WELCOME

Ask the FDA and CMS

2025 AABB Annual Meeting

Facility Disclosures

The following AABB Staff have no financial disclosures:

Karen Palmer MT(ASCP), CQA(ASQ)

- Director, Regulatory Affairs

Faiqa Sadique MS, SBB, MT(ASCP), CQA(ASQ)

- Director, CT Programs and Global Outreach

If you have questions following this session, please contact us:

regulatory@aabb.org

Learning Objectives

- Evaluate existing practices to establish alignment with current regulatory requirements and recommendations.
- Apply the Food and Drug Administration's (FDA) recommendations in recently-issued guidance to industry.
- Describe FDA's approach to policies, regulations, and inspection programs related to products regulated by the Center for Biologics Evaluation and Research (CBER).

Thank You!

We appreciate the support of our AABB members and the questions you submitted.

We also appreciate the support of the **FDA** and the **Centers for Medicare & Medicaid Services**.

Our FDA Participants:

The following speakers have no financial disclosures:

Office of Blood Research and Review (OBRR):

- **Anne Eder, M.D., Ph.D.**, CBER, OBRR, Office Director
- **Orieji Illoh, M.D.,** CBER, OBRR, Deputy Office Director

Office of Therapeutic Products (OTP):

- **Irma Sison MD,** CBER, OTP, Division of Human Tissues

Our CMS Participants:

The following participants have no financial disclosures:

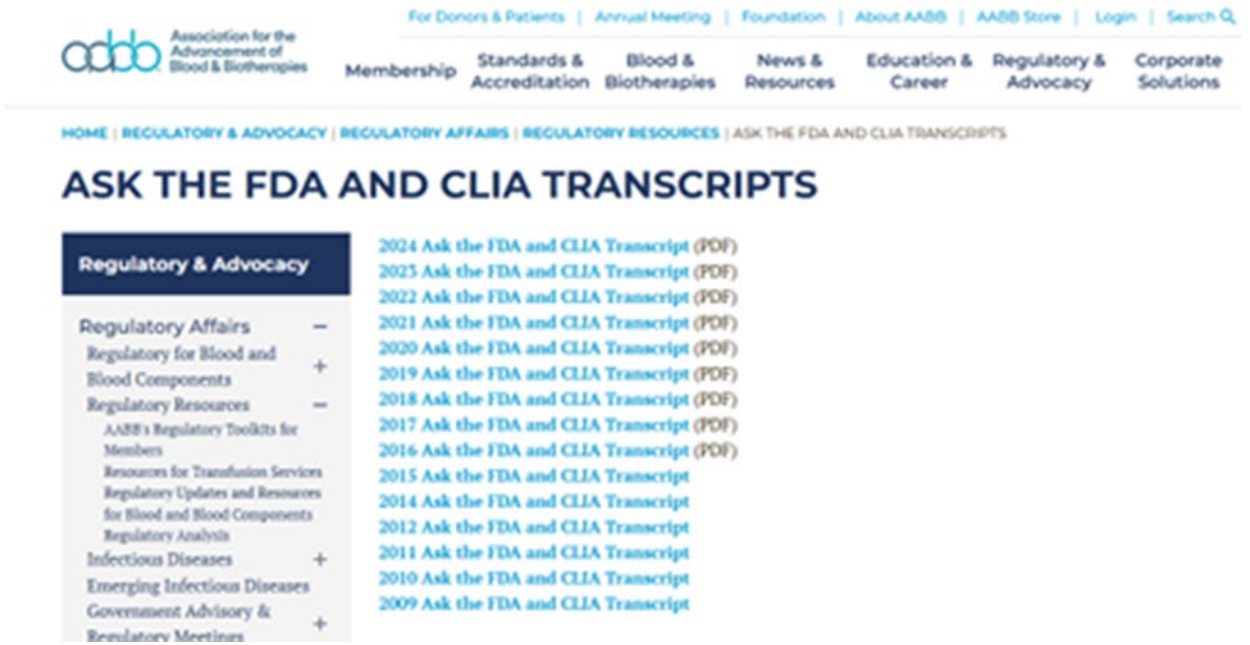
- **Lizet Estrada, MLS(ASCP)CM,** Clinical Laboratory Scientist, Department of Health and Human Services, Centers for Medicare and Medicaid Services

Look For:

AABB Weekly Report sent to your INBOX every Wednesday!

Ask the FDA & CMS/CLIA Transcripts

[Regulatory > Regulatory Resources > Ask The FDA and CLIA Transcripts]



Look For:

Regulatory Toolkits

Searchable PDFs of all Regulatory articles from Weekly Report

HOME | REGULATORY & ADVOCACY | REGULATORY AFFAIRS | REGULATORY RESOURCES | AABB'S REGULATORY TOOLKITS FOR MEMBERS

AABB'S REGULATORY TOOLKITS FOR MEMBERS

Regulatory & Advocacy

- Regulatory Affairs
  - Regulatory for Blood and Blood Components
  - Regulatory Resources
    - AABB's Regulatory Toolkits for Members
    - Resources for Transfusion Services
    - Regulatory Updates and Resources for Blood and Blood Components
    - Regulatory Analysis
  - Infectious Diseases
  - Emerging Infectious Diseases
  - Government Advisory & Regulatory Meetings
  - Regulatory for Cellular Therapies
- Advocacy

The AABB Regulatory Affairs staff have developed these Toolkits and "Member Offerings" to equip our members with the most up-to-date, practical tools to guide you through regulatory decision-making processes.

- Regulatory Update Toolkits: 2019-2020, 2021-2022, 2023-2024, 2025-2026 (member-protected)

What's New

- FDA Blood Establishment Registration Toolkit - September 18, 2025 (member-protected)
- Medication Deferral List v4.0 – Updated July 2025 Yeztugo (Lenacapavir) - Toolkit for Implementation - July 9, 2025 (open-access)
- Measles Virus Information and Resources - September 25, 2025 (member-protected)
- Blood Resiliency During Cybersecurity Events - April 2025 (open access)

Ask the FDA

Anne Eder, MD PhD
Director
Office of Blood Research and Review, CBER, FDA

October 28, 2025

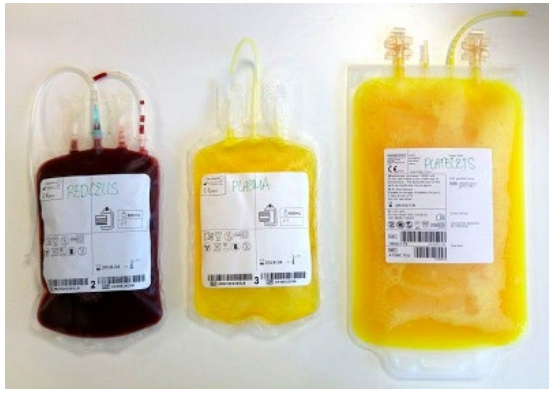
Office of Blood Research and Review (OBRR)

1. Overview of OBRR
   - Who we are
   - What we do
2. Questions sent to FDA
3. Questions sent to AABB

OBRR Mission and Scope

Ensure the safety, efficacy and availability of the U.S. blood supply, through:

1. Regulatory review
   - Blood and blood components, including Source Plasma
   - Devices related to blood manufacturing
     - Donor screening and confirmatory tests
     - Blood collection sets, anticoagulants
2. Inspections and compliance
3. Policy development and preparedness
4. Mission-related research



OBRR: Review Branches

Immediate Office of the Director		
	Anne Eder, M.D., PhD,	Director
	Orieji Illoh, M.D.	Deputy Director
	Jennifer Scharpf M.P.H.	Assoc. Dir., Policy
	Carlos Villa M.D., Ph.D.	Assoc. Dir., Special Programs
	Cherry Geronimo	Chief, Regulatory Project Management Staff

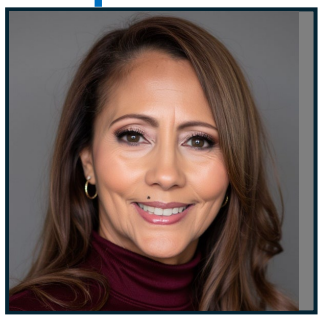
Division of Emerging & Transfusion Transmitted Disease (DETTD)	**Hira Nakhasi, Ph.D.,** Director **Peyton Hobson, Ph.D.,** Deputy Director

Product Review Branch

Division of Blood Components & Devices (DBCD)	**Wendy Paul, M.D.,** Director **Vacant,** Deputy Director

Device Review

Blood and Plasma Branch



Miriam Montes
Acting
Branch Chief

Camilla Smith
Team Lead

~ 12 Consumer Safety Officers (6 per team)

**Research Branches (4) not shown*

U.S. Blood Establishments

Products	License Holders (n)	Registered-only (n)	Establishments (n)
Source Plasma	**28**	--	**1204**
Blood and Components	**78***	--	**1002**
	--	**730**	**730**

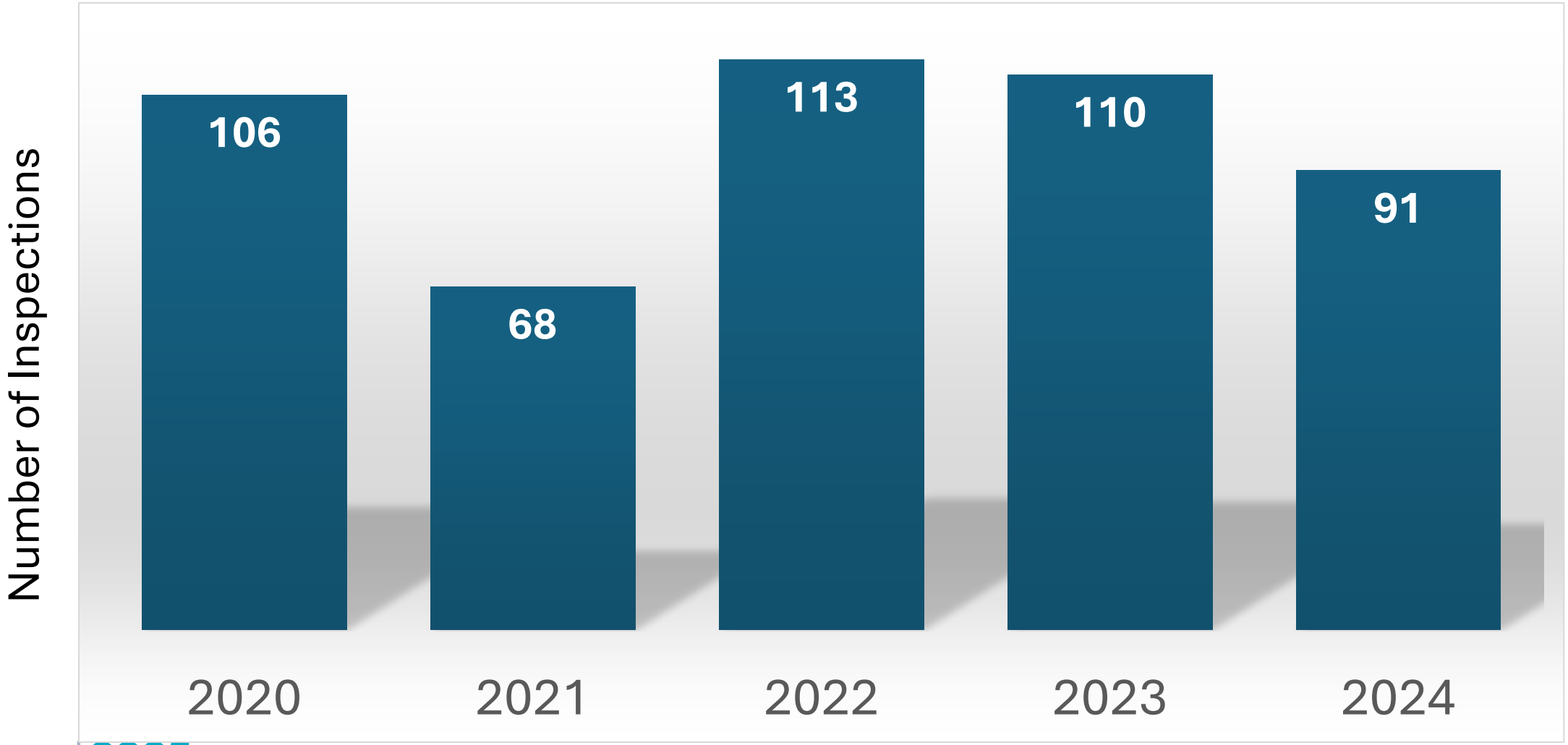
*** Of these, 4 licensed blood establishments provide about 60% of US blood supply**

Regulatory Review, BPB (FY2025)

Submission Type	Number
Original BLA	1
Prior Approval Supplement (PAS)	154
Changes Being Effected in 30 Days Supplement (CBE30)	90
Changes Being Effected Supplement (CBE)	72
Annual Reports	79
Product Correspondence	110
Total	506

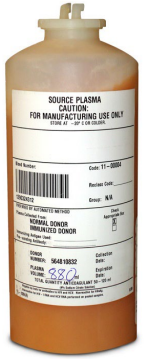
Oct. 1, 2024 – Sept. 30, 2025

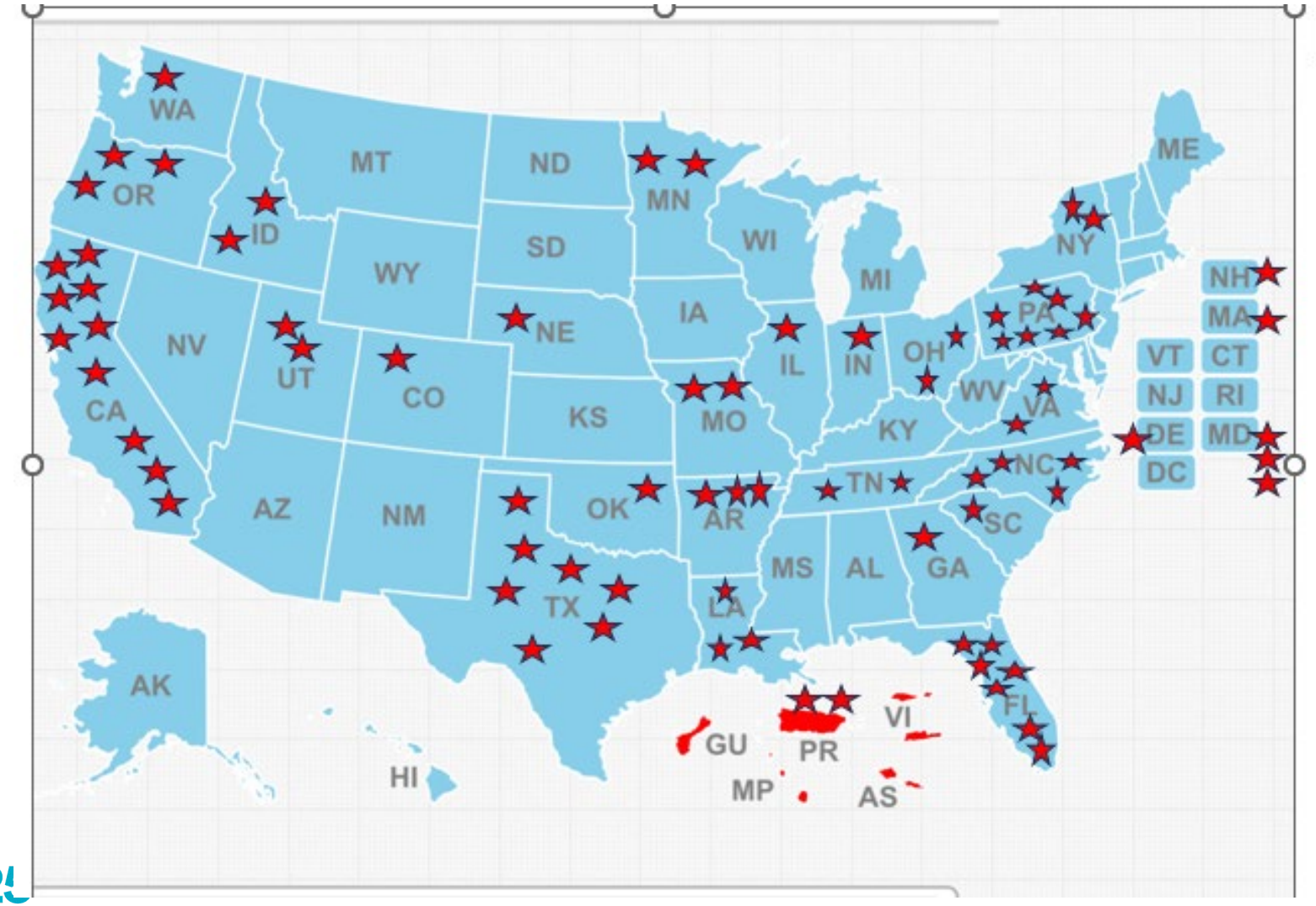
Inspections Conducted by BPB, 2020 - 2024



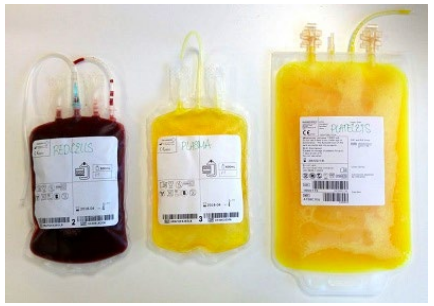
Preapproval Inspections, 2024

73
Source Plasma Establishments





18
Blood Establishments

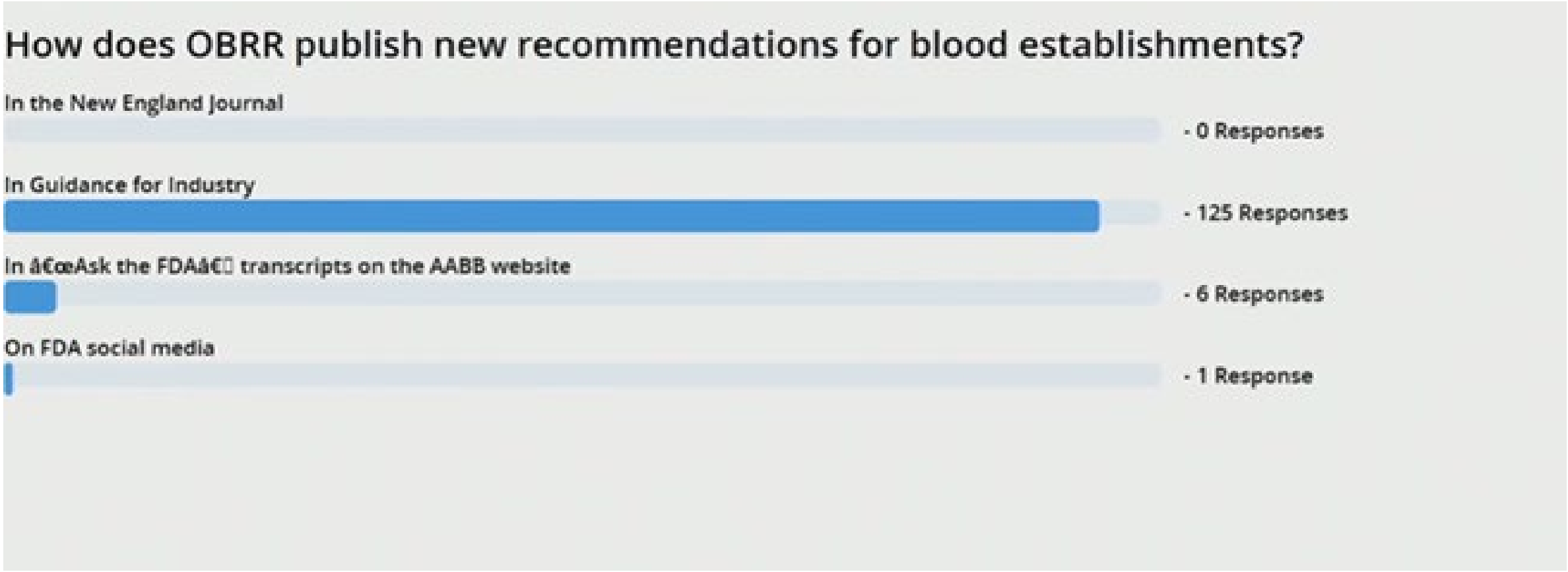


Audience participation

How does OBRR publish new recommendations for blood establishments?

A. In the New England Journal
B. In Guidance for Industry
C. In “Ask the FDA” transcripts on the AABB website
D. On FDA social media

Audience Participation



Correct Answer: In Guidance for Industry

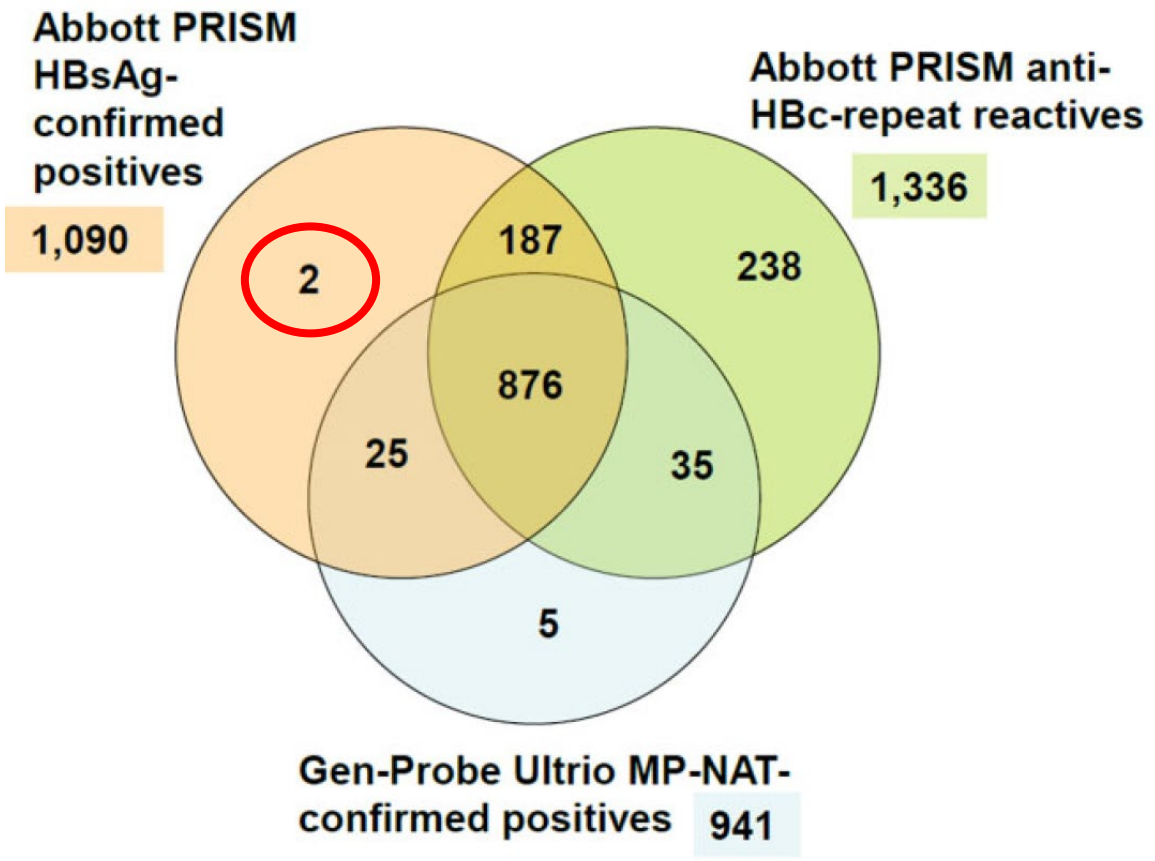
HBsAg Draft Guidance

Recommendations for Testing Blood Donations for Hepatitis B Surface Antigen, Draft Guidance for Industry (July 2025)

- Provides revised recommendations for adequate and appropriate testing for HBV (21 CFR 610.40 (a) & (b))
- FDA currently recommends testing for HBV markers:
  - HBsAg
  - HBV DNA by NAT
  - Antibody to hepatitis B core antigen (anti-HBc), except Source Plasma
- Draft guidance recommends that when donations are tested for HBV DNA and anti-HBc, testing for HBsAg is not necessary and may be discontinued

HBsAg Guidance – Supporting Data

- Decreasing incidence and prevalence of HBV in U.S. general population and blood donors (universal vaccination of newborns in 1991)
- Extensive experience of blood establishments in U.S. (American Red Cross), Germany and Netherlands with three-test algorithm since implementation of HBV NAT



12.8 million donations screened, 2009 to 2011
Stramer et al. Transfusion 2013;53:2449

HBsAg Guidance

Recommendations do not apply to Source Plasma

- No available data to evaluate discontinuing HBsAg testing for paid Source Plasma donors
- Paid donors have higher infectious disease marker rates
- Source Plasma donations are not tested for anti-HBc :

  Donors who have cleared HBV infection express anti-HBs (antibody to HBV surface antigen), in addition to anti-HBc, which neutralizes HBV and contributes to the safety of certain plasma products.

HBsAg Guidance – Next Steps

- Guidance comment period ended October 14, 2025
  - Docket FDA-2024-D-5942
- We intend to finalize recommendations to discontinue HBsAg testing when anti-HBc and HBV NAT is performed, and consolidate all HBV testing recommendations in one final guidance

AABB, ABC, ARC Comments

"AABB, ABC and ARC cautioned that the **differential treatment of source plasma versus recovered plasma** complicates fractionator acceptance and impedes harmonization efforts.

The organizations emphasized that recent scientific evidence and modeling from **Héma-Québec demonstrate that HBV NAT, when paired with pathogen inactivation (PI), provides a robust safety margin** for all plasma-derived medicinal products. The joint comments urge FDA to eliminate HBsAg testing requirements across all plasma types, recognizing HBV NAT and PI as sufficient safeguards. The blood community believes that **harmonizing U.S. standards with international practices would reduce unnecessary testing and support global consistency."**

Considerations

1. **“Differential treatment”** : Source plasma and recovered plasma (plasma collected for transfusion, later sent for fractionation) are fundamentally different and already treated differently.
2. **“Safety margin with pathogen inactivation” :**
   - No data have been submitted to the FDA on the incidence or prevalence of HBV among paid volunteers that present for Source Plasma donations.
   - Paid donors are known to have higher infectious disease marker rates compared to volunteer blood donors.
   - The rationale for eliminating HBV testing for blood donors is that the testing is redundant when HBV NAT and anti-HBc is performed, and the data support that there are essentially no HBV infected donors identified by testing.
3. **“Global consistency” :** Complicated

Screening Tests – Blood vs. Source Plasma

	Blood donation	Source Plasma
HBV	HBV DNA	HBV DNA
	HBsAg	HBsAg
	Anti-HBc	
HCV	HCV RNA	HCV RNA
	Anti-HCV	Anti-HCV
HIV 1, 2	HIV RNA	HIV RNA
	Anti-HIV 1,2	Anti-HIV 1,2
Syphilis	*T. pallidum* antibodies, RPR	*T. pallidum* antibodies, RPR
WNV	WNV RNA	
HTLV I, II	Anti-HTLV I, II	
Chagas	*T. cruzi* antibodies	
Babesia	*B. microti* antibody, endemic states	

Global Harmonization is Complicated

Table 1. Prevalence of transfusion-transmissible infections in blood donations (Median, Interquartile range (IQR)), by income groups (From WHO)

	HIV	HBV	HCV	Syphilis
High-income countries	0.002% (<0.001% – 0.01%)	0.02% (0.005% – 0.12%)	0.007% (0.002% – 0.06%)	0.02% (0.003% – 0.12%)
Upper middle-income countries	0.10% (0.03% – 0.23%)	0.29% (0.13% – 0.62%)	0.19% (0.07% – 0.36%)	0.35% (0.13% – 1.10%)
Lower middle-income countries	0.19% (0.04% – 0.62%)	1.70% (0.70% – 4.74%)	0.38% (0.12% – 0.99%)	0.69% (0.19% – 1.38%)
Low-income countries	0.70% (0.28% – 1.60%)	2.81% (2.00% – 6.02%)	1.00% (0.50% – 1.67%)	0.90% (0.60% – 1.81%)

https://www.who.int/news-room/fact-sheets/detail/blood-safety-and-availability

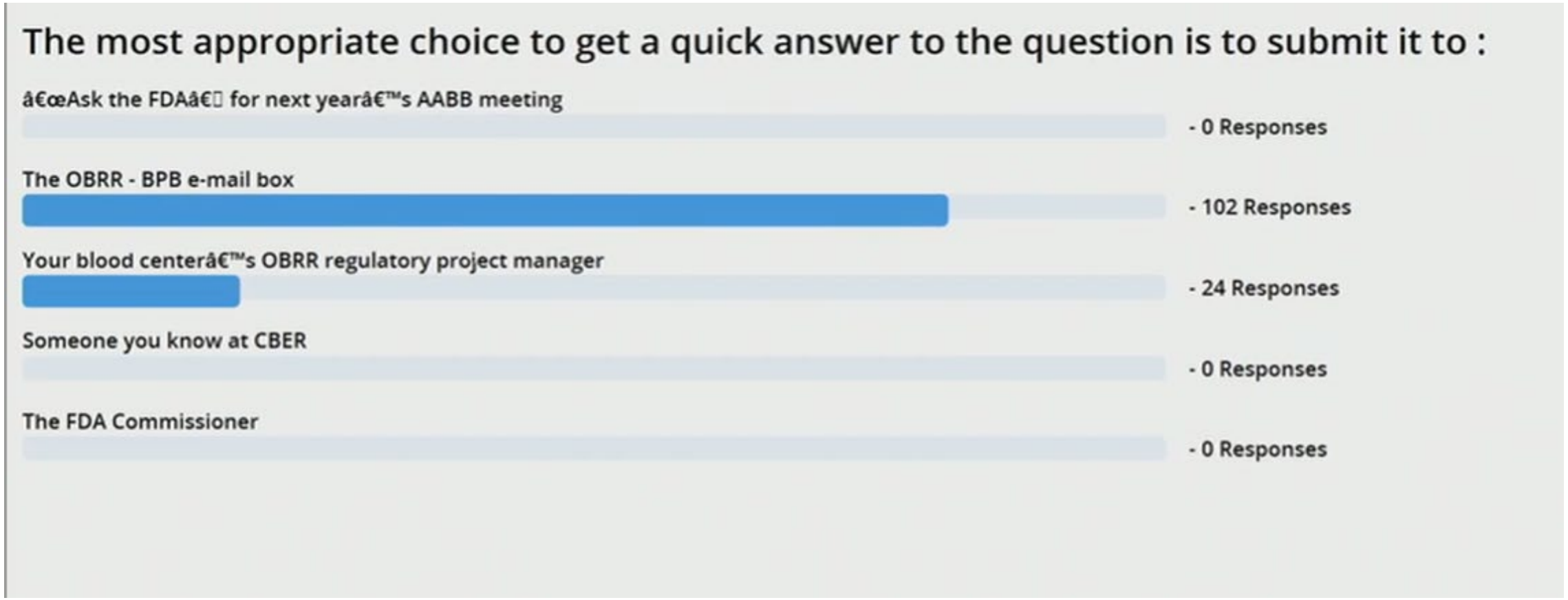
Audience participation

You are reading a newly released OBRR draft guidance and you have a question about how to interpret one of the recommendations.

The most appropriate choice to get a quick answer to the question is to submit it to:

1. “Ask the FDA” for next year’s AABB meeting
2. The OBRR - BPB e-mail box
3. Your blood center’s OBRR regulatory project manager
4. Someone you know at CBER
5. The FDA Commissioner

Questions about Draft Guidance



Correct Answer: The OBRR BPB email box

Contact OBRR

For regulatory submissions

- Contact Regulatory Project Management Staff
  Cherry.Geronimo@fda.hhs.gov

For general inquiries related to blood guidance or manufacturing

- BPB Inquiries mailbox*: **CBEROBRRBPB**Inquiries@fda.hhs.gov

*** CBEROBRRBPB** stands for
Centerfor**B**iologics**E**valuationand**R**esearch**O**fficeof**B**lood**R**esearch
Review**B**loodand**P**lasma**B**ranch

Re-Entry (Donor Requalification) HBsAg and anti-HBc

- A donor in 2024 had repeatedly-reactive HBsAg screening test results (all other infectious disease tests were non-reactive) did not neutralize (i.e., confirmatory testing was negative).
- From the FDA Memo 12-2-1987, and the donor was eligible to donate in 8 weeks.
- This donor then returned and all testing was non-reactive except anti-HBc, which was repeatedly reactive, for the first time
- The blood center looked at the Memo from12-2-1987 and a guidance from 7-19-1996 but they were not sure if the donor was eligible for re-entry.

Re-Qualification (Re-Entry) – anti-HBc

- Donors who test reactive for anti-HBc on **only one** occasion are not required to be deferred, under 21 CFR 610.41(a)(1).
- Guidance : Requalification Method for Reentry of Blood Donors Deferred Because of Reactive Test Results for Antibody to Hepatitis B Core Antigen (anti-HBc), May 2010
  - As an aside: The 7-19-1996 Memo addresses quarantine and disposition of prior donations from donors with repeatedly reactive screening tests for HBV, HCV and HIV, but does not address re-entry.
- The blood products from the anti-HBc reactive donation are not suitable for transfusion, under 21 CFR 610.40 (h)(1) and (2).

HBV : 1 RTTI=1 Guidance

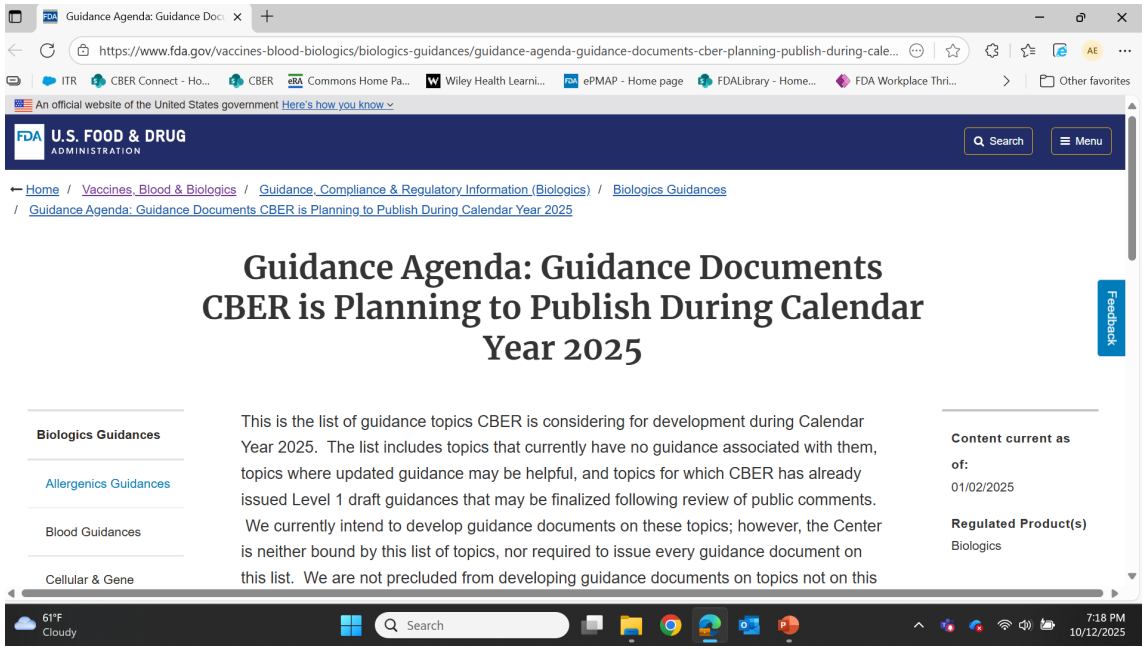
7 Current HBV Guidance Documents

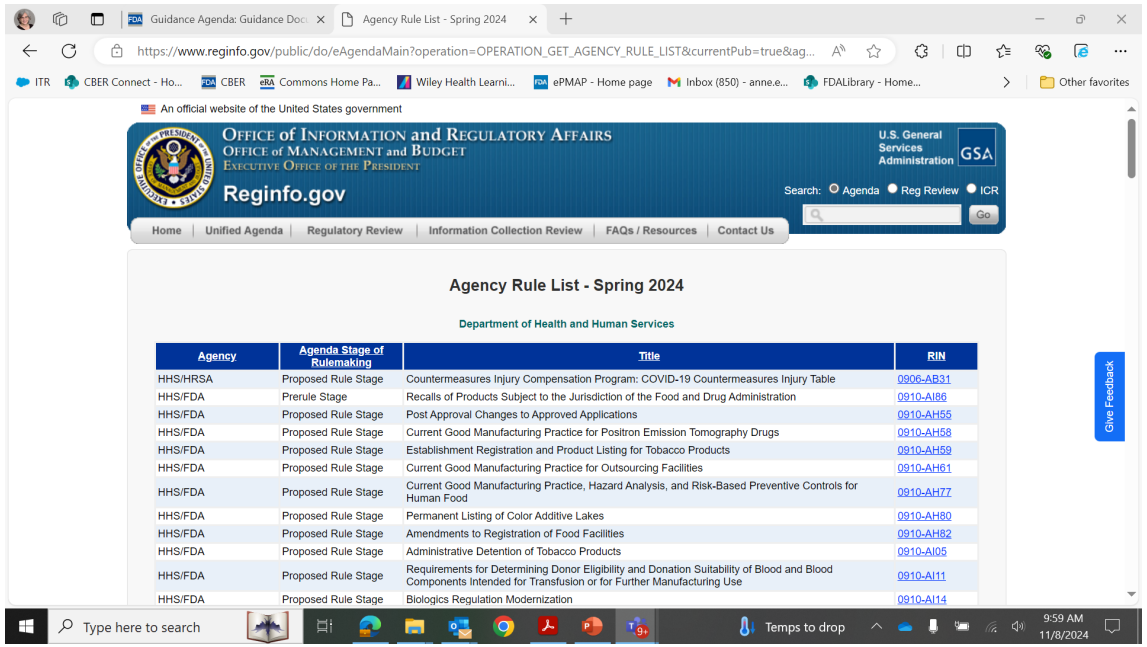
1. Recommendations for the Management of Donors and Units that are Initially Reactive for Hepatitis B Surface Antigen (HBsAg), Memorandum, December 2, 1987 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommendations-management-donor-and-units-are-initially-reactive-hepatitis-b-surface-antigen-hbsag
2. FDA Recommendations Concerning Testing for Antibody to Hepatitis B Core Antigen (Anti-HBc), Memorandum, September 10, 1991 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-recommendations-concerning-testing-antibody-hepatitis-b-core-antigen-anti-hbc
3. Recommendations for the Quarantine and Disposition of Units from Prior Collections from Donors with Repeatedly Reactive Screening Tests for Hepatitis B Virus (HBV), Hepatitis C Virus (HCV) and Human T-Lymphotropic Virus Type I (HTLV-I), Memorandum, July 19, 1996 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommendations-quarantine-and-disposition-units-prior-collections-donors-repeatedly-reactive
4. Requalification of Donors Previously Deferred for a History of Viral Hepatitis after the 11th Birthday; Guidance for Industry, September 2017 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requalification-donors-previously-deferred-history-viral-hepatitis-after-11th-birthday
5. Final Guidance for Industry: Use of Nucleic Acid Tests on Pooled and Individual Samples From Donors of Whole Blood and Blood Components, Including Source Plasma, to Reduce the Risk of Transmission of Hepatitis B Virus, November 15, 2012 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-nucleic-acid-tests-pooled-and-individual-samples-donors-whole-blood-and-blood-components
6. Guidance for Industry: Requalification Method for Reentry of Donors Who Test Hepatitis B Surface Antigen (HBsAg) Positive Following a Recent Vaccination against Hepatitis B Virus Infection (PDF - 50KB), November 2011 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requalification-method-reentry-donors-who-test-hepatitis-b-surface-antigen-hbsag-positive-following
7. Guidance for Industry: Requalification Method for Reentry of Blood Donors Deferred Because of Reactive Test Results for Antibody to Hepatitis B Core Antigen (Anti-HBc), April 30, 2010 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requalification-method-reentry-blood-donors-deferred-because-reactive-test-results-antibody

Coming (soon): One HBV Guidance Document

Table of Contents

Guidance and Regulatory Agendas





[Guidance Agenda: Guidance Documents CBER is Planning to Publish During Calendar Year 2025 | FDA]

[https://www.reginfo.gov/public/do/eAgendaMain]

Questions submitted to OBRR

“Walking Blood Banks”

Does FDA have a definition of a “walking blood bank”?

Does FDA intend to provide information to blood centers that would like to have a “walking blood bank” in the event of a disaster or on the battlefield?

Walking Blood Banks - Response

Response:

FDA does not have a definition of a walking blood bank.

FDA does not intend to release guidance on “walking blood banks" either in a civilian setting or a military setting. There is no consensus on the attributes of a “walking blood bank.”

FDA expects other preparedness options could ensure a safe and available blood supply during emergency situations.

If your blood establishment wishes to discuss your preparedness plans with FDA, you may request a formal meeting with OBRR by contacting your Regulatory Project Manager.

Audience Participation

Your registered-only blood bank wants to manufacture COVID-19 convalescent plasma. But you have never submitted a BLA.

The most appropriate next step is to submit the questions to:

A. Ask the FDA
B. The OBRR - BPB e-mail box
C. OBRR regulatory project management
D. Someone you know at OBRR
E. The FDA Commissioner

Licensed COVID-19 Convalescent Plasma

Correct Answer: OBRR regulatory project management

Contact OBRR

For regulatory submissions

- Contact Regulatory Project Management Staff
  Cherry.Geronimo@fda.hhs.gov

For general inquiries related to blood guidance or manufacturing

- BPB Inquiries mailbox: CBEROBRRBPBInquiries@fda.hhs.gov


FDA
U.S. FOOD & DRUG
ADMINISTRATION

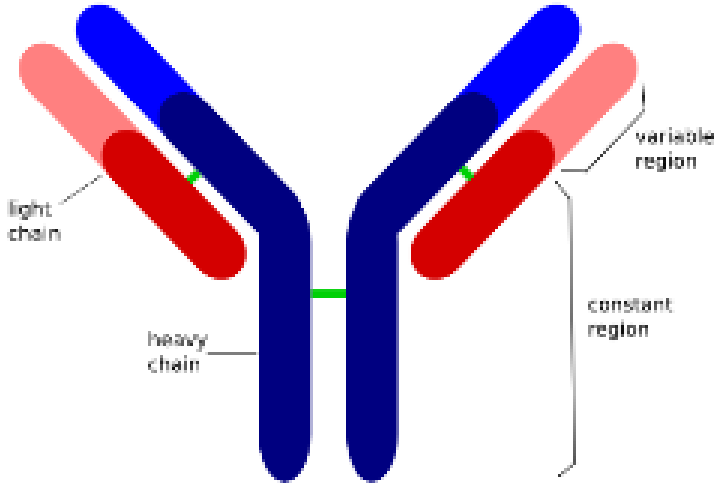
Ask the FDA

Blood and Blood Components

Unexpected Antibodies

Background: 21 CFR 606.121(e)
Container label requirements for particular products or groups of products requires:

> *(2) Except for frozen, deglycerolized, or washed Red Blood Cell products, Red Blood Cell labels must include:*
>
> > *ii) If tests for unexpected antibodies are positive and the product is intended for transfusion, the statement: "Contains (name of antibody)."*



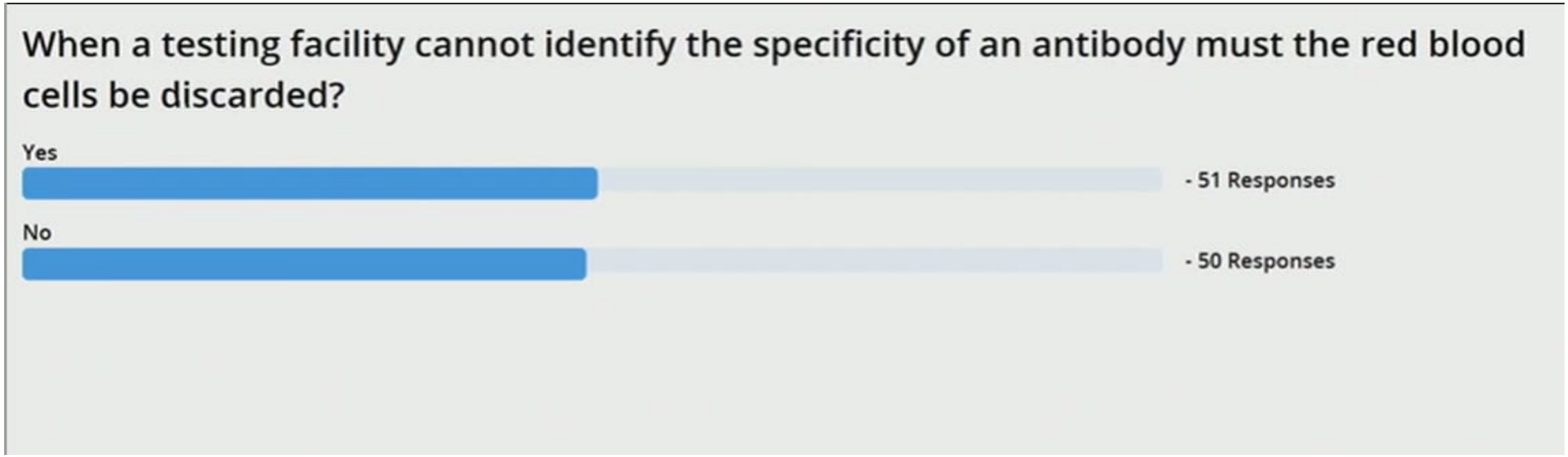
Cont'd on following page

Unexpected Antibodies *(cont'd)*

FOR AUDIENCE RESPONSE:

Question 1: When a testing facility cannot identify the specificity of an antibody must the red blood cells be discarded?

Unexpected Antibodies *(cont'd)*



Correct Answer: No

Unexpected Antibodies *(cont'd)*

FDA/OBRR Response Q1:

"No. 21 CFR 606.121(e)(2)(ii) describes labeling requirements when RBC specific antibodies can be identified before the unit is released for transfusion. This requirement does not apply to frozen, deglycerolized, or washed Red Blood Cell products. If you cannot identify the specificity of an antibody, you may wash the Red Blood Cells or freeze and subsequently deglycerolize them, so that the plasma is removed before transfusion and the unit does not require labeling. FDA does not require that Red Blood Cell units that contain antibodies be discarded."

Responsible Physician – Transfusion Service

Background: 21 CFR 630.3(h)(2)(B)(i) provides the definition of "responsible physician":

Responsible physician means an individual who is:

(1) Licensed to practice medicine in the jurisdiction where the collection establishment is located;

(2) Adequately trained and qualified to direct and control personnel and relevant procedures concerning the determination of donor eligibility; collection of blood and blood components; the immunization of a donor; and the return of red blood cells or other blood components to the donor during collection of blood component(s) by apheresis; and

(3) Designated by the collection establishment to perform the activities described in paragraph (i)(2) of this section.

Cont'd on following page

Responsible Physician – Transfusion Service
(cont'd)

There are multiple references to the duties of the "responsible physician" in relation to blood collection activities but no references to a "responsible physician" in relation to Transfusion Service activities.

Question 2: Must there be a responsible physician over Transfusion Service activities such as the interpretation of transfusion reactions including fatalities or other transfusion related clinical questions?

Responsible Physician – Transfusion Service
(cont'd)

FDA/OBRR Response Q2:

"FDA regulations for blood establishments (21 CFR 630.3(h)(2)(B)(i)) define a 'responsible physician' specifically in the context of blood collection activities.

Medical oversight for Transfusion Service activities, such as the interpretation of transfusion reactions (including fatalities) or other transfusion-related clinical questions remains a responsibility of qualified medical staff within the transfusion service according to applicable CLIA and institutional requirements.

Transfusion services must comply with other applicable FDA regulations, including Current Good Manufacturing Practice for Blood and Blood Components in 21 CFR Part 606."

Pathogen Reduced Platelets – Extending the Expiration

Background: We are a Transfusion Service with a 100% pathogen reduced Platelet inventory. We routinely find ourselves with only expired platelets in our inventory. Our blood supplier recommends that we perform rapid testing to extend the expiration from day-5 to day-6.

Question 3: Is this an acceptable practice?

Cont'd on following page

Pathogen Reduced Platelets – Extending the Expiration
(cont'd)

FDA/OBRR Response Q3:

"No, this is not acceptable practice. The INTERCEPT Pathogen Reduction system for platelets is approved for a maximum of 5 days of storage. Extended storage beyond manufacturer specifications must not be performed because we are not aware of data that this is safe or effective. The recommendations from your blood supplier conflicts with the manufacturer's instructions for use, the code of federal regulations (21 CFR 606.65 (e)), and FDA's guidance.

Regarding transfusion of expired platelets products in an *emergency*, when no alternative is available, your Medical Director should make that decision. We expect that such emergencies happen on an infrequent basis and not routinely. The decision by the Medical Director on whether to allow emergency transfusion of expired platelets is a clinical decision that should be made on a case-by-case basis and based on an individual risk-benefit assessment for each patient. The decision should be documented and include the rationale. All documentation should be available on-site for review at the time of FDA inspections."

FDA Registration and License

Background: The following questions are based on information on FDA registration and licensing shared during the 2021 Ask the FDA session:

FDA's response to questions 24-26 on licensure of the facility versus the component:

> "...*In general, Apheresis Red Blood Cell and Apheresis Platelet product licenses are establishment specific – they apply only to location(s) for which process validation and product quality control data have been submitted and found to be acceptable in a formal supplement to a firm's BLA...*"

FDA's response to questions 31 and 32 on licensure of components manufactured from Whole Blood:

> "*Liquid Plasma, as well as other manually-collected Whole Blood-derived products, such as RBCs and plasma products, are approved at the applicant level under a BLA or changes submitted to an approved BLA. Once approved, the components are licensed throughout all of the facilities under your license.*"

Cont'd on following page

FDA Registration and License (cont'd)

Our main collection facility is FDA licensed for whole blood collection and component manufacturing. This facility is also licensed to collect and manufacture apheresis platelets with both a 5-day dating period and a 7-day dating period. We are planning to open an additional collection site.

Question 4: Based on the FDA's 2021 responses, are we correct in our understanding that whole blood units collected at the new FDA registered collection facility and sent to the main facility for processing into components may be labeled with the facility license number without a prior approval supplement?

FDA/OBRR Response Q4:

"Yes, you are correct. Whole Blood (WB) units, WB derived Red Blood Cells (RBCs) and Plasma can be labeled with your establishment's license number without a prior approval supplement. You should include this change in your annual report."

Cont'd on following page

FDA Registration and License (cont'd)

Question 5: Are we correct in our understanding that apheresis products (platelets and RBCs) collected at the new FDA registered collection facility and sent to the main facility for processing cannot be labeled with the main facility license number without first submitting a PAS and receiving approval?

FDA/OBRR Response Q5:

"Yes, you are correct. This represents a major change requiring the submission of a prior approval supplement (21 CFR 601.12(b))."

Cont'd on following page

FDA Registration and License (cont'd)

Question 6: The new collection facility will only collect apheresis platelets with 7-day dating using the large volume delayed sampling as provided by the 2020 Bacterial Risk Control guidance. There are no plans to collect 5-day platelets at this facility. Must this facility first submit a PAS for 5-day platelets before applying for 7-day platelets?

FDA/OBRR Response Q6:

"No, your establishment does not need to submit a PAS for 5-day platelets before applying for 7-day platelets. Your PAS for 7-day platelets should include information on the specific apheresis device(s) used at the new facility."

Question 7: Is it acceptable for the new collection facility to collect and distribute 7-day platelets for intrastate commerce (within the state) before FDA approval of the PAS?

FDA/OBRR Response Q7:

"Yes. The new collection facility can collect and distribute 7-day apheresis platelets intrastate, before FDA approval of the PAS."

Quality Control Testing - Apheresis Platelets

Background: The 2007 Guidance for Industry and FDA Review Staff Collection of Platelets by Automated Methods, page 19, section VII.C.2. states:

> "*As part of your QC protocol you should: define a plan for non-selectively identifying collections to be tested. This should ensure testing of components collected on each individual automated blood cell separator device, each collection type, and each location.*"

As a blood center that collects Platelets, Leukocytes Reduced by Apheresis at over a dozen blood establishments, our monthly QC sampling plan includes testing of randomly selected collections from all establishments. Policies are in place to ensure that each collection type (single, double, triple) and each location (each establishment) is represented in the QC data. At the end of each month a typical data set has each collection type represented at most locations, but not all. For example, a few locations may only have one to two collection types represented, not all three.

Cont'd on following page

Quality Control Testing - Apheresis Platelets

(cont'd)

Question 8: Does this QC sampling plan meet the recommendations for 2007 Guidance for QC monitoring? Specifically, is it acceptable to represent each collection type and each location per month as compared to ensuring each collection type per each location is represented?

FDA/OBRR Response Q8:

"Based on the information you presented, the sampling approach sounds acceptable, provided you test components from all locations and all collection types on a regular basis. If there is a collection type (single/double/triple) from a particular location that is not sampled in a month, for example, if no triple collections were performed at that location during the month, we recommend that you include components from that type of collection at the location in your testing the following month. You should document the reason why a particular collection type/location was not included in your sampling for the month."

FDA Registration

Background: 21 CFR 607.65(f) describes exemptions for FDA registration for Transfusion Services:

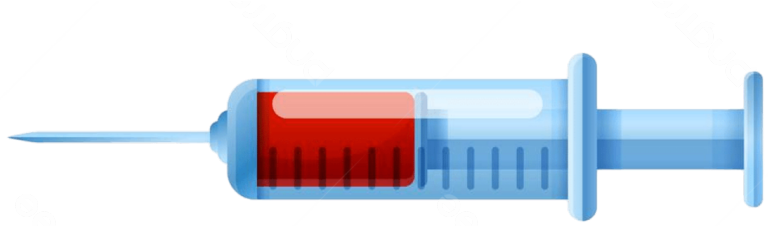
> *"Transfusion services which are a part of a facility that is certified under the Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 263a) and 42 CFR part 493 or has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services and which are engaged in the compatibility testing and transfusion of blood and blood components, but which neither routinely collect nor process blood and blood components. The collection and processing of blood and blood components in an emergency situation as determined by a responsible person and documented in writing, therapeutic collection of blood or plasma, the preparation of recovered human plasma for further manufacturing use, or preparation of red blood cells for transfusion are not acts requiring such transfusion services to register."*

Cont'd on following page

FDA Registration *(cont'd)*

We are a Transfusion Service located in a medical facility which also includes a Hospital-Based Blood Collection Center. There are separate medical directors responsible for the Transfusion Service and Blood Collection Center, but otherwise both operate under the same executive management.

The Transfusion Service is considering reconstituting RBCs and plasma for neonatal transfusion. We understand this is a manufacturing step which requires FDA registration.



Cont'd on following page

FDA Registration *(cont'd)*

Question 9: Is the Transfusion Service required to register separately with FDA or are we considered an extension of the FDA registration held by the Hospital-Based Blood Collection Center?

FDA/OBRR Response Q9:

"In the scenario described, the transfusion service and the collection center may register as a single establishment. When a transfusion service and hospital blood donor center operate under the same hospital management or company ownership, in the same general physical location (see 21 CFR 607.3(c)), they may function under a single FDA Blood Establishment Registration Number. However, the Blood Establishment Registration must document all operational activities and list all blood products that are manufactured as defined per 21 CFR 607.3(d) by the transfusion service and hospital blood donor center."

Therapeutic Phlebotomy – Testosterone Therapy Donors

Background: 21 CFR 630.15(a)(2) describes the requirements for a donor undergoing therapeutic phlebotomy including that:

…

ii. "The donor undergoes a therapeutic phlebotomy as prescribed by a licensed health care provider treating the donor for:

(A) Hereditary hemochromatosis; or

(B) Another disease or condition, when the health of a donor with that disease or condition will not be adversely affected by donating, and the donor's disease or condition will not adversely affect the safety, purity, and potency of the blood and blood components, or any products manufactured from them, and the collection is in accordance with a procedure that has been found acceptable for this purpose by FDA;"

Cont'd on following page

Therapeutic Phlebotomy – Testosterone Therapy Donors (cont'd)

Our facility received FDA approval for an alternative procedure more than 10 years ago to perform phlebotomy of donors on testosterone therapy more frequently than every 8 weeks. Our FDA submission at the time did not state that our medical director would complete a review and signature of each prescription order, but our current policy does require this review and sign off.

Based on the sheer volume of these requests, we are considering a change to our procedure so that the medical director is not responsible for the review of each order form.

Question 10: Is the blood center medical director responsible for the review and approval of each therapeutic phlebotomy order or may this responsibility be delegated to a trained individual if defined in an updated policy and procedure?

Therapeutic Phlebotomy – Testosterone Therapy Donors (cont'd)

FDA/OBRR Response Q10:

"According to 21 CFR 630.15(a)(2), you may perform therapeutic phlebotomy if the donor presents with a prescription from a licensed health care provider treating the donor. FDA regulations do not describe how to review the prescription. Your procedures should include the process to review and document the prescription."

Therapeutic Phlebotomy – Testosterone Therapy Donors (cont'd)

Background: 21 CFR 630.15(a)(2) describes the requirements for therapeutic phlebotomy:

> *(2) Therapeutic phlebotomy. When a donor who is determined to be eligible under § 630.10 undergoes a therapeutic phlebotomy under a prescription to promote the donor's health, you may collect from the donor more frequently than once in 8 weeks for collections resulting in a single unit of Whole Blood or Red Blood Cells, or once in 16 weeks for apheresis collections resulting in two units of Red Blood Cells, provided that the container label conspicuously states the disease or condition of the donor that necessitated phlebotomy.*

And (i) and (ii), as described above in Question 10, the conditions under which "no labeling for the disease or condition" is required."

Cont'd on following page

Therapeutic Phlebotomy – Testosterone Therapy Donors (cont'd)

Our FDA registered collection facility is considering the start of a whole blood therapeutic phlebotomy program for testosterone donors who are determined to be eligible under 21 CFR 630.10. Our program will NOT collect donors more frequently than every 8 weeks.

Question 11: Would these donors, collected less frequently than every 8 weeks, require a prescription from a licensed health care provider?

FDA/OBRR Response Q11:

"Yes. When an individual presents for therapeutic phlebotomy, that is they are under a physician's care for a medical condition treated by therapeutic phlebotomy, a prescription from a licensed health care provider is required according to 21 CFR 630.15(a)(2). Further, you must meet all the conditions in 21 CFR 630.15 (a)(2) if you intend to not label the units with the disease or condition that necessitates the phlebotomy."

Therapeutic Phlebotomy – Testosterone Therapy Donors (cont'd)

Question 12: Are we required to submit our procedures for FDA review and approval prior to the start of the program?

FDA/OBRR Response Q12:

"Yes, in accordance with 21 CFR 630.15(a)(2)(ii)(B), FDA must review and approve your procedures."

Organ Perfusion Devices

Background: We are seeing growing adoption of organ perfusion devices used in organ transplantation to maintain organ viability between donation and implantation. These devices can extend preservation time beyond what traditional cold storage allows.

Blood collection facilities and Transfusion Services are increasingly being asked to provide blood for these devices. We have several questions surrounding our responsibilities.

Cont’d on following page

Organ Perfusion Devices *(cont'd)*

Question 13: Is there guidance now or will there be future guidance surrounding blood usage in organ donors during organ harvest?

FDA/OBRR Response Q13:

"OBRR does not intend to issue specific guidance on this topic. We are aware that certain organ perfusion devices specify the use of allogeneic blood components as perfusates. You should refer to the instructions for use of the device for perfusate requirements. Your medical director should determine whether it is necessary to perform further processing of the blood component such as irradiation."

FDA Responses cont'd on following page

Organ Perfusion Devices *(cont'd)*

Question 14: How do we maintain continuity of patient identification and document traceability of blood products supplied for these organ perfusion devices?

FDA/OBRR Response Q14:

"You must establish procedures relating a unit of blood or blood component from the donor to its final disposition in accordance with 21 CFR 606.100 (b)(13). We recommend creating a detailed documentation process that track each blood component from collection through perfusion device use, including lot numbers, expiration dates, and staff involved in preparation and delivery. Additionally, you should implement a verification system to confirm organ recipient/organ identification before releasing blood products for organ perfusion use, similar to standard transfusion protocols."

FDA Responses cont'd on following page

Organ Perfusion Devices *(cont'd)*

Question 15: Are errors (blood product deviations) reportable in the same manner as when the product is destined for a living patient if the product is used with a perfusion device?

FDA/OBRR Response Q15:

"Yes. Under 21 CFR 606.171, establishments are required to report specific events associated with the manufacturing processes of blood and blood components, including testing, processing, packing, labeling, storage, holding, or distribution activities that may affect the safety, purity, or potency of distributed products. This Biological Product Deviation (BPD) reporting requirement applies to all products regardless of their intended use, including those utilized in conjunction with perfusion devices."

Donor Eligibility – Proof of Postal Address

Background: 21 CFR 630.10(g)
General donor eligibility requirements describes:

(1) *"**Proof of identity and postal address.*** You must obtain proof of identity of the donor and a postal address where the donor may be contacted for 8 weeks after donation;"

Cont'd on following page

Donor Eligibility – Proof of Postal Address *(cont'd)*

Question 16: In today's digital age, would it be acceptable for a donor to show proof a valid email address (i.e. business card) in place of a postal address?

John Q. Public
XYZ Company/CEO

999.999.9999 | Jpublic@xyzcompany.com
123 5th Ave New York, NY 10021, USA

Cont'd on following page

Donor Eligibility – Proof of Postal Address *(cont'd)*

FDA/OBRR Response Q16:

"FDA requires provision of a postal address to support effective communication on issues that may be important to the donor and his or her contacts. Specifically, Establishments may use this information to contact the donor to communicate regarding test results for evidence of infection, as required under 21 CFR 630.40.

In addition to obtaining the donor's postal address, blood establishments may also request an email address or telephone number and describe in their SOPs how the donor will be notified by these means and steps to follow if the donor is not successfully contacted. If the donor has been successfully contacted by other means, then we do not require that contact be made using the postal service."

Emergency Release of Blood – Physician Signature

Background: 21 CFR 606.160 provide records which must be maintained.

> "(b)(3) Storage and distribution records:
>
> (v) Emergency release of blood, including signature of requesting physician obtained before or after release."

We are a Transfusion Service supporting a large trauma center. Multiple times a day we issue validated trauma coolers, packed with emergency release blood, to the emergency room. Frequently, these coolers are returned to us unused and unopened. We inspect and return the blood to inventory storage according to our SOPs for the next trauma.

Cont'd on following page

Emergency Release of Blood – Physician Signature

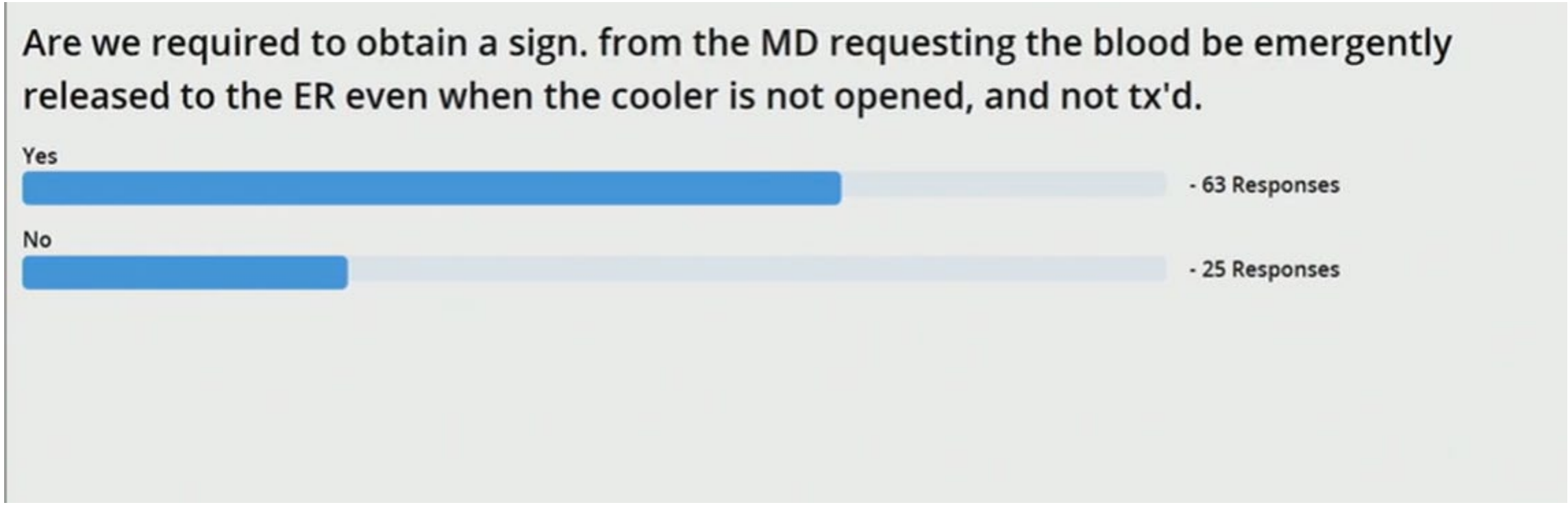
(cont'd)

AUDIENCE RESPONSE

Question 17: Are we required to obtain a signature from the physician requesting the blood be emergently released (sent) to the ER even when the cooler is not opened, and the blood is not transfused?

Emergency Release of Blood – Physician Signature

(cont'd)



Emergency Release of Blood – Physician Signature

(cont'd)

FDA/OBRR Response Q17:

"FDA regulations for compatibility testing require procedures to expedite transfusions in life threatening situations, including a physician's signature documenting the emergency action (21 CFR 606.151 (e)). You must maintain records on the emergency release of blood, including the signature of the requesting physician, which can be obtained before or after release of the blood product (21 CFR 606.160 (b)(3)(v). While a physician's signature documenting the emergency action may not be necessary if a unit is not transfused, your procedures must clearly describe situations when this signature will not be obtained and how you will record the disposition of a unit that was not transfused."

Blood Group Labeling

Background: 21 CFR 640.5 ***Testing the blood*** states:

"All laboratory tests shall be made on a specimen of blood taken from the donor, and these tests shall include the following:

(a) [Reserved]

(b) ***Determination of blood group.*** *Each container of Whole Blood shall be classified as to ABO blood group. At least two blood group tests shall be made and the unit shall not be issued until grouping tests by different methods or with different lots of antiserums are in agreement. Only those Anti-A and Anti-B Blood Grouping Reagents licensed under, or that otherwise meet the requirements of, the regulations of this subchapter shall be used, and the technique used shall be that for which the serum is specifically designed to be effective."*

Cont'd on following page

Blood Group Labeling *(cont'd)*

Assuming results are in agreement, please provide further clarification of what would represent two tests and/or two different methods.

Question 18: Would testing the donor red blood cells with licensed anti-A and anti-B reagents (forward type) and testing the donor plasma/serum with A1 and B cells (reverse type) constitute two different methods and be compliant?

FDA/OBRR Response Q18:

"Yes. Performing a "forward type" with licensed antisera and a "reverse" type with licensed A and B cells would fulfill the requirement in 21 CFR 640.5(b)."

Blood Group Labeling *(cont'd)*

Question 19: Would testing the donor red blood cells with licensed anti-A and Anti-B reagents by an automated method and testing the donor red blood cells with the same reagents/lot #s by a different technology, e.g., tube testing, constitute two different methods and be compliant?

FDA/OBRR Response Q19:

"FDAs' current consideration and the general practice is that you perform a forward type and reverse type with licensed reagents antisera. Blood establishments that wish to use a different approach should contact FDA with their specific questions."

Directed Donation – Not Medically Necessary

Background: In Oct 2023, FDA issued a Safety and Availability communication titled, "Important Information About Directed Blood Donations That Are Not Medically Indicated." It stated:

> *"Directed blood donations requested for certain donor characteristics (e.g., vaccination status, sex, sexual orientation, religion) lack scientific support … There is no evidence that directed donation provides safer blood … Studies suggest that directed donations may carry greater risk of transmitting infectious diseases than the general blood supply."*

The information cautioned against commercial "membership" sites that promise "COVID-19 unvaccinated" donor blood, making clear that labeling or segregating blood based on vaccination status is misleading and not medically justifiable. The agency advised against accepting directed donations based on donor characteristics—such as COVID-19 vaccination status—due to a lack of scientific basis.

Cont'd on following page

Directed Donation – Not Medically Necessary *(cont'd)*

Question 20: Does FDA plan additional education measures to ensure consistent compliance across all collection centers?

FDA/OBRR Response Q20:

"No, FDA is not currently planning additional educational activities on this topic. We expect blood establishments to comply with applicable regulations regarding the manufacture of blood and blood components, including the prohibition against false or misleading labeling."

FDA Responses cont'd on following page

Directed Donation – Not Medically Necessary *(cont'd)*

Question 21: What framework does FDA use to reconcile patient-centered decision making with the need to maintain public health integrity?

FDA/OBRR Response Q21:

"There hasn't been a need for such a general framework. Donors can request their own directed donors, for whatever reason, and it is not always appropriate to allow directed donation (e.g., donor ineligibility, wrong blood type). It isn't clear how this will threaten public health integrity or blood availability.

But this question might be a legal one related to the various legislative efforts in states to facilitate patient centered decision making and seeking to restrict or dictate the use of blood products based on donors' COVID-19 vaccination status.

FDA Response cont'd on following page

Directed Donation – Not Medically Necessary *(cont'd)*

From a practical perspective, there is currently no assay that can determine a donor's COVID-19 vaccination status or discern which vaccine they received.

From a high-level perspective, federal law would generally preempt state law that is in conflict with federal requirements, including FDA's regulations, particularly as related to interstate commerce. Each state or local legislative proposal would need to be considered individually on how it relates to existing federal law and regulations. We will continue to monitor these developments."

Ask the FDA Transcripts

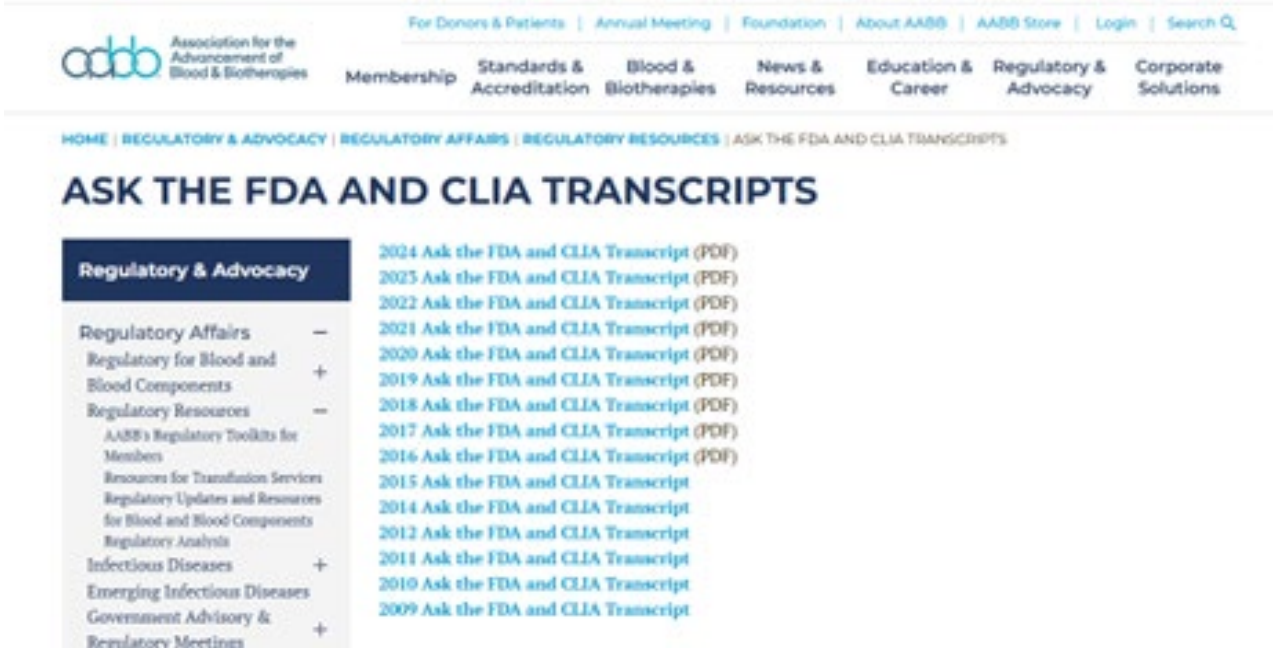
Background: We greatly appreciate FDA's willingness to participate and answer our questions in this public setting. It is our understanding that FDA's responses to the questions serve as an official public record and provide "FDA's current thinking". The Ask the FDA Transcripts posted on AABB's website are a great way to reference these official records.

We recently underwent an FDA inspection and were cited for not being in compliance with a regulation.

Cont'd on following page

Ask the FDA Transcripts *(cont'd)*

Question 22: During an FDA onsite inspection, is it appropriate to cite an Ask the FDA Transcript in support of our position?



Cont'd on following page

Ask the FDA Transcripts *(cont'd)*

FDA/OBRR Response Q22:

FDA's requirements and recommendations are in the CFR and guidance documents, respectively. Ask the FDA transcripts are not requirements or recommendations. Ask the FDA transcripts represent informal FDA communications that are often tailored to specific scenarios described by the questioner which can differ from your circumstances. Additionally, the information provided may be subject to change as FDA policy develops or as new information becomes available to the agency.

Ask the FDA

Office of Therapeutic Products

FDA.gov

Is it Minimally Manipulated? – Examples are helpful *(cont'd)*

Background: In the FDA 2020 guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, page 16, paragraph (c) describes an HCT/P derived from cord blood that is "*generally considered more than minimally manipulated" as a result of processing that alters "the cells' relevant biological characteristics of multipotency and capacity for self-renewal"* :

Cont'd on following page

Is it Minimally Manipulated? – Examples are helpful *(cont'd)*

"(c) A manufacturer of a placental/umbilical cord blood product performs cell selection and incubates the selected cells in a laboratory vessel containing culture media and growth factors to achieve large numbers of cells capable of long-term repopulation of the bone marrow. ***This HCT/P derived from cord blood would generally be considered more than minimally manipulated because the processing affects*** *the production of intracellular or cell-surface proteins and other markers of cell lineage, activation state, and proliferation****, thereby altering the cells' relevant biological characteristics of multipotency and capacity for self-renewal.****"*

Cont'd on following page

Is it Minimally Manipulated? – Examples are helpful *(cont'd)*

Queston 1: We have a question about (c) quoted from page 16 of the 2020 Guidance, stating "*This HCT/P derived from cord blood would* ***generally be considered more than minimally manipulated****…"* which suggests that there might be some circumstances when an **HCT/P derived from cord blood might not be considered "more than minimally manipulated**." Under what circumstances would an HCT/P derived from cord blood be considered minimally manipulated vs more than minimally manipulated?

FDA/OTP Response Q1:

"Thank you for your question regarding Example 16-1(c) in the 2020 guidance document. This example explains, in general, the criterion of more than minimal manipulation for hematopoietic stem/progenitor cells, whose relevant biological characteristics include their ability to repopulate bone marrow through self-renewal and differentiating along myeloid and lymphoid cell lines. Considerations for minimal manipulation depend on the manufacturing process and must be evaluated individually."

Is it Minimally Manipulated? – Examples are helpful

Background: 21 CFR 1271.3(f) provides the definition of minimal manipulation:

"***Minimal manipulation*** *means:*

(1) ***For structural tissue, processing that does not alter*** *the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement; and*

(2) ***For cells or nonstructural tissues, processing that does not alter*** *the relevant biological characteristics of cells or tissues."*

Cont'd on following page

Is it Minimally Manipulated? – Examples are helpful *(cont'd)*

Question 2: As we try to verify our understanding 1271.3(f), can you please provide some examples that are captured in 1271.3(f)(1) and (f)(2) to help us visualize the differences?

FDA/OTP Response Q2:

"Several examples of minimal manipulation for both structural and nonstructural tissues are provided in the guidance document titled *Regulatory Considerations for Human Cells, Tissue, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, published in July 2020, which is available on the FDA Tissue Guidances website."

Leukapheresis Starting Material - Donor Eligibility

Background: As outlined in the FDA's 2024 Guidance, *Considerations for the Development of Chimeric Antigen Receptor (CAR) T Cell Products*, donor eligibility for leukocytes collected via apheresis must comply with 21 CFR Part 1271. The guidance, Section IV, B. Collection, Handling, and Testing of Cellular Starting Material page 7 states:

> *"Collection of the leukapheresis starting material should be conducted in accordance with the regulations in 21 CFR part 1271. Autologous leukapheresis starting material does not require a donor eligibility determination (21 CFR 1271.90(a)(1) and Ref. 20), but you may consider a risk-based approach for screening or testing (Ref. 3).*

Cont'd on following page

Leukapheresis Starting Material - Donor Eligibility (cont'd)

> ***Allogeneic leukapheresis starting material, on the other hand, does require a donor eligibility determination****, including screening and testing for relevant communicable disease agents and diseases (21 CFR part 1271, Subpart C).*"

Our blood collection facility intends to collect apheresis leukocytes (leukopacks) and/or other blood-derived biologics as starting material **under agreement for further manufacture of HCT/P products (e.g., CAR T cells) *and other biological products*.**

Cont'd on following page

Leukapheresis Starting Material - Donor Eligibility (cont'd)

Question 3: Please clarify if we use the HCT/P DHQ or the Blood DHQ for donor eligibility determination for allogeneic donors when collecting blood-derived cellular materials intended as starting material for HCT/P manufacturing?

FDA/OTP Response Q3:

"Starting materials for HCT/P manufacturing are considered HCT/Ps and must comply with the regulations described in 21 CFR part 1271. The 21 CFR part 1271 regulations do not prescribe specific questionnaires that establishments must use to perform donor eligibility related activities. It is the establishment's responsibility to ensure that the donor medical history interview questionnaire they use complies with the regulations applicable to the products they manufacture."

Leukapheresis Starting Material - Donor Eligibility (cont'd)

Question 4: For acellular components of blood collected as starting material for biologics that are not classified as HCT/Ps, should donor eligibility be assessed using the Blood DHQ under the criteria for "blood products" outlined in 21 CFR Part 630, or does 21 CFR Part 1271 still apply?

FDA/OTP Response Q4:

"The information provided is insufficient for us to provide a response. It is unclear what acellular components the question is referring to.

We suggest submitting the question with more detail about the acellular components to the Office of Communication, Outreach, and Development (OCOD) at Industry.Biologics@fda.hhs.gov, where our subject matter experts can provide a response to your specific question."

Leukapheresis Starting Material - Donor Eligibility (cont'd)

Question 5: Are there circumstances under which the FDA-approved AABB Blood Donor History Questionnaire (DHQ) would be considered sufficient to meet donor eligibility requirements for blood-derived cellular materials (e.g., leukopacks or apheresis leukocytes) used in the manufacture of HCT/Ps?

FDA/OTP Response Q5:

"The 21 CFR part 1271 regulations do not prescribe a specific questionnaire that establishments must use to perform donor eligibility related activities. The acceptability of any donor history questionnaire depends on whether it comprehensively captures all the information required by 21 CFR part 1271."

Manufacturing Agreements and Deviation Reporting under IND

Background: Based on our understanding of 21 CFR 600.14 and 21 CFR 606.171, FDA does not require reporting for biologic deviations involving products manufactured under an Investigational New Drug (IND) application.

We manufacture unrelated allogeneic stem cell products under an agreement with the supplier who has an FDA-approved IND. A deviation occurred at our facility during manufacturing.

Question 6: Are we obligated to notify the IND holder if a deviation occurs in our facility during manufacturing processes under the supplier's IND, given that the IND holder is not required to report a deviation under 21 CFR 600.14 and 21 CFR 606.171?

Manufacturing Agreements and Deviation Reporting under IND

FDA/OTP Response Q6:

"You should notify the IND sponsor of manufacturing deviations. Manufacturing deviations should be investigated to identify root cause, and appropriate corrective actions should be taken to avoid repeat occurrences in the future. Appropriate change control procedures should be in place to manage risk associated with these corrective actions. IND sponsors should provide a description of the risk management and change control procedures for how to address manufacturing deviations in their IND. Therefore, your reporting of manufacturing deviations could be important for the IND sponsor to understand if anything needs to be adjusted to their manufacturing process to maintain their drug product quality due to potential difference in the starting or source material."

Ask CMS/CLIA

CMS.gov

CMS Final Rule

Background: On December 28, 2024, the Centers for Medicare & Medicaid Services (CMS) final rule became effective, updating laboratory personnel requirements under Subpart M of the Clinical Laboratory Improvement Amendments (CLIA) for the first time since 1992.

The CLIA 42 CFR 493.1405(b) qualifications Standard; Laboratory Director (LD) qualifications for a nonwaived/Moderate Complexity testing lab on/after Dec 24, 2024, include:

Cont'd on following page

CMS Final Rule (cont'd)

"(5)(i)

(A) Have earned a bachelor's degree in a chemical, biological, clinical or medical laboratory science or medical technology from an accredited institution; or

(B) At least 120 semester hours, or equivalent, from an accredited institution that, at a minimum, includes either—...

(ii) Have at least 2 years of laboratory training or experience, or both, in nonwaived testing; and

(iii) Have at least 2 years of supervisory laboratory experience in nonwaived testing; and

(iv) Have at least 20 CE credit hours in laboratory practice that cover the director responsibilities defined in § 493.1407."

Cont'd on following page

CMS Final Rule (cont'd)

Question 1: Does the employment summary (iii) of supervised testing experience determine the moderate complexity testing (analytes) that can be performed in the laboratory under the directorship of an LD with a bachelor's degree?

CMS Response Q1:

"The 2 years of experience for a laboratory director with a bachelor's degree does not dictate what analytes can be performed in the laboratory."

Question 2: Does it change with a PhD in clinical laboratory science?

CMS Response Q2:

"The 1 year of experience for a PhD in clinical laboratory science does not dictate what analytes can be performed in the laboratory."

Competency Assessment

Background: The 2025 CLIA Assessing Personnel Competency brochure, page 3 states:

> *"If the laboratory acquires new analyzers or changes methodology, testing personnel should be trained and competent before reporting patient results."*

The laboratory:

- Implements a new high complexity test system, including new instrumentation with new methodology (not just a new analyte on current instrument).

The laboratory trains all staff on the new test system.

Cont'd on following page

Competency Assessment (cont'd)

Question 3: Does the laboratory need to assess the competency of the staff, using the 6 elements a second time in the first year of the test system implementation and then annually thereafter?

CMS Response Q3:

"Yes, for all testing personnel trained on a new test system (whether the employee is new or the test system is new), competency must be assessed twice in the first year."

Competency Assessment (cont'd)

Background: 42 CFR 493.1451(b)(8)(9) describe the requirements for Competency Assessment:

(b) The technical supervisor is responsible for—
(8) Evaluating the competency of all testing personnel and assuring that the staff maintain their competency to perform test procedures and report test results promptly, accurately and proficiently. The procedures for evaluation of the competency of the staff must include, but are not limited to—
(i) Direct observations of routine patient test performance, including patient preparation, if applicable, specimen handling, processing and testing;
(ii) Monitoring the recording and reporting of test results;
(iii) Review of intermediate test results or worksheets, quality control records, proficiency testing results, and preventive maintenance records;
(iv) Direct observation of performance of instrument maintenance and function checks;
(v) Assessment of test performance through testing previously analyzed specimens, internal blind testing samples or external proficiency testing samples; and
(vi) Assessment of problem solving skills; and

Cont'd on following page

Competency Assessment (cont'd)

(9) Evaluating and documenting the performance of individuals responsible for high complexity testing at least semiannually during the first year the individual tests patient specimens. Thereafter, evaluations must be performed at least annually unless test methodology or instrumentation changes, in which case, prior to reporting patient test results, the individual's performance must be reevaluated to include the use of the new test methodology or instrumentation.

The regulation does not specify what qualifies as "documentation" of competency assessment.

Question 4: Please clarify with an example, if possible, what would CMS consider acceptable documentation. Is a spreadsheet with dates and references for each element for each test method acceptable? Or would it need to be more granular/in depth with checklists for each test method with critical steps outlined, initialed and dated, etc.?

Cont'd on following page

Competency Assessment (cont'd)

CMS Response Q4:

"Competency assessment documentation must include who performed the competency assessment and the date each item (I through vi) is assessed."

Quality Control Testing (cont'd)

Background: 42 CFR 493.1256(d)(3)(iii) requires:

(3) At least once each day patient specimens are assayed or examined perform the following for—

...

(iii) Test procedures producing graded or titered results, include a negative control material and a control material with graded or titered reactivity, respectively;

...

Question 5: To meet this requirement, do high-titer low-avidity antibodies also need controls if titered as part of an antibody identification?

Cont'd on following page

Quality Control Testing (cont'd)

CMS Response 5:

"Yes. The reagents used to test titers are subject to the CLIA control requirements.

The regulation at 42 CFR §493.1256(h) states, "If control materials are not available, the laboratory must have an alternative mechanism to detect immediate errors and monitor test system performance over time. The performance of alternative control procedures must be documented." Ultimately, it is the laboratory's responsibility to meet the requirements at 42 CFR §493.1256 by performing and documenting QC or alternative control procedures.

Several types of titers are commonly performed in blood banks, including prenatal antibody titers, cold agglutinin titers, and high-titer low-avidity antibody titers. These titers are typically performed using textbook procedures, and a laboratory's written policies and procedures should reference the publication from which the procedure was obtained. The textbook or publication may provide recommendations for quality control."

Quality Control Testing (cont'd)

Background: Referring specifically to the requirements of 42 CFR 493.1256(d)(3)(iii) listed above:

Question 6: Does performing testing with one antigen-positive cell and one antigen-negative cell for the antibody to be titered satisfy the requirement for titer controls—on the basis that the antigen-positive cell demonstrates reactivity of the titered antibody and the antigen-negative cell shows no reactivity?

CMS Response Q6:
"No, this would not satisfy the requirement as the control test would not produce a titered reactivity."

Cont'd on following page

Quality Control Testing (cont'd)

Question 7: For titration testing in which no prior patient sample is available for parallel testing, would performing duplicate testing of the same sample by the same technologist be sufficient?

CMS Response Q7:
"No, this would not be sufficient as the sample serving as the control would not have a known reactivity."

Question 8: Is the daily testing of non-diluted anti-A and anti-B reagents with corresponding A and B cells sufficient to meet these control requirements?

CMS Response Q8:
"No, this would not satisfy the requirement as the control test would not produce a titered reactivity."

Cont'd on following page

Quality Control Testing (cont'd)

Question 9: For control testing of low-titer whole blood, would preparing a single dilution of anti-A and anti-B, tested with A and B cells to demonstrate the expected positive and negative reactivity during titration—irrespective of the endpoint—be sufficient?

CMS Response Q9:

"Yes, this would meet the intent of the regulation for a negative control material and a control material with graded or titered reactivity."

Equipment Verification

Background: 42 CFR 493.1252(b) describes the requirement for the verification of performance specifications:

(1) Verification of performance specifications. Each laboratory that introduces an unmodified, FDA-cleared or approved test system must do the following before reporting patient test results:

(i) Demonstrate that it can obtain performance specifications comparable to those established by the manufacturer for the following performance characteristics:

(A) Accuracy.

(B) Precision.

(C) Reportable range of test results for the test system.

(ii) Verify that the manufacturer's reference intervals (normal values) are appropriate for the laboratory's patient population."

Cont'd on following page

Equipment Verification (cont'd)

With respect to antibody panels, some Transfusion Services are performing equipment verifications across methodologies (i.e. testing type and screen in gel and tube testing). It is difficult getting the same donor for each of the cells in the panel between methodologies because a solid phase panel for the instrument probably is a different set of cells. It is next to impossible to "bake" exact cell populations into solid phase as prepared in suspensions to compare apples to apples.

Question 10: Is verifying the type and screen adequate when performing verifications across methodologies or do antibody panels need to be tested as well?

CMS Response Q10:

"Antibody panels need to be tested as well."

Questions

Thank You!

Contact AABB's Regulatory Staff at

regulatory@aabb.org