Compliance Policy Regarding Blood and Blood Component Donation Suitability, Donor Eligibility and Source Plasma Quarantine Hold Requirements

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Guidance for Industry

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 1-800-835-4709 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.

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Guidance for Industry

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

This guidance addresses certain requirements that apply to blood establishments that collect blood and blood components, including Source Plasma. Specifically, the guidance explains the conditions under which FDA does not intend to take regulatory action for a blood establishment's failure to comply with certain requirements in Title 21 of the Code of Federal Regulations 630.30 (21 CFR 630.30) regarding donation suitability; 21 CFR 630.10(c)(2) regarding donor eligibility; and 21 CFR 640.69(f) regarding quarantine hold for Source Plasma.

This guidance finalizes the draft guidance of the same title, dated May 2022, and supersedes the guidance entitled, "Alternative Procedures for Blood and Blood Components During the COVID-19 Public Health Emergency; Guidance for Industry," dated April 2020.[1]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency'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 Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

To address the urgent and immediate need for blood and blood components during the Coronavirus Disease 2019 (COVID-19) public health emergency, FDA (we) issued certain

[1] The April 2020 guidance was revised to continue in effect until November 7, 2023 (180 days after the public health emergency declaration expired), unless superseded by a revised final guidance before that date. For further information, see 85 FR 15417 (March 13, 2023).

exceptions and alternatives to the requirements regarding blood and blood components under 21 CFR 640.120(b). Through the guidance entitled, "Alternative Procedures for Blood and Blood Components During the COVID-19 Public Health Emergency; Guidance for Industry" dated April 2020 (April 2020 guidance), we issued the following exceptions and alternative procedures:

- Permitted the release of certain donations for transfusion or further manufacturing when the review of records, required after donation under 21 CFR 630.30(a)(2), identified a donation as unsuitable because of failure to follow certain procedures to ensure that the donation would not adversely affect the health of the donor. Provided that the donor is otherwise eligible and the donation is otherwise suitable, we granted exceptions for the following requirements:
    - blood pressure (21 CFR 630.10(f)(2));
    - pulse (21 CFR 630.10(f)(4));
    - weight (21 CFR 630.10(f)(5)); and
    - donation frequency (21 CFR 630.15(a)(1)).
- Permitted blood establishments to clarify a donor's response or obtain omitted information required to determine donor eligibility and component suitability within 72 hours of the time of collection, instead of within 24 hours of the time of collection (21 CFR 630.10(c)(2)).
- Permitted the release of Source Plasma donated by paid donors and determined to be suitable for further manufacturing into injectable products after a quarantine hold of 45 calendar days, instead of 60 calendar days, provided all other donor eligibility and donation suitability requirements are met (21 CFR 640.69(f)).

Since publication of the April 2020 guidance, we received numerous comments from the blood industry requesting that we continue to permit the exceptions and alternatives beyond the public health emergency related to COVID-19 because the changes have increased availability of blood and blood components while maintaining safety of blood and blood components and without compromising the health of blood donors. Further, blood establishments requested that we provide our recommendations before the end of the public health emergency to reduce the operational burdens associated with changes in standard operating procedures and blood establishment computer systems. On March 13, 2023, we announced that the April 2020 guidance would remain in effect until November 7, 2023, unless superseded by a revised final guidance before that date.[2]

After considering the public comments and the available data on donor health and the safety and availability of blood and blood components since publication of the April 2020 guidance, as well as our overall experience with these regulations since they became effective in May 2016[3], we

[2] *Id.*

[3] See Requirements for Blood and Blood Components Intended for Transfusion or for Further Manufacturing Use, May 22, 2015; 80 FR 29841 ("Donor Eligibility Final Rule"), https://www.govinfo.gov/app/details/FR-2015-05-22/2015-12228.

are issuing this guidance to explain the conditions under which FDA does not intend to take regulatory action for a blood establishment's failure to comply with certain requirements in 21 CFR 630.30 regarding donation suitability; 21 CFR 630.10(c)(2) regarding donor eligibility; and 21 CFR 640.69(f) regarding quarantine hold for Source Plasma.

Consequently, we expect that the compliance policy described in this guidance will increase the availability of blood and blood components, including Source Plasma, while maintaining the health of blood donors and the safety of blood and blood components. If, based upon the available scientific evidence, FDA determines that the risk to the safety of the blood supply or the risk to donors' health significantly changes as a result of this compliance policy, FDA may revise this compliance policy as warranted. Further, we will continue to evaluate whether permanent changes to the regulations would be appropriate.

III. COMPLIANCE POLICY

A. Donation Suitability Requirements (21 CFR 630.30(a)(2) and 21 CFR 630.30(b)(1))

Blood establishments must determine donation suitability as prescribed in 21 CFR 630.30(a)(1)-(5). When a donation is not suitable, blood establishments must not release the donation for transfusion or further manufacturing use, unless it is an autologous donation, or an exception is provided (21 CFR 630.30(b)(1)).

FDA does not intend to take regulatory action for a blood establishment's failure to comply with certain regulations for donation suitability in 21 CFR 630.30 provided certain conditions are met. Specifically, when the donation is otherwise suitable under 21 CFR 630.30(a), we do not intend to take regulatory action if blood establishments release certain donations for transfusion or further manufacture when the review of records, required after donation under 21 CFR 630.30(a)(2), identifies the donation as unsuitable because of inadvertent failure to follow procedures to ensure that the donation would not adversely affect the health of the donor, namely for:

- blood pressure (21 CFR 630.10(f)(2));
- pulse (21 CFR 630.10(f)(4));
- weight (21 CFR 630.10(f)(5));
- donation frequency for Whole Blood and Red Blood Cells collected by apheresis (21 CFR 630.15(a)(1));
- pregnancy (21 CFR 630.10(e)(2)(v)); and
- red blood cell loss for plasma collected by plasmapheresis (21 CFR 630.15(b)(6)).

To ensure that the health of the donor is not adversely affected by the donation, blood establishments must continue to determine donor eligibility consistent with 21 CFR 630.10 and 21 CFR 630.15 and must not collect blood from a donor found to be

ineligible prior to collection. In other words, blood establishments must continue to assess donors' blood pressure, pulse, weight, donation frequency, pregnancy history and red blood cell loss on the day of donation and prior to collection, and not collect from ineligible donors, as described in 21 CFR 630.10 and 21 CFR 630.15. However, in the following circumstances, we do not intend to take regulatory action regarding the release of blood components collected from certain ineligible donors as described above:

> (1) an error occurred during the donor eligibility determination that is discovered upon record review, and such error resulted in a blood establishment incorrectly determining that a donor met the eligibility criteria; or
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> (2) the establishment received post donation information from a donor or third party with respect to the requirements in 21 CFR 630.10 and 21 CFR 630.15 described above (e.g., for donation frequency (21 CFR 630.15(a)(1)) or pregnancy (21 CFR 630.10(e)(2)(v)), and such information would have resulted in that donor being determined to be ineligible during the establishment's evaluation of the criteria.

This compliance policy does not apply to donations found unsuitable because of screening test results or risk factors for relevant transfusion-transmitted infections (RTTI) or other factors that have the potential to affect the safety, purity or potency of the blood or blood component, including but not limited to the requirements with respect to donation testing in 21 CFR 610.40 and 21 CFR 640.65(b); the requirement for educational material in 21 CFR 630.10(b); the requirements for assessing a donor's medical history in 21 CFR 630.10(e)(1) and certain requirements in (e)(2); and donor's body temperature in 21 CFR 630.10(f)(1).

The compliance policy also does not apply to donations found unsuitable because of hemoglobin levels or hematocrit values in 21 CFR 630.10(f)(3); the determination of a plasma donor's total protein level as required in 21 CFR 630.15(b)(4); or, the requirements for syphilis testing, total plasma or serum protein determination, and plasma or serum protein electrophoresis or quantitative immuno-diffusion test or equivalent test in 21 CFR 640.65(b). An establishment's failure to comply with these regulations has the potential to adversely affect a donor's health, and the ability of a blood establishment to maintain control of good manufacturing practices.

- Record Maintenance, Investigation and Annual Reporting

We intend to apply this compliance policy, as described above, provided blood establishments that elect to release unsuitable units report the errors and the release of unsuitable donations to FDA annually. The submission of reports will allow FDA to monitor error rates associated with the collection of unsuitable units across the blood industry. FDA will also use this information to assess an individual establishment's

compliance with the donor eligibility requirements and identify the need for corrective actions, if necessary.

Specifically, FDA does not intend to take regulatory action against a blood establishment's failure to comply with certain regulations for donation suitability as described above provided that, among other conditions, licensed and registered-only blood establishments investigate the error that resulted in the collection of an unsuitable donation under 21 CFR 630.30(a)(2); and submit a summary report to FDA annually. The report, in summary format, should describe the number and type of donations released under these conditions. The report should also describe the corrective actions taken to prevent recurrence of errors and to ensure compliance with the applicable regulations. In submitting the report to FDA, establishments may rely on investigations already conducted and information already developed as part of their deviation management and corrective action program.

- Licensed establishments who release unsuitable donations under this compliance policy should include such a report as part of their Annual Report required under 21 CFR 601.12(d).

- We recommend that registered-only establishments who release unsuitable donations under this compliance policy submit the report annually between October 1 and December 31. Registered-only establishments should clearly label the submission as "New URVR Submission – Report of Released Unsuitable Units" and submit to the Office of Blood Research and Review at the following address:

  Food and Drug Administration
  Center for Biologics Evaluation and Research
  Document Control Center
  10903 New Hampshire Ave.
  WO71-G112
  Silver Spring, MD 20993-0002

Blood establishments must continue to maintain records as required under 21 CFR 606.160. This compliance policy does not extend to blood establishments that wish to release unsuitable donations under circumstances other than those described in this section. Blood establishments wishing to release unsuitable donations in other circumstances may submit a request for an alternative procedure under 21 CFR 640.120(a).

B. Donor Eligibility (21 CFR 630.10(c)(2))

Section 21 CFR 630.10(c) generally requires blood establishments to determine donor eligibility on the day of donation and before collection. However, 21 CFR 630.10(c)(2) permits a blood establishment to clarify a donor's responses or obtain omitted information within 24 hours after collection in the event that, upon review, an establishment finds that a donor's responses to the donor questions were incomplete. This permitted clarification applies only to responses to donor questions. It does not apply to information establishments are required to obtain as part of the physical assessment of donors required in 21 CFR 630.10(f).

With respect to the timeframe described in 21 CFR 630.10(c)(2), FDA does not intend to take regulatory action if a blood establishment clarifies a donor's response or obtains omitted information required to determine donor eligibility and donation suitability within 72 hours of the time of collection, instead of within 24 hours of the time of collection, provided all other donor eligibility requirements are met.

C. Source Plasma Quarantine Hold (21 CFR 640.69(f))

Under 21 CFR 640.69(f), Source Plasma donated by paid donors and determined to be suitable for further manufacturing into injectable products must be held in quarantine for a minimum of 60 calendar days before it is released for further manufacturing. With respect to the timeframe for the hold required in 21 CFR 640.69(f), FDA does not intend to take regulatory action if Source Plasma is released after a quarantine hold of 45 calendar days, instead of 60 calendar days, provided all other steps in 21 CFR 640.69(f) are followed and all other donor eligibility and donation suitability requirements are met.

IV. IMPLEMENTATION

Licensed establishments that intend to implement changes described in this guidance must report changes to their standard operating procedures (SOPs) to reflect this compliance policy guidance as Changes Being Effected (CBE) supplements under 21 CFR 601.12(c)(5) (see 21 CFR 601.12(a)(3)).

If, consistent with the April 2020 guidance, a licensed establishment reported changes to their SOPs under 21 CFR 601.12(c)(5), a new CBE supplement does not need to be submitted to reflect this compliance policy guidance. However, the establishment should report that they are retaining the SOPs in their Annual Report under 21 CFR 601.12(d).

V. PAPERWORK REDUCTION ACT

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 (44 U.S.C. 3501-3521). The time required to complete this information collection is estimated to average 4 hours per response, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. Send comments regarding

this burden estimate or suggestions for reducing this burden to:

Food and Drug Administration
Center for Biologics Evaluation and Research
10903 New Hampshire Ave., Bldg. 71, Rm. 7301
Silver Spring, MD 20993-0002

This guidance also refers to previously approved FDA collections of information. The collections of information in 21 CFR part 601 have been approved under OMB control number 0910–0338 and the collections of information in 21 CFR parts 606, 630, and 640 have been approved under OMB control number 0910–0116.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0116. To find the current expiration date, search for this OMB control number at https://www.reginfo.gov).