www.fda.gov/regulatoryinformation/dockets/default.htm.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *http://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Tami Belouin, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993–0002, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Executive Summary

A. Purpose of Direct Final Rule

FDA is issuing this direct final rule because revision and removal of certain general biological products standards will update outdated requirements and accommodate new and evolving technology and testing capabilities without diminishing public health protections. FDA is taking this action because the existing codified requirements are duplicative of requirements that are also specified in biologics license applications (BLAs) or are no longer necessary or appropriate to help ensure the safety, purity, and potency of licensed biological products.

B. Summary of the Major Provisions of the Direct Final Rule

This direct final rule removes the requirements contained in § 610.20 (21 CFR 610.20) from the regulations. FDA is taking this action because the standard preparations listed in the regulation are obsolete, no longer available, or described on a product specific basis in BLAs. In addition, FDA believes that it is no longer necessary to restrict the source of standard preparations to the Center for Biologics Evaluation and Research (CBER), since

appropriate standard preparations can often be obtained from other sources. Section 610.21 is removed because these potency limits are either obsolete or best described on a product specific basis in the BLA. Section 610.50 is amended to remove references to §§ 610.20 and 610.21 and official potency tests and to reflect FDA's updated approach to establishing dates of manufacture. Section 610.53 is amended to remove products no longer manufactured and products for which dating information is identified in the BLA of each individual product, and to reflect updated practices for the remaining products.

C. Legal Authority

FDA is taking this action under the biological products provisions of the Public Health Service Act (PHS Act), and the drugs and general administrative provisions of the Federal Food, Drug, and Cosmetic Act (the FD&C Act).

D. Costs and Benefits

Because this direct final rule does not impose any additional regulatory burdens, this regulation is not anticipated to result in any compliance costs and the economic impact is expected to be minimal.

II. Direct Final Rulemaking

In the document entitled ''Guidance for FDA and Industry: Direct Final Rule Procedures,'' announced and provided in the **Federal Register** of November 21, 1997 (62 FR 62466), FDA described its procedures on when and how the Agency will employ direct final rulemaking. The guidance may be accessed at: *http://www.fda.gov/RegulatoryInformation/Guidances/ucm125166.htm.* We have determined that this rule is appropriate for direct final rulemaking because we believe that it includes only noncontroversial amendments and we anticipate no significant adverse comments. Consistent with our procedures on direct final rulemaking, FDA is also publishing elsewhere in this issue of the **Federal Register** a companion proposed rule proposing to amend the general biological products standards relating to dating periods and to remove those relating to standard preparations and limits of potency. The companion proposed rule provides a procedural framework within which the rule may be finalized in the event that the direct final rule is withdrawn because of any significant adverse comments. The comment period for the direct final rule runs concurrently with the companion proposed rule. Any comments received in response to the companion proposed rule will be considered as comments regarding the direct final rule.

We are providing a comment period on the direct final rule of 75 days after the date of publication in the **Federal Register**. If we receive any significant adverse comments, we intend to withdraw this direct final rule before its effective date by publication of a notice in the **Federal Register**. 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, we 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 regulation change in addition to those in this direct final rule would not be considered a significant adverse comment unless the comment states why the rule would be ineffective without the additional change. In addition, if a significant adverse comment applies to part of this rule and that part can be severed from the remainder of the rule (*e.g.,* where, as here, a direct final rule deletes several unrelated regulations), we may adopt as final those provisions of the rule that are not the subject of the significant adverse comment.

If any significant adverse comments are 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 we withdraw 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 notice-and-comment procedures.

If FDA receives no significant adverse comments during the specified comment period, FDA intends to publish a document confirming the effective date within 30 days after the comment period ends.

III. Background

On January 18, 2011, President Barack Obama issued Executive Order 13563, ''Improving Regulation and Regulatory Review'' (76 FR 3821, January 21, 2011). One of the provisions in the Executive Order requires Agencies to consider how best to promote the retrospective analysis of rules that may be outmoded, ineffective, insufficient, or excessively burdensome, and to modify, streamline, expand, or repeal them in accordance with what has been learned (76 FR 3821 at 3822). As one step in implementing the Executive Order, FDA published a notice in the **Federal Register** of April 27, 2011 (76 FR 23520) entitled ''Periodic Review of Existing Regulations; Retrospective Review Under E.O. 13563.'' In that notice, FDA announced that it was conducting a review of existing regulations to determine, in part, whether they can be made more effective in light of current public health needs and to take advantage of, and support, advances in innovation that have occurred since those regulations took effect. As part of this initiative, FDA is updating outdated regulations as specified in this rule.

FDA's general biological products standards in part 610 are intended to help ensure the safety, purity, and potency of biological products administered to humans. The revision and removal of certain general biological products standards are designed to update outdated requirements and accommodate new and evolving manufacturing and control testing technology. The rule provides manufacturers of biological products with flexibility, as appropriate, to employ advances in science and technology as they become available, without diminishing public health protections.

A. Sections 610.20 and 610.21

Standard preparations are generally used to perform lot release testing or other specific product characterization assays. Under the current standard preparations, § 610.20, FDA requires specific standard preparations to be used for a small number of the biological products FDA regulates unless a modification is permitted under § 610.9. Specifically, according to current § 610.20 *Standard preparations,* standard preparations, made available by CBER, are required to be used in the testing of potency or opacity of certain biological products, mostly biological products that were initially licensed several decades ago. Most of these standard preparations requirements are now obsolete, because either CBER no longer provides the listed standard preparations, or the specific biological products are no longer manufactured, or both. In addition, standard preparations to help ensure the safety, purity, and potency of particular biological products can often be obtained from sources other than CBER now, including international sources, or can be

developed internally by the applicant. Thus, FDA believes it is no longer necessary to specify CBER as the source of standard preparations in § 610.20. For these reasons, FDA is removing § 610.20. Consistent with current practice and BLAs, CBER will continue to make and supply standard preparations when appropriate, as well as continue to collaborate with external organizations in the development and assessment of physical standard preparations for biological products.

Under the current § 610.21 *Limits of potency,* FDA specifies minimal potency limits to be met for the antibodies and antigens listed. However, most of the biological products subject to the specified potency limits are no longer manufactured. In addition, for those that are still manufactured, or for anyone wanting to manufacture the listed products, FDA's updated practice is to have the potency limit also be specified in the BLA. For this reason, FDA is removing § 610.21. As a result of removing §§ 610.20 and 610.21, part 610, subpart C is removed and reserved.

In addition to sometimes being duplicative of information provided in the BLA and unnecessarily restrictive regarding the source of standard preparations, the codification by regulation of many of the standard preparations and limits of potency for certain biological products sometimes does not keep abreast of technological advances in science related to manufacturing and testing. For many years, because of the potential for impeding scientific progress, FDA has not codified additional specific standard preparations and limits of potency for licensed biological products, but instead the standards are established in the BLA. Failure to conform to applicable standards established in the license is grounds for revocation under § 601.5(b)(1)(iv) (21 CFR 601.5(b)(1)(iv)). Notwithstanding the changes in this rule, FDA will continue to require that each biological product meet standards to assure that the product is safe, pure, and potent, and will continue to require that each lot demonstrate conformance with the standards applicable to that product (see § 610.1) through appropriate testing. Therefore, we expect that standard preparations and potency limits will be established in the BLA and may be changed only in accordance with regulations for reporting post-approval changes (see § 601.12). Furthermore, no lot of any licensed product may be released by the manufacturer prior to the completion of tests for conformity with standards applicable to such product (see § 610.1).

FDA is therefore amending its regulations to remove §§ 610.20 and 610.21 because appropriate standard preparations and potency limits for any listed product are specified during the licensing process on a product specific basis. The removal of §§ 610.20 and 610.21 will also increase regulatory flexibility by allowing industry and FDA to more readily use and incorporate current scientific technology and other appropriate reference materials in the manufacture and regulation of licensed biological products.

B. Sections 610.50 and 610.53

A biological product is expected to remain stable and retain its identity, strength, quality, and purity for a period of time after manufacture when it is properly stored. The dating period limitations regulations provided at §§ 610.50 and 610.53 specify how the date of manufacture for biological products will be determined, when the dating begins, and dating periods for certain biological products. The existing § 610.50 prescribes how the date of manufacture is determined for biological products and relies in part upon §§ 610.20 and 610.21 or official standards of potency (*i.e.,* a specific test method described in regulation). With the removal of §§ 610.20 and 610.21 for reasons described in this document, FDA is revising § 610.50 to reflect FDA's updated approach to establishing dates of manufacture.

In addition, current § 610.50(b) does not provide FDA or applicants with flexibility to consider the variety of manufacturing situations and technologies that exist today and which may occur in the future. Since 1977, when the regulation was last amended, new methods of manufacture and testing often associated with new biological products have been developed. The revisions to § 610.50 provided in this direct final rule therefore allow additional manufacturing activities other than those currently listed to be used to determine the date of manufacture.

Under the revised regulation, the date of manufacture must be identified in the approved BLA. FDA recommends that applicants discuss a suitable date of manufacture with FDA during late clinical development and propose a date of manufacture in the BLA. We consider the underlying science and manufacturing process testing methods in determining the date of manufacture for each specific product. The approved BLA will specify how the date of manufacture is determined. A paragraph is being added, § 610.50(c), specifying how the date of manufacture for Whole Blood and blood components is determined. This will assist in complying with the dating periods prescribed for Whole Blood and blood components in the revised table in redesignated § 610.53(b).

The current table at § 610.53(c) lists dating periods, manufacturer's storage periods, and storage conditions for many biological products. The table in § 610.53(c) (which is redesignated as § 610.53(b)) is revised to remove products where storage conditions and dating periods are established to help ensure the continued safety, potency, and purity of each individual product, based upon information submitted in the relevant BLA. The dating period and storage conditions for these products will be identified in the BLA. The table in § 610.53(c) is also revised to delete those products that are no longer manufactured. We are retaining those products, specifically Whole Blood and blood components, whose dating periods are based upon data relating to the anticoagulant or preservative solution in the product, usage, clinical experience, laboratory testing, or further processing. The list is updated to include currently licensed Whole Blood and blood component products with their applicable storage temperatures and dating periods.

In listing the dating periods for Whole Blood and blood component products, we took into account existing regulations, guidance documents, package inserts for solutions used for manufacture or storage of Whole Blood and blood components, and operator instruction manuals for devices used in the manufacture of Whole Blood and blood component products. Because we understand from these materials that these dating periods are in current use, and because blood establishments can request an exception under § 640.120 (21 CFR 640.120), we do not anticipate significant objections to codifying this information. Similarly, we are removing § 610.53(d) because it is duplicative of § 640.120. In addition, we recognize that future scientific understanding and new technology, such as the implementation of pathogen reduction technology or the approval of extended storage systems, could affect what dating periods would be necessary, as a scientific matter, for Whole Blood and blood components. For this reason, the rule allows for changes to the dating periods specified in § 610.53(b) when the dating period is otherwise specified in the instructions for use by the blood collection, processing, and storage system approved or cleared for such use by FDA.

In conclusion, the amendments to the regulations provided by this rule are designed to be consistent with updated practices in the biological product industry and to remove unnecessary or outdated requirements. FDA is taking this action as part of our continuing effort to reduce the burden of unnecessary regulations on industry and to revise outdated regulations to provide flexibility without diminishing public health protection. Given the additional flexibility provided by these revised regulations, FDA does not anticipate that applicants for licensed biological products will need to revise information in BLAs in order to conform to the revised regulations.

IV. Highlights of the Direct Final Rule

FDA is revising the general biological products standards relating to dating periods and removing certain standard preparations and limits of potency. These changes are designed to remove unnecessary or outdated requirements, and accommodate new and evolving technology and testing capabilities without diminishing public health protections. FDA is issuing these revisions directly as a final rule because the Agency believes they include only noncontroversial amendments and FDA anticipates no significant adverse comments.

FDA is removing § 610.20 because the standard preparations listed are obsolete or no longer available; standard preparations to ensure the safety, purity, and potency of a product can best be determined on a product specific basis; and standard preparations may be obtained from other sources. Applicants for biological product licenses currently identify standard preparations in the BLA, and the proposed standard preparations and their purpose are reviewed by FDA during the regulatory process. The standard preparations may include standard preparations developed by the applicant as well as appropriate standard preparations that can be obtained from other sources. Consistent with current practice, CBER will continue to make and supply standard preparations when appropriate, as well as continue to collaborate with external organizations in the development and assessment of physical standard preparations for licensed biological products.

We are removing § 610.21 because these potency limits are best described in the BLAs on a product specific basis. Applicants for biological product licenses already identify standards for potency to help ensure the safety, purity, and potency of the product within their BLA, and the proposed standards are reviewed by FDA during the regulatory process. The use of a potency limit is suitably described in the specific product's BLA and allows for its continued and appropriate use in the absence of § 610.21.

We are revising § 610.50 by making a minor amendment to the section heading, removing the current language, redesignating § 610.53(b) as § 610.50(a) with edits, revising § 610.50(b), and adding new § 610.50(c). Current § 610.53(b), which applies to all biological products, has been moved to § 610.50(a) and edits have been made for better organization and clarification. Section 610.50(b) is being revised and § 610.50(c) is being added to clarify how the date of manufacture is set for purposes of determining the dating period for general biological products and for Whole Blood and blood components, respectively.

We are amending the section heading of § 610.53 to reflect that it only addresses dating periods for Whole Blood and blood components. We are revising § 610.53(a) since this section only applies to the dating periods for Whole Blood and blood components. We are redesignating § 610.53(c) as § 610.53(b) and revising the text to provide an explanation on using the table and to correspond with 21 CFR 606.121(c)(7). We are revising the text and table to eliminate those products for which storage periods, storage conditions, and dating periods are better established by data submitted in the BLA, and to delete those products which are no longer manufactured. The dating period and storage conditions for these products are identified in the BLA. We are including an updated list of Whole Blood and blood component products with their applicable storage temperatures and dating periods, which are based upon available information, including data relating to the anticoagulant or preservative solution in the product, usage, clinical experience, laboratory testing, or further processing. The table contains a list of storage temperatures and dating periods for Whole Blood and blood components that FDA has reviewed and determined to be necessary to help ensure the safety, potency, and purity of these products. In listing the dating periods for the Whole Blood and blood component products, we took into account existing guidance documents, package inserts for solutions used for manufacture or storage of Whole Blood and blood components, and operator instruction manuals for devices used in the manufacture of Whole Blood and blood component products. We are redesignating § 610.53(c) as § 610.53(b) and removing all products regulated by FDA's Center for Drug Evaluation and Research (CDER) from the table. Finally, we are removing § 610.53(d) because it is duplicative of § 640.120.

V. Legal Authority

FDA is issuing this rule under the biological products provisions of the PHS Act (42 U.S.C. 216, 262, 263, 263a and 264) and the drugs and general administrative provisions of the FD&C Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360c, 360d, 360h, 360i, 371, 372, 374, and 381). Under these provisions of the PHS Act and the FD&C Act, we have the authority to issue and enforce regulations designed to ensure that biological products are safe, pure, and potent, and prevent the introduction, transmission, and spread of communicable disease.

VI. Economic Analysis of Impacts

We have examined the impacts of the direct final rule under Executive Order 12866, Executive Order 13563, and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4). Executive Orders 12866 and 13563 direct us 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; distributive impacts; and equity). We believe that this direct final rule is not a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the direct final rule is removing regulations and revising regulations to be consistent with updated practice, we certify that this direct final rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before issuing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $144 million, using the most current (2014) Implicit Price Deflator for the Gross Domestic Product. This direct final rule would not result

in an expenditure in any year that meets or exceeds this amount.

VII. Analysis of Environmental Impact

We have 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.

VIII. Federalism

We have analyzed this direct 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, we conclude that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

IX. Paperwork Reduction Act of 1995

This direct final rule contains collections of information 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 collections of information in part 610 have been approved under OMB control number 0910–0338. The removal of § 610.53(d) impacts OMB control number 0910–0338. We are removing § 610.53(d) because it is duplicative of § 640.120, which is also approved under the same collection of information. While there is no net change in the burden estimate, the current approved collection of information will be updated to reflect this removal. The actions taken by this direct final rule do not create a substantive or material modification to this approved collection of information. Therefore, FDA concludes that OMB has already approved this information collection and the requirements in this document are not subject to additional review by OMB.

List of Subjects in 21 CFR Part 610

Biologics, Labeling, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 610 is amended as follows:

PART 610—GENERAL BIOLOGICAL PRODUCTS STANDARDS

■ 1. The authority citation for part 610 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360c, 360d, 360h, 360i, 371, 372, 374, 381; 42 U.S.C. 216, 262, 263, 263a, 264.

Subpart C [Removed and Reserved]

■ 2. Remove and reserve subpart C, consisting of §§ 610.20 and 610.21.

■ 3. Revise § 610.50 to read as follows:

§ 610.50 Date of manufacture for biological products.

(a) *When the dating period begins.* The dating period for a product must begin on the date of manufacture as described in paragraphs (b) and (c) of this section. The dating period for a combination of two or more products must be no longer than the dating period of the component with the shortest dating period.

(b) *Determining the date of manufacture for biological products other than Whole Blood and blood components.* The date of manufacture for biological products, other than Whole Blood and blood components, must be identified in the approved biologics license application as one of the following, whichever is applicable: The date of:

(1) Potency test or other specific test as described in a biologics license application or supplement to the application;

(2) Removal from animals or humans;

(3) Extraction;

(4) Solution;

(5) Cessation of growth;

(6) Final sterile filtration of a bulk solution;

(7) Manufacture as described in part 660 of this chapter; or

(8) Other specific manufacturing activity described in a biologics license application or supplement to the biologics license application.

(c) *Determining the date of manufacture for Whole Blood and blood components.* (1) The date of manufacture for Whole Blood and blood components must be one of the following, whichever is applicable:

(i) Collection date and/or time;

(ii) Irradiation date;

(iii) The time the red blood cell product was removed from frozen storage for deglycerolization;

(iv) The time the additive or rejuvenation solution was added;

(v) The time the product was entered for washing or removing plasma (if prepared in an open system);

(vi) As specified in the instructions for use by the blood collection, processing, and storage system approved or cleared for such use by FDA; or

(vii) As approved by the Director, Center for Biologics Evaluation and Research, in a biologics license application or supplement to the application.

(2) For licensed Whole Blood and blood components, the date of manufacture must be identified in the approved biologics license application or supplement to the application.

■ 4. Revise § 610.53 to read as follows:

§ 610.53 Dating periods for Whole Blood and blood components.

(a) *General.* Dating periods for Whole Blood and blood components are specified in the table in paragraph (b) of this section.

(b) *Table of dating periods.* In using the table in this paragraph, when a product in column A is stored at the storage temperature prescribed in column B, storage of a product must not exceed the dating period specified in column C, unless a different dating period is specified in the instructions for use by the blood collection, processing and storage system approved or cleared for such use by FDA. Container labels for each product must include the recommended storage temperatures.

WHOLE BLOOD AND BLOOD COMPONENTS STORAGE TEMPERATURES AND DATING PERIODS

A	B	C
Product	Storage temperature	Dating period
Whole Blood		
ACD, CPD, CP2D	Between 1 and 6 °C	21 days from date of collection.

WHOLE BLOOD AND BLOOD COMPONENTS STORAGE TEMPERATURES AND DATING PERIODS—Continued

A	B	C
Product	Storage temperature	Dating period
CPDA–1	do [1]	35 days from date of collection.
Red Blood Cells		
ACD, CPD, CP2D	Between 1 and 6 °C	21 days from date of collection.
CPDA–1	do	35 days from date of collection.
Additive solutions	do	42 days from date of collection.
Open system (e.g., deglycerolized, washed)	do	24 hours after entering bag.
Deglycerolized in closed system with additive solution added.	do	14 days after entering bag.
Irradiated	do	28 days from date of irradiation or original dating, whichever is shorter.
Frozen	−65 °C or colder	10 years from date of collection.
Platelets		
Platelets	Between 20 and 24 °C	5 days from date of collection.
Platelets	Other temperatures according to storage bag instructions.	As specified in the instructions for use by the blood collection, processing and storage system approved or cleared for such use by FDA.
Plasma		
Fresh Frozen Plasma	−18 °C or colder	1 year from date of collection.
Plasma Frozen Within 24 Hours After Phlebotomy.	do	1 year from date of collection.
Plasma Frozen Within 24 Hours After Phlebotomy Held at Room Temperature Up To 24 Hours After Phlebotomy.	do	1 year from date of collection.
Plasma Cryoprecipitate Reduced	do	1 year from date of collection.
Plasma	do	5 years from date of collection.
Liquid Plasma	Between 1 and 6 °C	5 days from end of Whole Blood dating period.
Source Plasma (frozen injectable)	−20 °C or colder	10 years from date of collection.
Source Plasma Liquid (injectable)	10 °C or colder	According to approved biologics license application.
Source Plasma (noninjectable)	Temperature appropriate for final product	10 years from date of collection.
Therapeutic Exchange Plasma	−20 °C or colder	10 years from date of collection.
Cryoprecipitated AHF		
Cryoprecipitated AHF	−18 °C or colder	1 year from date of collection of source blood or from date of collection of oldest source blood in pre-storage pool.
Source Leukocytes		
Source Leukocytes	Temperature appropriate for final product	In lieu of expiration date, the collection date must appear on the label.

[1] The abbreviation "do." for ditto is used in the table to indicate that the previous line is being repeated.

Dated: April 27, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016–10385 Filed 5–3–16; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF THE INTERIOR

Bureau of Indian Affairs

[167A2100DD/AAKC001030/ A0A501010.999900 253G]

25 CFR Part 20

RIN 1076–AF29

Financial Assistance and Social Services Programs; Burial Assistance

AGENCY: Bureau of Indian Affairs, Interior.

ACTION: Final rule; confirmation.

SUMMARY: The Bureau of Indian Affairs (BIA) is confirming the interim final rule published on March 1, 2016, extending the deadline for filing an application for burial assistance to 180 days to address hardships resulting from the current short timeframe. The Department of the Interior (Department) did not receive any significant adverse comments during the public comment period on the interim final rule, and