

**AABB
VIRTUAL**
2021 OCT
17-19

WELCOME

Ask the FDA and CMS/CLIA

2021 AABB Virtual Annual Meeting

October 17-19, 2021



Faculty Disclosure

*In compliance with ACCME policy,
AABB requires the following
disclosures to the session audience*

The following Regulatory Affairs Staff have no financial disclosures:

Senior Director:

- Sharon Carayiannis, MT(ASCP)HP

Director:

- Karen Palmer, MT(ASCP), CQA(ASQ)

If you have questions following this session, please contact us:
regulatory@aabb.org



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 (CMS)

And thank you to our colleague, Arnold McKinnon, for proofreading our slides every year!

Our FDA Attendees:

The following speakers have no financial disclosures:

Michelle Gutierrez, BS, MT(AMT), Consumer Safety Officer (CSO)
Center for Biologics Evaluation and Research (CBER), Office of Blood
Research and Review (OBRR) Division of Blood Components and Devices
(DBCD), Blood and Plasma Branch (BPB)

Christopher Cox, BS, Biology, CSO
CBER, OBRR, DBCD, BPB

Sharon O'Callaghan, CSO
CBER, Office of Compliance and Biologics Quality (OCBQ), Division of
Inspections and Surveillance, Program Surveillance Branch

Our FDA OTAT Participant:

Hanh Khuu, MD, Office of Tissues and Advanced Therapies (OTAT)



Our CMS Participants:

Daralyn Hassan, M.S., MT(ASCP), Medical Technologist
Center for Clinical Standards and Quality (CCSQ), Quality,
Safety & Oversight Group (QSOG), Division of Clinical
Laboratory Improvement and Quality (DCLIQ)

Mary L. Hasan, MPA, MT (ASCP), Clinical Laboratory Scientist
CCSQ, QSOG, DCLIQ

Jelani R. Sanaa ([She/Her](#)), MS, MLS(ASCP)^{CM}SBB^{CM}, SH^{CM}, Clinical
Laboratory Scientist
CCSQ, QSOG, DCLIQ



Questions and responses will be posted in the slide deck following the meeting and can be found on the AABB web page, [Ask the FDA and CLIA Transcripts:](#)

The screenshot shows a web browser window displaying the AABB website. At the top, a dark purple banner reads: "Blood donations are urgently needed now to ensure blood is available for patients in need. [Make an appointment to donate now.](#)" Below this is the AABB logo and a navigation bar with links: "For Donors & Patients", "Annual Meeting", "National Blood Foundation", "AABB Store", "Login", and "Search". A secondary navigation bar includes: "Membership", "Standards & Accreditation", "News & Resources", "Education", "Regulatory & Advocacy", "About AABB", and "Get Involved". The main content area is titled "ASK THE FDA AND CLIA TRANSCRIPTS" and lists transcripts from 2009 to 2020, each with a PDF icon. A left sidebar menu is open, showing "Regulatory & Advocacy" selected, with sub-items: "Regulatory Affairs", "Regulatory for Blood and Blood Components", and "Regulatory Resources". A right sidebar menu is also open, showing "Regulatory Affairs" selected, with sub-items: "Regulatory for Blood and Blood Components", "Regulatory Resources", "Infectious Diseases", "Government Advisory & Regulatory Meetings", and "Regulatory for Cellular Therapies". Below this is an "Advocacy" section with sub-items: "Advocacy Agenda", "Comments to FDA", "Blood Sustainability", "Patient & Donor Safety", and "Cellular Therapies & Biotherapies". The Windows taskbar at the bottom shows the date as 8/19/2021 and the time as 9:32 AM.

Look for the AABB Weekly Report:

Our announcement that these slides and agency responses have been posted on the AABB website in November.

Sent to your INBOX every Wednesday!



To find Regulatory Content on our Website:

The screenshot shows a web browser window with the URL [aabb.org/home](https://www.aabb.org/home). The website header includes the AABB logo and navigation links: For Donors & Patients, Annual Meeting, National Blood Foundation, AABB Store, Login, and Search. The main navigation menu includes: Membership, Standards & Accreditation, News & Resources, Education, Regulatory & Advocacy (highlighted), About AABB, and Get Involved. A dropdown menu for Regulatory & Advocacy is open, listing the following items:

- Regulatory Affairs
 - Regulatory for Blood and Blood Components
 - Regulatory Resources
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 - Government Advisory & Regulatory Meetings
 - Regulatory for Cellular Therapies
- Advocacy
 - Advocacy Agenda
 - Comments to FDA
 - Blood Sustainability
 - Patient & Donor Safety
 - Cellular Therapies & Biotherapies
 - Coverage & Reimbursement

A red arrow points to the 'Regulatory Resources' link in the dropdown menu. The background of the page features a banner with the text 'Be a Part of the AABB Community' and a 'LEARN MORE' button. The URL bar at the bottom shows <https://www.aabb.org/regulatory-and-advocacy>.



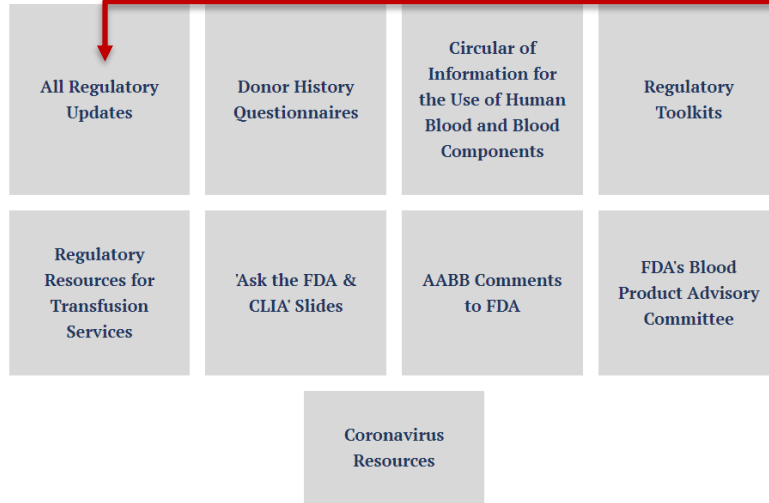
REGULATORY RESOURCES

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 - Regulatory Resources for Transfusion Services
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- Advocacy +

COVID-19 Resources for Blood Donor Centers

Developed with input from federal regulators, AABB's regulatory resources are clear, user-friendly tools that help blood centers and transfusion services protect donor and patient safety at each step in the transfusion chain.





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| REGULATORY UPDATES AND RESOURCES FOR BLOOD AND BLOOD COMPONENTS

REGULATORY UPDATES AND RESOURCES FOR BLOOD AND BLOOD COMPONENTS

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Toolkits Developed Exclusively for AABB Members, Including:

- [2021 Regulatory Updates Toolkit](#) - a searchable pdf of all Regulatory articles from *Weekly Report*
- [Regulatory Updates 2019-2020](#)



The best Tool EVER!

Recent Regulatory Newsfeed

REGULATORY UPDATE: Status of Cold-Stored Platelets and the Next Circular

08/04/2021

AABB requested a clarification from the Food and Drug Administration to address recurring member questions regarding the agency's approval of variance requests under 21 CFR 640.120 for cold-stored platelets (CSP).

REGULATORY UPDATE: FDA Updates List of Variance Approvals

08/02/2021

The Food and Drug Administration's Center for Biologics Evaluation and Research (CBER) recently updated its list of exceptions and alternative procedures approved under 21 CFR 640.120.

REGULATORY UPDATE: FDA Authorizes Imported Becton Dickinson Sodium Citrate/Light Blue Top Tubes Due to Shortage

07/23/2021

The Food and Drug Administration determined that, "due to an increase in demand and recent vendor supply challenges, there is a shortage of the sodium citrate (light blue top) tubes at this time."

REGULATORY UPDATE: FDA Issues Required Labeling Changes for Hydroxyethyl Starch Products

07/23/2021





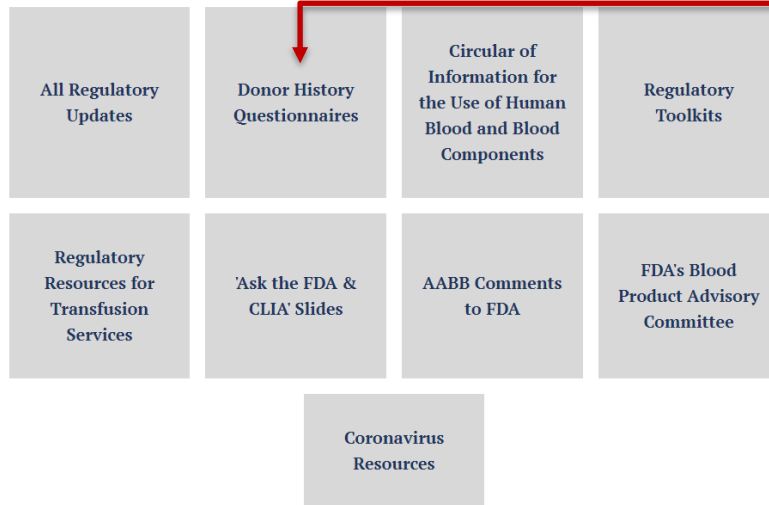
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Donor History Questionnaires x +

aabb.org/news-resources/resources/donor-history-questionnaires

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DONOR HISTORY QUESTIONNAIRES

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 - Patient Blood Management +
 - Hemovigilance +
 - Clinical Resources
 - Association Bulletins
 - Circular of Information
 - Donor History

Summary: Donation of CCP, Blood Components and HCT/Ps, Including Information on COVID-19 Vaccines or Treatment with CCP or Monoclonals (updated 04/14/21)

This section contains information on questionnaires used to screen prospective donors and help ensure the safety of the donation process as well as the product being donated. AABB has played a leadership role in the development of model questionnaires for blood collection facilities as well as for facilities involved in the collection of hematopoietic progenitor cells (HPCs).

- [Blood Donor History Questionnaires, v2.1](#)
 - [Evaluating Donors for Risk of Ebola Virus Infection](#)
- [HPC, Apheresis and Marrow Donor History Questionnaire](#)
- [HPC, Cord Blood Donor History Questionnaire](#)

BLOOD DONOR HISTORY QUESTIONNAIRES

News & Resources

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Evaluating Donors for Risk of Ebola Virus Infection	
Hematopoietic Progenitor Cell, Apheresis and Marrow Donor History Questionnaire	
Hematopoietic Progenitor Cell, Cord Blood Donor History Questionnaire	
Billing Guide	
Job Board	

The volunteer member experts of the [Donor History Task Force](#), in collaboration with AABB's Regulatory Affairs staff, have developed the current Blood Donor History Questionnaire(s) (DHQs) and Related Materials to provide a system:

- That is submitted by AABB Regulatory Affairs for FDA review as an acceptable mechanism for collecting blood donor history information from donors of blood and blood components that is consistent with the FDA requirements and recommendations. [[21 CFR 630.10](#)] and [AABB Standards](#).
- That is posted on the AABB website and where it remains publicly available, along with the [DHQ v2.1 Implementation Toolkit](#).
- That may be reported by licensed manufacturers as a minor change in a facility's annual report to FDA under [§601.12\(d\)](#) *if implemented as accepted by FDA* (refer to the Implementation section of the guidance)

On 05/05/2020, the [FDA formally recognized the v2.1 DHQ](#) and Related Materials as acceptable for use. **Blood collection establishments are responsible for:**

- Reviewing the [guidance](#) to ensure compliance with FDA's recommendations, and reporting and implementation requirements.
- Reviewing the [DHQ User Brochure](#) for detailed instructions on the limitations and appropriate use of AABB's FDA-recognized DHQ(s) (for example, adding questions, reformatting materials).
- Reporting the implementation of AABB's DHQ and related documents as a minor change in the Annual Report [[§601.12\(d\)](#)] to FDA when **implemented as accepted by FDA** and without modifications of the version v2.1 documents posted by AABB.
- Compliance with additional FDA requirements under [§601.12](#), as noted in the [guidance](#), for licensed blood establishments **implementing a modified version** of the FDA accepted v2.1 DHQ materials, such as submission of a PAS [[§601.12\(b\)](#)] for FDA approval prior to implementation of major changes.

Please don't hesitate to send your questions regarding the v2.1 documents to Regulatory Affairs at





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[COVID-19 Resources](#) for Blood Donor Centers

Developed with input from federal regulators, AABB's regulatory resources are clear, user-friendly tools that help blood centers and transfusion services protect donor and patient safety at each step in the transfusion chain.

All Regulatory Updates	Donor History Questionnaires	Circular of Information for the Use of Human Blood and Blood Components	Regulatory Toolkits
Regulatory Resources for Transfusion Services	'Ask the FDA & CLIA' Slides	AABB Comments to FDA	FDA's Blood Product Advisory Committee
Coronavirus Resources			



← → aabb.org/news-resources/resources/circular-of-information

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CIRCULAR OF INFORMATION FOR THE USE OF HUMAN BLOOD AND BLOOD COMPONENTS

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This webpage provides the background information for compliance with FDA requirements under [21 CFR 606.122](#) for a *Circular of Information* (the *Circular*), including information on purchase options, implementation, and updated language. AABB encourages you to review the information for important changes.

Please contact Regulatory Affairs with your questions at regulatory@aabb.org.

Proper Use of the *Circular*

The *Circular* was designed as an extension of container labeling to provide specific instructions for the administration and use of blood and blood components intended for transfusion (as required in [§606.122](#)). The *Circular* must be available for review by Transfusion Services, prescribing physicians, and staff anywhere blood is issued or transfused. If the environment includes blood transfusion, the *Circular* should be available.

The [User Guide for the Circular](#) provides blood collection establishments, transfusion services and clinical staff with information to supplement their understanding of the regulatory responsibilities for implementation and use of the *Circular*. The [User Guide](#) also provides information about the electronic version of the *Circular* (e*Circular* provided in USB format to blood manufacturers).

Purchase

Please visit the [AABB Store](#) to order the current *Circular of Information for the Use of Human Blood and Blood Components*, dated October 2017, as a [brochure](#) or [brochure/electronic bundle](#).

View Posted Version

AABB has made the *Circular* publicly available for [review \(as a pdf document\)](#) to ensure access to the content. This nested watermarked version may not be copied, printed or used as the extension of labelling.



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Coronavirus Resources



AABB's Regulatory Toolkits for Members

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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.

- [Toolkit for Transfusion Services: FDA Registration Requirements when Extending Platelet Expiration to Day-6 or Day-7 - June 23, 2021](#)
- [Toolkit: Checklist for Biologics License Application \(BLA\) for Platelets, Leukocytes Reduced Collected by Apheresis - June 30, 2021](#)
- [Toolkit: Spanish Translation of Blood Donor Screening Tools: Examples to Consider - June 30, 2021](#)
- [Regulatory Resources for Transfusion Services](#)
- [2021 Regulatory Updates Toolkit](#)
- [Toolkit for December 2020 Syphilis Guidance - December 9, 2020](#)
- [Toolkit for COVID-19 Convalescent Plasma under Emergency Use Authorization - April 14, 2021](#)
- [Live with FDA on the CCP Regulatory Landscape - October 28, 2020](#)
- [Toolkit: Compliance Options for Implementation of FDA's August 2020 HIV Risk Guidance - October 16, 2020](#)
- [DHQ v2.1 Implementation Toolkit - May 5, 2020](#)
- [HCV Further Testing Toolkit - November 2019](#)
- [Babesia Toolkit - September 2019](#)
- [AABB Checklist for Historic Antigen Labeling - January 2019](#)
- [User Guide for the Circular - September 2018](#)

Related News



AABB Regulatory Affairs Introduction [slides 2-17]

AABB/Regulatory Affairs Sharon Carayiannis:

“We will remind you, if you have any questions following this session, or really at any time, you can reach out to directly to us by email to regulatory@aabb.org. Our objectives today are to evaluate existing practices to establish alignment with current regulatory requirements and recommendations, to apply FDA recommendations in recently issued guidance, and to describe FDA’s approach to policies, regulations, and inspection programs related to products regulated by CBER.

Thank you so much for the important work you do. We stay amazed at your commitment to patients. Karen and I remember all too well what it’s like to be in your shoes and the difficult work that you do everyday for patients. We are so impressed by what we’ve seen you achieve under the most adverse circumstances for over a

AABB Regulatory Affairs Introduction [slides 2-17] (cont'd)

AABB/Regulatory Affairs Sharon Carayiannis: (cont'd)

year and a half. So, we want to recognize you and thank you at the beginning of our session for all that you've done.

We certainly appreciate the AABB members who submitted questions that make this session possible. We also appreciate the continued support of FDA and CMS who put a lot of work into making this such a successful session. And, of course, we always like to thank our colleague Arnold McKinnon for proofreading our slides every year and for every other thing he does over the course of the year to support us as we try to support you.

We have three FDA attendees today. We'll begin with the first two, Michelle Gutierrez and Christopher Cox. Both Michelle and Chris are consumer safety officers in the



AABB Regulatory Affairs Introduction [slides 2-17] (cont'd)

AABB/Regulatory Affairs Sharon Carayiannis: (cont'd)

Blood and Plasma Branch of the Division of Blood Components and Devices within the Office of Blood Research and Review at CBER. Thank you so much Michelle and Chris for being with us today. And we have Sharon O'Callaghan who comes to us from the Office of Compliance and Biologics Quality. Sharon is in the Program Surveillance Branch of the Division of Inspections and Surveillance. Thank you, Sharon, for supporting this session and many other sessions that you have in years past.

We did get several questions for CLIA and will have CMS responses posted in the slide deck on the AABB website at 'Ask the FDA and CLIA Transcripts'. Look for the AABB Weekly Report. We're going to announce when these slides are posted. We expect it to be in November. You should get the Weekly Report in your inbox every

AABB Regulatory Affairs Introduction [slides 2-17] (cont'd)

AABB/Regulatory Affairs Sharon Carayiannis: (cont'd)

Wednesday. If you're not receiving this, please let us know. There's important information and we want to make sure that you're receiving it every week.

Because we so often hear that people never realize that we have so much regulatory content posted on the AABB website, we're going to make a quick run through one of our regulatory pages, the 'Regulatory Resource' page. Beginning with the 'All Regulatory Updates', you can see our regulatory newsfeed and you can also see what we think are two kind of golden nuggets that we developed for AABB members. The first bullet is the '[2021 Regulatory Updates Toolkit](#)' which is a searchable PDF with all of the regulatory updates we've published this year, and the second bullet is the very same thing, all '[Regulatory Updates for 2019-2020](#)'. We think that these two documents are very easy to use and will take you to information when you have a



AABB Regulatory Affairs Introduction [slides 2-17] (cont'd)

AABB/Regulatory Affairs Sharon Carayiannis: (cont'd)

question or think you may have missed something along the way. We hope you'll make sure to remember where they are and try to use them whenever you need them.

Of course, the '[Regulatory Resources](#)' page includes the donor history questionnaires. For the purposes of today, we will just look at the 'Blood Donor History Questionnaires' page. The '[Blood Donor History Questionnaires](#)' webpage has all kinds of supporting documents. It has the documents that are used along with the DHQ. It has links to FDA's website and FDA guidance documents and anything else that you would need to implement the questionnaires or if you have questions and need additional understand for staff training, etc.

AABB Regulatory Affairs Introduction [slides 2-17] (cont'd)

AABB/Regulatory Affairs Sharon Carayiannis: (cont'd)

Likewise, the [Circular of Information for Blood and Blood Components](#) also has a webpage with supporting information including a [User Guide for the Circular](#) which helps you understand FDA's expectations for the use of this extension of container labeling. Again, we have a lot of links to important information from FDA all throughout this webpage.

The last thing I'll show you is the '[Regulatory Toolkits](#)' page. This list has gotten longer since we first started creating toolkits. Back in 2019, when FDA issued guidance on *Babesia* testing and HCV further testing, we created flowcharts to help our members visualize how these recommendations would come together to operationalize the information in the guidance. These toolkits are not ever intended to replace FDA guidance but to supplement your understanding. So, throughout the

AABB Regulatory Affairs Introduction [slides 2-17] (cont'd)

AABB/Regulatory Affairs Sharon Carayiannis: (cont'd)

toolkits, we reference specific pages and specific sections where you can go and read exactly what FDA has said as you're using the toolkit. We are planning to update this page with an additional toolkit related to testing for RTTIs and lookback and reentry as well. We're looking forward to that. That should happen in the next couple of months.

All of us that you see here today were reminiscing just the other day about how this session has such a consistently huge audience, and we really do enjoy seeing all of you. So, we're certainly looking forward to when we'll see you in person again, but until then, we're just really happy that we can continue to bring you this important information from FDA and CMS. And with that, Karen will quick off our questions.”



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Advancing

Ask the FDA

Blood and Blood Components

IRRADIATION – Manufacturers Package Inserts

Background: The 1993 FDA Memorandum, [Recommendations Regarding License Amendments and Procedures for Gamma Irradiation of Blood Products](#), Section III. License Amendments for Irradiation of Blood and Blood Products recommends:

C. RADIATION DOSAGES AND VALIDATION [page 7]

“...The dose of irradiation delivered should be 2500 cGy targeted to the central portion of the container and 1500 cGy should be the minimum dose at any other point.”

E. LABELING [page 8]

“ ...

4. The dating period for red blood cell products (Red Blood Cells, Whole Blood) should be not more than 28 days from the date of irradiation, but otherwise not more than the dating period of the non-irradiated product.”

IRRADIATION – Manufacturers Package Inserts (cont'd)

Note: AABB notes that in order to meet the 2500 centigray (cGy) recommendation, many irradiators target a higher central dose. However, the 1993 Memorandum does not describe a limitation for a maximum central dose of irradiation.

Example: The ALYX Operator's Manual and the package insert of the ALYX 2RBC LR Kit both contain specific directions related to the irradiation and expiration dating of these products when the irradiation dose is 3000 cGy:

Package Insert:

ACD-A/ADSOL Red Cells may be irradiated. If irradiation dose is 3000 cGy, Red Cells should be transfused within 28 days from date of collection.

Operator's Manual:

Note: *There is no restriction on red blood cells irradiated using 2500 cGy. The restriction to 28 days from collection is limited to red blood cells irradiated using 3000 cGy.*

IRRADIATION – Manufacturers Package Inserts (cont'd)

Blood products are routinely irradiated by hospital Transfusion Services. At the time of irradiation, the facility is responsible for relabeling the unit with the new expiration date based on the irradiator central dose. At the time of relabeling with the new expiration, the Transfusion Service has no way to know which platform was used to collect the red blood cells (RBCs), nor that specific FDA required instructions exist in a manufacturer's package insert for the collection set or Operator's Manual.

Question 1: For this example, how are the FDA expectations in this approved package insert/Operator's Manual to be communicated to a Transfusion Service when applicable to manufacturing steps performed after distribution by the collection establishment?

FDA/OBRR Christopher Cox Q1:

“The blood center should communicate with their customers about the components that they provide.”



IRRADIATION - Pathogen Reduced Platelets

Background: As required by [21 Code of Federal Regulations \(CFR\) 606.121\(c\)\(2\)](#), the container label for pathogen reduced apheresis platelets provided by our licensed Blood Supplier includes the license number of the manufacturer:

c) The container label must include the following information, as well as other specialized information as required in this section for specific products:

...

(2) The name, address, unique facility identifier, and, if a licensed product, the license number of each manufacturer;...

Question 2: Our inventory is 100% pathogen reduced apheresis platelets. A staff physician insists on irradiating pathogen reduced apheresis platelets despite education provided by the Transfusion Service medical director and the FDA approved package insert language that pathogen reduced components may serve “*as an alternative to gamma irradiation for*

IRRADIATION - Pathogen Reduced Platelets (cont'd)

prevention of transfusion-associated graft versus host disease.” Please clarify the Transfusion Service’s regulatory responsibilities under these circumstances.

FDA/OBRR Christopher Cox Q2:

“As you noted, the package insert for the processing set used to manufacture Psoralen-treated Apheresis Platelets states that pathogen reduction is an alternative to gamma irradiation for prevention of transfusion-associated GVHD.

FDA would expect the transfusion medicine physician and/or treating physician to make the decision as to whether to irradiate pathogen-reduced blood products to prevent TA-GVHD for a patient.”



IRRADIATION - Pathogen Reduced Platelets (cont'd)

Question 3: Is irradiation of a pathogen reduced apheresis platelet component acceptable and, if so, how is the expiration date determined?

If performed, should the Transfusion Service cross out the license number of the blood collection establishment following irradiation?

FDA/OBRR Christopher Cox Q3:

“If the Transfusion Service decides to irradiate, the expiration date will be the same as a conventional irradiated apheresis platelet unit. If the Transfusion Service is not licensed to irradiate blood products, the FDA license number must be crossed out.”

IRRADIATION - Platelet Bacterial Risk Guidance

Background: The [December 2020 Platelet Bacterial Risk Control guidance](#), Section III.B.2 describes the use of secondary rapid testing of apheresis platelets to extend expiration dating to day 6 and day 7. The guidance states on page 8:

Note: “Bacterial testing to extend dating beyond day 5 and up to day 7 should be performed with devices labeled as safety measure⁶. Platelet storage containers must be cleared or approved by FDA for 7-day storage.”

Example: Our Blood Supplier provides our Transfusion Service with apheresis platelets labeled with a 5-day expiration following primary culture at 36 hours. It is our practice to routinely irradiate several platelets a day to ensure they are readily available for our large oncology service. FDA guidance does not provide recommendations for irradiated platelet components.

IRRADIATION - Platelet Bacterial Risk Guidance (cont'd)

Question 4: Is it acceptable to extend dating of irradiated platelets labeled with a 5-day expiration to day 6 or day 7 using secondary, rapid testing or secondary culture on day 4? Are there additional considerations?



IRRADIATION - Platelet Bacterial Risk Guidance (cont'd)

FDA/OBRR Christopher Cox Q4:

“Yes. The secondary rapid testing and secondary culture performed no sooner than Day 4 applies to apheresis platelets and irradiated apheresis platelets. Both strategies can be used to extend the dating period beyond 5 days.

For platelet products, the dating period is not affected by irradiation.

Additional considerations for labeling: If dating is extended beyond 5 days, the Transfusion Service that performs the secondary testing must update the container label to reflect the new expiration date ([21 CFR 606.121\(c\)\(4\)\(i\)](#)).”

PLATELET BACTERIAL RISK GUIDANCE - FDA Registration

Background: A Transfusion Service currently exempt from [FDA registration and blood product listing](#) under provisions of [21 CFR 607.65\(f\)](#) implements bacterial detection testing to extend expiration dating of apheresis platelet products to day 6 or day 7. As described in the [December 2020 Platelet Bacterial Risk Control guidance](#), Section V. Transfusion Services - Registration and Blood Product Listing, page14:

“...you are no longer considered exempt because you are engaging in blood product manufacturing under [21 CFR 607.3\(d\)](#). You must therefore register your blood establishment with FDA and list the blood products you manufacture, pursuant to [21 CFR 607.7](#). Indicate that you are performing bacterial detection testing on platelet products by selecting ‘Bacterial Testing’ as a process for the platelet products.”



PLATELET BACTERIAL RISK GUIDANCE - FDA Registration (cont'd)

Example: We are a Transfusion Service newly registered to extend platelet dating to day 6 or day 7. We understand the registration requirement necessary to perform this manufacturing step. We do not know how our recent FDA registration changes our regulatory responsibilities and inspections process etc.

Question 5: Are we now subject to FDA inspection of ALL activities including RBC crossmatch, storage and issue, plasma storage and thawing, and pooling or will FDA inspection be limited to bacterial testing of platelets?



PLATELET BACTERIAL RISK GUIDANCE - FDA Registration (cont'd)

FDA/OCBQ Sharon O'Callaghan Q5:

“FDA conducts Current Good Manufacturing Practice (CGMP) inspections on a risk-based schedule.

A firm's registration status is reviewed for active, inactive, and pre-registered establishments according to the CBER Blood Establishment Registration database, and ORA and CBER jointly develop an annual inspection workplan.

The Inspection of Licensed and Unlicensed Blood Banks, Brokers, Reference Laboratories, and Contractors- Compliance Program 7342.001, (<https://www.fda.gov/media/84887/download>), outlines a systems-based approach to conducting a CGMP inspection. It identifies five potential systems in an establishment's operation for inspection. The inspection is a comprehensive evaluation of the critical areas in each system used by the establishment. The program provides three surveillance

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PLATELET BACTERIAL RISK GUIDANCE - FDA Registration (cont'd)

FDA/OCBQ Sharon O'Callaghan Q5: (cont'd)

inspection options (Level 1, Level 2, and Donor Center) and the investigator will inspect each system to the extent necessary to determine whether the establishment complies with all applicable regulations, including [21 CFR Parts 606](#), [610](#), [630](#), and [640](#), and is a comprehensive inspection of all systems employed at the establishment.

While all manufacturing steps associated with blood and blood components are subject to FDA's oversight, the activities referenced in your question fall under the following systems, which would potentially be the focus of an inspection:

- Product Testing Systems that includes properly testing products collected for transfusion or for further manufacture for control of bacterial contamination of platelets consistent with [21 CFR 606.145](#), blood grouping and typing ([21 CFR 640.5](#)), and compatibility testing by serologic or electronic crossmatch ([21 CFR 606.151](#)).

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PLATELET BACTERIAL RISK GUIDANCE - FDA Registration (cont'd)

FDA/OCBQ Sharon O'Callaghan Q5: (cont'd)

- Quarantine/Storage/Disposition System - the system that manages product quarantine, storage, and distribution, and prevents release of unsuitable products.”

PLATELET BACTERIAL RISK GUIDANCE - FDA Registration (cont'd)



Background: We are in the process of completing our FDA registration. The [2020 guidance](#) directs us to select “Bacterial Testing” as our process for the platelet products. The [Blood Establishment Registration Instructions](#) Process Definitions define “Bacterial Testing” as:

“a qualitative immunoassay for the detection of aerobic and anaerobic Gram-positive and Gram-negative bacteria in leukocyte reduced apheresis platelets or pre-storage pools of up to six (6) leukocyte reduced whole blood derived platelets within 24 hours prior to transfusion as a safety measure following testing with a growth-based quality control test cleared by the FDA for platelet components.”

PLATELET BACTERIAL RISK GUIDANCE - FDA Registration (cont'd)

Example: Our Transfusion Service plans to implement secondary culture on day 4 of storage to extend apheresis platelet dating to day 7.

Question 6: Is “Bacterial Testing” the correct process to choose for a culture-based detection method when we complete the [Electronic Blood Establishment Registration and Product Listing process](#) online?

FDA/OBRR Michelle Gutierrez Q6:

“Yes, as explained in our instructions for completing the eBER and Product Listing form which can be accessed through the weblink we will provide to AABB for the transcript: <https://www.fda.gov/vaccines-blood-biologics/biologics-establishment-registration/blood-establishment-registration-and-product-listing>”

PLATELET BACTERIAL RISK GUIDANCE - Labeling with License or Registration Number

Background: [21 CFR 610.60](#) Container Label describes:

- (a) Full label. The following items shall appear on the label affixed to each container of a product capable of bearing a full label:*
- (1) The proper name of the product;*
 - (2) The name, address, and license number of manufacturer;*

Example: We are an FDA registered Transfusion Service that receives licensed apheresis platelets labeled with a 5-day expiration from our Blood Supplier. We have implemented secondary rapid testing to extend apheresis platelet dating to day 6 and day 7.

Question 7: When we extend the expiration date to day 6 or day 7 do we need to cross out the license number of our Blood Supplier and relabel the platelet with our FDA registration number?

PLATELET BACTERIAL RISK GUIDANCE - Labeling with License or Registration Number (cont'd)

FDA/OBRR Michelle Gutierrez Q7:

“Because you are not licensed to perform testing and relabeling of platelet products, you should strike out the US License Number on the original product labels, since they are no longer licensed products. You do not need to add your registration number to the product labels as long as the Apheresis Platelets are used in your facility.”

PLATELET QUALITY CONTROL – Manufacturer Responsibility

Background: For Platelets quality control (QC), [21 CFR 640.25\(b\)](#) General requirements include:

(b) Quality control testing. Each month four units prepared from different donors shall be tested at the end of the storage period as follows:

(1) Platelet count.

(2) pH of not less than 6.2 measured at the storage temperature of the unit.

(3) Measurement of actual plasma volume.

Example: The platelet supplier ships apheresis platelets to a Transfusion Service labeled with a 5-day expiration and is responsible for compliance with [21 CFR 640.25\(b\)](#) for a storage period of 5 days.

PLATELET QUALITY CONTROL – Manufacturer Responsibility (cont'd)

Question 8: Is an FDA registered Transfusion Service that performs the manufacturing steps to extend platelet expiration to day 6 or day 7 required to perform the monthly QC testing as outlined in [21 CFR 640.25\(b\)](#) for the storage periods of day 6 and/or day 7?



PLATELET QUALITY CONTROL – Manufacturer Responsibility (cont'd)

FDA/OBRR Michelle Gutierrez Q8:

“No, the FDA-registered Transfusion Service is not required to perform monthly quality control testing under [21 CFR 640.25\(b\)](#).

However, you must update your registration. FDA regulations under [21 CFR 607](#) require establishments that engage in the manufacture of blood products to update their registration and list their products and activities with the agency within 5 days of beginning blood manufacturing operations.”

LICENSE AND REGISTRATION

Background: FDA regulation [21 CFR 607.7](#) describes:

Establishment registration and product listing of blood banks and other firms manufacturing human blood and blood products. All owners or operators of establishments that engage in the manufacturing of blood products are required to register, pursuant to Section 510 of the Federal Food, Drug, and Cosmetic Act. Registration and listing of blood products must comply with this part. Registration does not permit any blood bank or similar establishment to ship blood products in interstate commerce.



LICENSE AND REGISTRATION (cont'd)

Example: We are an FDA registered (but not licensed) hospital-based blood collection facility. For the most part we are able to supply our own needs. However, there are times when we must purchase blood from outside sources. The purchased RBCs are labeled with the Blood Supplier license number.

Question 9: As an FDA registered only collection facility can we ship RBC inventory labeled with the license number of the supplier across state lines to a “sister” hospital Transfusion Service using shipping containers that we have validated for this purpose?

FDA/OBRR Michelle Gutierrez Q9:

“Yes. The registered-only facility may distribute blood products from their supplier to a ‘sister’ facility in another state, as long as the products are FDA-licensed.”

LICENSE AND REGISTRATION (cont'd)

Question 10: As an FDA registered only collection facility, can we conduct a mobile blood drive in a neighboring state if all the blood collected is returned to the location of the FDA registered facility for processing and labeling, but never distributed across state lines following labeling and lot release?

FDA/OBRR Michelle Gutierrez Q10:

“Yes, components collected on mobiles are associated with the registration number/FEI of the facility from which they originate. The components, however, are not considered licensed and cannot be distributed in interstate commerce.”

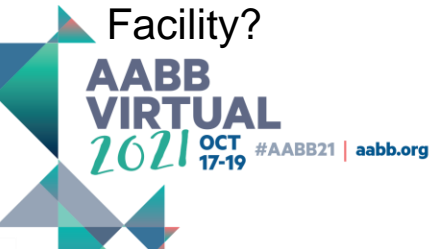
HELICOPTERS – License and Registration

Background: Again referencing [21 CFR 607.7](#) which describes:

...Registration and listing of blood products must comply with this part. Registration does not permit any blood bank or similar establishment to ship blood products in interstate commerce.

For this section, we are seeking clarification for a variety of issues related to registration and licensure. We are seeking clarification on at exactly what point in the processes described in the examples, would FDA consider the blood to be introduced into interstate commerce and require licensure. To begin, we have a few general overarching questions:

Question 11: If looking at the definitions for Hospital Transfusion Service, Non-hospital Transfusion Service, Blood Bank, or Distribution Center, all of which store and distribute blood, what definition, if any, describes an Emergency Transport Service (ETS) with interim storage of blood supplied by a Hospital Transfusion Service, Blood Bank or Blood Collection Facility?



HELICOPTERS – License and Registration (cont'd)

FDA/OBRR Christopher Cox Q11:

“The ETS function is to ‘transport’ blood and blood components during emergency situations and is not required to be registered under any of the specified categories.”

HELICOPTERS – License and Registration (cont'd)



Question 12: Under what circumstances would a Blood Collection Facility be considered responsible as both Blood Supplier and Transfusion Service? For example, if the blood collector's Immunohematology Reference Laboratory performs testing to confirm the ABO/Rh status of the blood products supplied directly to the ETS, would that collector also assume all of the responsibilities of a Transfusion Service?

FDA/OBRR Christopher Cox Q12:

“If the blood collection facility performs confirmation of the ABO/Rh status of the blood products supplied directly to the ETS, they are conducting the functions of a Transfusion Service.”

HELICOPTERS – License and Registration (cont'd)

Example: Our FDA compliant process was developed to ensure patients receive safe transfusions in the field, at the site of an accident with traumatic injuries, with a commitment to remaining compliant with FDA regulations regarding interstate commerce. The hospital blood bank issues Whole Blood to an ETS helicopter air base within the same state. Upon receipt of the product, the ETS will follow our standard operating procedures (SOPs) and will store the Whole Blood in a continuously monitored refrigerator at the air base. When in flight, the Whole Blood product is stored in a validated cooler, which is continuously temperature monitored, where it is available for transfusion in the field after arrival to the scene of the accident. Any blood product that is not transfused will be returned to our hospital blood bank (the blood bank issuing the product to the air base facility).

There are multiple scenarios that can take place and we want to ensure compliance with our FDA registration regarding distribution of blood products. If you find that any of these scenarios render the hospital blood bank out of compliance, please advise how to proceed to ensure FDA compliance with provision of these lifesaving products.



HELICOPTERS – License and Registration (cont'd)

Scenario 1) One unit of Whole Blood from interim storage at the in-state ETS air base facility accompanies the ETS team in the event transfusion is required in the field after arrival at the scene of the accident. The Whole Blood is not transfused and is returned to the issuing hospital blood bank prior to outdate for final disposition.

Question 13: What is the definition of “interstate commerce” as it applies to an ETS and their supplier, whether transport is by air or ground?

Question 14: In this example, are we correct in concluding that this untransfused unit of Whole Blood, returned to us, is never introduced into interstate commerce at the time of distribution to the in-state ETS air base that maintains an interim storage, as described?

Question 15: In this example, is the ETS air base serving as a Distribution Center that requires registration or does another definition of this air base facility apply?

HELICOPTERS – License and Registration (cont'd)

Scenario 2) One unit of Whole Blood is issued to the in-state ETS air base facility for transfusion in the field after arrival at the scene of the accident. The transfusion is initiated in the field and the blood product is infusing when the patient arrives at an in-state hospital.

Question 16: In this example, are we correct in concluding that this transfused unit of Whole Blood remained in-state and was not introduced into interstate commerce at the time of distribution to the in-state ETS air base that maintains an interim storage, as described?

Question 17: If correct, would that change if the transfusion was initiated out of state by the ETS team before the patient was transported to an in-state hospital?



HELICOPTERS – License and Registration (cont'd)

Scenario 3) One unit of Whole Blood is issued to the in-state ETS air base facility for transfusion in the field after arrival at the scene of the accident. The transfusion is initiated in the field and the blood product is infusing when the patient arrives at an out of state hospital.

Question 18: In this example, are we correct in concluding that this unit of Whole Blood, distributed to the in-state ETS air base for interim storage, infusing at the time the patient was received at an out of state hospital was not introduced into interstate commerce?

Question 19: If correct, would the determination regarding interstate commerce change if:

- the transfusion was initiated in-state, but the patient was taken to the closest hospital which happened to be out of state?
- a second unit was left at the out of state hospital because it was not transfused in the field?

HELICOPTERS – License and Registration (cont'd)

FDA/OBRR Christopher Cox Q13, Q14, Q15, Q16, Q17, Q18, Q19:

“We are going to give one response here, which addresses all of these various scenarios.

Unscheduled and infrequent interstate shipments of blood products for use in medical emergencies, for which documentation is maintained and made available for Agency examination, do not ordinarily constitute the types of transactions that would require licensure.

The shipment of the unlicensed blood product(s) would be covered under the FDA Compliance Policy Guide 220.100 for Interstate Shipment Biologicals for Medical Emergency: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cpg-sec-220100-shipment-biologicals-medical-emergency>

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HELICOPTERS – License and Registration (cont'd)

FDA/OBRR Christopher Cox Q13, Q14, Q15, Q16, Q17, Q18, Q19: (cont'd)

The Agency reserves the right to review the documentation relating to such incidents on an individual basis, to prevent the interstate shipment of unlicensed blood products under the guise of responding to a medical emergency. Such documentation must be maintained at the establishment that ships the product in response to the emergency. A blood product deviation report would not be required, provided the product was distributed using an emergency protocol, it was labeled appropriately, and all documentation is maintained.

The receiving hospital should develop their own policies and procedures related to the management and final disposition of blood and blood products that were intended for the patient being transported but were not transfused and left at the facility.”

HELICOPTERS – Emergency Release Signature for Emergency Transport Services

Background: FDA regulations require a signed statement in the records from the physician indicating the clinical situation was sufficiently urgent to require release of blood before completion of compatibility testing:

[21 CFR 606.151\(e\)](#) Procedures to expedite transfusion in life-threatening emergencies. Records of all such incidents shall be maintained, including complete documentation justifying the emergency action, which shall be signed by a physician.

[21 CFR 606.160\(b\)\(3\)\(v\)](#) Emergency release of blood, including signature of requesting physician obtained before or after release.



HELICOPTERS – Emergency Release Signature for Emergency Transport Services (cont'd)

Question 20: What physician(s) is responsible for providing authorization for emergency transfusion by the ETS team and retaining records of these emergency transfusions?

FDA/OBRR Christopher Cox Q20:

“Establishments should establish procedures defining which physician is responsible for providing authorization for emergency transfusions and retaining records during emergency transport by the ETS team.”

HELICOPTERS – Fatality Reporting

Background: [21 CFR 606.170\(b\)](#) requires reporting of fatalities confirmed to be caused by blood donation or blood transfusion:

(b) When a complication of blood collection or transfusion is confirmed to be fatal, the Director, Office of Compliance and Biologics Quality, CBER, must be notified by telephone, facsimile, express mail, or electronically transmitted mail as soon as possible.

Question 21: What facility(ies) is responsible for this investigation, assessment, and report to CBER when a fatality is caused by a transfusion initiated by the ETS team?

HELICOPTERS – Fatality Reporting (cont'd)

FDA/OCBQ Sharon O'Callaghan Q21:

“[21 CFR 606.170\(b\)](#) states ‘When a complication of blood collection or transfusion is confirmed to be fatal, the Director, Office of Compliance and Biologics Quality, CBER must be notified by telephone, facsimile, express mail, or electronically transmitted mail as soon as possible. A written report of the investigation must be submitted to the Director, Office of Compliance and Biologics Quality, CBER, by mail, within 7 days after the fatality by the collecting facility in the event of a donor reaction, or by the facility that performed the compatibility tests in the event of a transfusion reaction’.

Therefore, the facility that performed the compatibility testing, or provided the units under emergency release in accordance with [§606.151\(e\)](#), is responsible for reporting to FDA any fatal complication associated with the products administered by the Emergency Transport Services.”

ELECTRONIC CIRCULAR OF INFORMATION – Distribution in Lieu Of Hard Copies

Background: [21 CFR 606.122 Circular of information](#) states:

“A circular of information must be available for distribution if the product is intended for transfusion.”

At AABB’s [2017 Ask the FDA session](#), FDA stated:

*“...With that said, the Circular of Information for the Use of Human Blood and Blood Components is considered to be labeling. It was developed as an extension of the blood bag container label, because the space on these labels is limited. FDA believes that the Circular should be distributed to customers. **We believe availability of a hard copy Circular should be part of the overall distribution process, in accordance with §606.122, to include distribution on a yearly basis or whenever a change is made to the Circular or upon request from your customers.**”*

ELECTRONIC CIRCULAR OF INFORMATION – Distribution in Lieu Of Hard Copies (cont'd)

[Refer to additional details and background provided by FDA and posted on AABB's [Circular of Information \(COI\) webpage](#)]

Current technologies support the effectiveness and broad accessibility of electronic instructions for use for many products, including FDA regulated medical devices. Distribution of a Blood Center COI by electronic methods, e.g., a link to the Blood Center website or as a PDF file, can be much more timely and readily accessible to a wider end-user audience than relying on distribution of hard copy COIs. Electronic distribution is also much more cost effective than distribution of hard copies.

ELECTRONIC CIRCULAR OF INFORMATION – Distribution in Lieu Of Hard Copies (cont'd)

Question 22: Given that FDA supports electronic instructions for use in labeling for other regulated products, when will CBER support the option to use an electronic COI without first requiring a hard copy to be distributed annually *or whenever a change is made...., as noted in the Background?*



ELECTRONIC CIRCULAR OF INFORMATION – Distribution in Lieu Of Hard Copies (cont'd)

FDA/OBRR Christopher Cox Q22:

“FDA/CBER has stated that the availability of a hard copy Circular should be part of the overall distribution process, in accordance with [§606.122](#), to include distribution on a yearly basis or whenever a change is made to the Circular, or upon request from your customers. We understand your concerns and acknowledge that we need to provide additional guidance.”

LICENSING – Facility Versus Component

Background: Current regulations require an FDA license before a blood component can be shipped across state lines as discussed earlier.

Example: A Blood Center initially submitted a Blood License Application (BLA) which was approved by FDA to include collection of RBCs using apheresis Platform A. Blood products collected using Platform A are labeled with the facility license number assigned by FDA in the approved BLA.

At a later time, this facility implements:

- a second apheresis platform, Platform B, to collect RBCs.

Followed by:

- new procedures for apheresis platelet collections using Platform A.

LICENSING – Facility Versus Component (cont'd)

Question 23: Does FDA license the facility itself or the components we collect? Please explain the difference.

FDA/OBRR Michelle Gutierrez Q23:

“The term generally applies to both facilities and blood products.

More specifically, through the approval of Biologics License Applications (BLAs), FDA issues a license to a blood establishment to manufacture certain blood components to distribute into interstate commerce.

FDA licenses biological products, including blood components, under the authority of section 351(a) of the PHS Act. The PHS Act requires that biological products be licensed and be safe, pure, potent, and manufactured in facilities designed to ensure that the product continues to be safe, pure, and potent. Accordingly, [21 CFR 601.2\(d\)](#) states that approval of a Biologics License Application (BLA) or issuance of a biologics license constitutes a

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LICENSING – Facility Versus Component (cont'd)

FDA/OBRR Michelle Gutierrez Q23: (cont'd)

determination that the establishment(s) and the product meet applicable requirements to ensure the safety, purity, and potency of such products.

Therefore, blood establishments only need to submit one BLA to request approval to market one or more blood or blood components, or submit a supplement to the BLA for a manufacturing change in accordance with [21 CFR 601.12](#). You can also refer to our December 2014 Guidance for Industry: Changes to an Approved Application: Biological Products: Human Blood and Blood Components Intended for Transfusion or for Further Manufacture (<https://www.fda.gov/media/86137/download>), on reporting changes to an approved application.”

LICENSING – Facility Versus Component (cont'd)

Question 24: Using the FDA approved BLA in the example above, does the license number assigned by FDA in the BLA apply to additional collections sites, including both fixed and mobile operations, for RBC collections using apheresis Platform A under the direction of the licensed facility, following the same SOPs and performed by the same trained and competent staff?

Question 25: When adding Platform B at our collection sites currently licensed for collection of apheresis RBCs using Platform A, will apheresis RBC collections from Platform B be automatically considered licensed apheresis RBCs? If not, what is required for FDA approval of apheresis components collected at our licensed facility using Platform B?

Question 26: Likewise, what is required to achieve licensure for a second component, apheresis platelets, collected on Platform A or are they already licensed under our FDA approved BLA?



LICENSING – Facility Versus Component (cont'd)

FDA/OBRR Michelle Gutierrez Q24, Q25, Q26:

“For questions 24, 25 and 26, we are going to provide a general response.

Based on the information provided, we understand that you are asking if blood establishments can collect apheresis products on mobile blood collection drives or at other fixed blood collection establishments that are not licensed for the specific apheresis products, using different apheresis collection devices, and consider the apheresis products licensed, based on the license approvals at the original fixed establishment where the mobile originates.

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. Mobile collection operations, by definition, occur at locations that are not fixed blood establishments and have no registration numbers/FEIs. The

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LICENSING – Facility Versus Component (cont'd)

FDA/OBRR Michelle Gutierrez Q24, Q25, Q26: (cont'd)

locations are used only temporarily for blood collections. For this reason, components collected on mobiles are associated with the registration number/FEI of the establishment from which they originate and are considered licensed only if the originating establishment is already licensed for the same products.

FDA cannot provide feedback without additional information on the specific circumstances of each establishment. Individual blood establishments should contact FDA to discuss the facts and circumstances related to the specific situation.”

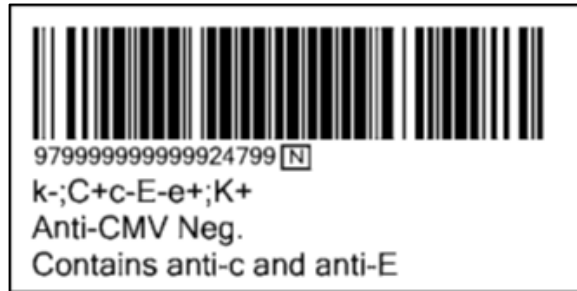
LABELING – Red Blood Cells

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).”



LABELING – Red Blood Cells (cont'd)

Question 27: The current policy at our Blood Center is to label a unit of packed RBCs with the name of the antibody when the antibody screen is positive. We destroy the plasma made from the collection. However, if a donor with history of a clinically significant antibody returns for another donation and the antibody screen is negative, is there a requirement to label RBCs with a donor's historical antibody?



LABELING – Red Blood Cells (cont'd)

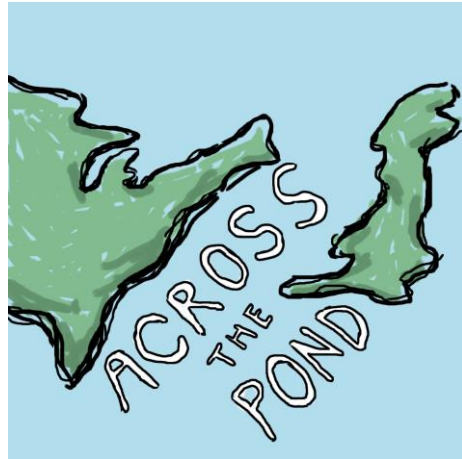
FDA/OBRR Michelle Gutierrez Q27:

“There is no FDA requirement to label Red Blood Cell units with a donor’s historical antibody based on records. Units must be labeled based on current antibody test results, as described in [21 CFR 606.121\(e\)\(2\)\(ii\)](#).”

IMPORTING A VERY RARE UNIT OF BLOOD

Background: A patient presents for surgery with extremely rare, clinically significant antibodies. The surgery is not urgent, but it is serious and necessary. The surgery supports the need for 4 units of RBCs to be crossmatched and available. The entire United States (U.S.) rare donor registry has been searched and 2 units are available. Two additional units are located in the United Kingdom.

Question 28: Is there an FDA approved process to import these rare donor units into the U.S.?



IMPORTING A VERY RARE UNIT OF BLOOD (cont'd)

FDA/OBRR Christopher Cox Q28:

“For such medical emergencies, there is a streamlined approach to request approval for an individual patient expanded access IND under [21 CFR 312.23](#) for importation of rare blood units for patients with extremely rare, clinically significant antibodies for emergency use, when suitable units are not available in the United States.

For further information, please refer to our Guidance for Industry: Individual Patient Expanded Access Applications: Form FDA 3926, updated October 2017:

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/individual-patient-expanded-access-applications-form-fda-3926>

Approved requests require submission of follow-up information regarding patient status after treatment is concluded, and whether or not the patient received the product.

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IMPORTING A VERY RARE UNIT OF BLOOD (cont'd)

FDA/OBRR Christopher Cox Q28: (cont'd)

Should the imported blood product not be transfused, FDA requires email notification indicating final disposition of the blood product, i.e., disposed of/destroyed/returned to the manufacturer.”

ELECTRONIC RECORDS AND SIGNATURES

Background: [21 CFR 11](#) provides FDA regulations for Electronic Records and Electronic Signatures and [21 CFR 630.10\(g\)](#) describes the Donor's acknowledgement:

...You must establish procedures in accordance with §606.100 of this chapter to assure that the donor has reviewed this material, and provide for a signature or other documented acknowledgement.

Question 29: As a large volume of the workforce continues to work remotely during the COVID-19 public health emergency, would FDA provide clarity regarding its current expectations for electronic record review to ensure that policies, processes, and procedures are in compliance?

FDA/OBRR Christopher Cox Q29:

“FDA's recommendations for maintaining electronic records under [21 CFR Part 11](#) are in the guidance document, titled, ‘Part 11, Electronic Records; Electronic Signatures — Scope

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ELECTRONIC RECORDS AND SIGNATURES

FDA/OBRR Christopher Cox Q29: (cont'd)

and Application' and accessible at <https://www.fda.gov/media/75414/download>. The recommendations have not been revised or updated during the COVID-19 public health emergency.”

Question 30: If defined in policy, is an electronic signature an acceptable method to capture donor acknowledgement, and are there other alternative methods to capture signatures?

FDA/OBRR Christopher Cox Q30:

“As stated in the preamble to the Donor Eligibility Final Rule ([80 FR 29870](#), May 22, 2015), an electronic signature satisfies the requirement in [21 CFR 630.10\(g\)\(2\)](#) that the donor’s acknowledgement be provided by signature or other documented acknowledgement. Other methods for documenting the donor’s acknowledgment may be acceptable provided you have established such procedures in accordance with [21 CFR 606.100](#).”

LIQUID PLASMA

Background: We are a licensed firm that is considering Liquid Plasma licensure for use during emergency and massive transfusion protocols.

Question 31: Does our current licensure for Whole Blood-derived plasma cover Liquid Plasma intended for interstate distribution?

FDA/OBRR Christopher Cox Q31:

“Yes: 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.”

Question 32: What would be required to license Apheresis Liquid Plasma?

LIQUID PLASMA (cont'd)

FDA/OBRR Christopher Cox Q32:

“Currently FDA would not approve the collection and manufacture of this component, based on the following:

Liquid Plasma, as defined at [21 CFR 640.34\(c\)](#) must be separated from the Red Blood Cells and stored at a temperature of 1-6 C within 4 hours of filling the final container. In [21 CFR 610.53\(b\)](#), Liquid Plasma must be stored at 1-6 C and has an expiration date of 5 days from the end of the Whole Blood dating period.

There are no apheresis devices that are 510(k) cleared/approved for the collection of Liquid Plasma. In addition, Liquid Plasma collected by apheresis has not been defined or characterized.”

ARM SCRUB

Background: We are currently looking at donor arm preparation alternatives. I can't seem to find the CBER website where FDA used to list approved arm prep products.

Question 33: Is this website still available?

FDA/OBRR Michelle Gutierrez Q33:

“No. FDA removed the website because it was outdated.”

Question 34: Can you provide some guidance or point in the direction of where to find FDA's currently approved antiseptic scrubs for use on blood donor arms to minimize bacterial contamination and should the method be validated?



ARM SCRUB (cont'd)

FDA/OBRR Michelle Gutierrez Q34:

“FDA does not provide ‘pre-clearance’ or ‘pre-approval’ for antiseptic products since they are considered over the counter (OTC) products. Use of an OTC antiseptic product would be acceptable for the skin scrub provided that the intended use of the antiseptic product describes skin preparation prior to surgery or injection, or for blood donor collection.

You should validate the arm scrub method used in manufacturing blood components.”

COLD-STORED PLATELETS

Background: We would like to receive clarification about the Cold-Stored Platelets (CSP) licensure. We have been previously informed by industry that these products cannot be licensed.

Question 35: Is CSP a licensed product?

FDA/OBRR Christopher Cox Q35:

“FDA has approved some blood establishments for an alternative procedure to [21 CFR 606.65\(e\)](#) and [21 CFR 610.53\(b\)](#), under the provisions in [21 CFR 640.120\(a\)](#), to manufacture Platelets stored at 1-6 C for the treatment of actively bleeding patients for up to 14 days, when conventional platelets are unavailable, or their use is not practical.”

Question 36: If a licensed blood establishment recently received this approval to manufacture CSP under a [21 CFR 640.120\(a\)](#) variance, does that mean the establishment can distribute these products in interstate commerce?

COLD-STORED PLATELETS (cont'd)

FDA/OBRR Christopher Cox Q36:

“Yes. A blood establishment that has received approval for the alternative procedure can distribute the cold stored platelets in interstate commerce, provided that establishment is licensed to manufacture conventional, room-temperature platelets. If the firm is not licensed to distribute conventional, room-temperature platelets in interstate commerce, they should first submit a biologics license application (BLA) or a supplement to their approved BLA for conventional platelets, in addition to the request for the alternative procedure.”

PATHOGEN REDUCED PLATELETS AND CMV STATUS

Background: I am trying to determine if psoralen-treated platelets are considered “CMV negative” or “CMV-safe”?

Question 37: Can we label pathogen-reduced platelet products as “CMV Negative” or “CMV Safe”?



PATHOGEN REDUCED PLATELETS AND CMV STATUS (cont'd)

FDA/OBRR Michelle Gutierrez Q37:

“No, you cannot label pathogen-reduced platelets as ‘CMV Negative’ or ‘CMV-safe.’

To label the unit as ‘CMV Negative’, FDA requires that the unit be tested by an FDA-approved or cleared anti-CMV donor screening assay. FDA does not recognize the term ‘CMV-safe’ for blood components.

However, the package inserts for the processing sets to manufacture Psoralen-treated Apheresis Platelets (<https://intercept-usa.com/resources/?topic=package-inserts>) describes the effect of pathogen reduction on viruses, including CMV, in reducing the viral load in the product.”

COLLECTION OF DONORS WITH HEREDITARY HEMOCHROMATOSIS AND DONORS ON TESTOSTERONE THERAPY

Background: We would like to be able to draw platelets from donors who have Hereditary Hemochromatosis and Red Blood Cells from donors on testosterone replacement therapy.

Question 38: Would we need to file a variance with the FDA for:

- The collection of platelets from donors who are diagnosed with Hereditary Hemochromatosis?
- The collection of RBCs from donors on Testosterone Replacement Therapy?

COLLECTION OF DONORS WITH HEREDITARY HEMOCHROMATOSIS AND DONORS ON TESTOSTERONE THERAPY (cont'd)

FDA/OBRR Christopher Cox Q38:

- The collection of platelets from donors who are diagnosed with Hereditary Hemochromatosis?

“No, you do not need to file a variance. You should evaluate donors with hereditary hemochromatosis according to your standard operating procedures for determining eligibility for platelet donation.

In addition, you do not need a variance to provide therapeutic phlebotomy for more frequent collections of Whole Blood or apheresis red cells from individuals with hereditary hemochromatosis, provided your program meets the specifications in [21 CFR 630.15\(a\)\(2\)](#) and you report it in your Annual Report under [21 CFR 601.12\(d\)](#).”

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COLLECTION OF DONORS WITH HEREDITARY HEMOCHROMATOSIS AND DONORS ON TESTOSTERONE THERAPY (cont'd)

FDA/OBRR Christopher Cox Q38: (cont'd)

- The collection of RBCs from donors on Testosterone Replacement Therapy?

“No, you do not need to file a variance.

However, therapeutic phlebotomy collections from donors undergoing testosterone replacement therapy or from individuals with any other type of disease or condition, other than Hereditary Hemochromatosis, must be performed using a procedure that has been reviewed and approved by FDA ([21 CFR 630.15\(a\)\(2\)\(ii\)\(B\)](#)), which will require a Prior Approval Supplement (PAS) submission.”

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VIRTUAL**

2021 OCT
17-19

Advancing

Ask the FDA

Cellular Therapy

CELLULAR THERAPY

Background: Regulations on human cells, tissues, and cellular and tissue-based products (HCT/Ps) are described in [Title 21 of the Code of Federal Regulations \(CFR\) Part 1271](#).

[21 CFR 1271.145](#) Prevention of the introduction, transmission, or spread of communicable diseases states:

You must recover, process, store, label, package, and distribute HCT/Ps, and screen and test cell and tissue donors, in a way that prevents the introduction, transmission, or spread of communicable diseases.

The following regulations also apply:

- [21 CFR 1271.10\(a\)](#) Are my HCT/P's regulated solely under section 361 of the PHS Act and the regulations in this part, and if so what must I do?
- [21 CFR 1271.150](#) Current good tissue practice requirements
- [21 CFR 1271.155](#) Exemptions and alternatives

CELLULAR THERAPY (cont'd)

Question 39: Does a specimen container for a biological designated for banking purposes (semen, cord blood, tissue, etc.) specifically need to be a sterile container?

FDA/OTAT Hanh Khuu Q39:

“Human cells, tissue, or cellular or tissue-based products (HCT/Ps) are regulated solely under the authority of section 361 of the Public Health Service Act (the PHS Act) (361 HCT/Ps) and the regulations in [21 CFR part 1271](#) when all criteria in [§1271.10\(a\)](#) are met and an exception under [§1271.15](#) does not apply.

The Current Good Tissue Practice (CGTP) regulation in [21 CFR part 1271](#), subpart D includes requirements for supplies and reagents that are used during manufacture of HCT/Ps. The CGTPs do not specify use of sterile HCT/P containers, however, under [§1271.210](#), HCT/P manufacturers must not use supplies or reagents until they have been verified to meet specifications designed to prevent situations that increase the risk of

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CELLULAR THERAPY (cont'd)

FDA/OTAT Hanh Khuu Q39: (cont'd)

introduction, transmission, or spread of communicable diseases. The guidance titled '[Current Good Tissue Practice \(CGTP\) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products \(HCT/Ps\)](#)', section XI includes helpful recommendations as to how manufacturers can verify supplies and reagents they receive from vendors meet relevant specifications of the HCT/P manufacturer. As explained in this guidance, use of a contaminated or otherwise defective supply or reagent in the manufacture of an HCT/P could lead to such problems as the introduction of a communicable disease agent or the failure to properly preserve the HCT/P.

With the exception of [§§1271.150\(c\)](#) and [1271.155](#), the CGTP requirements in subpart D are not applicable to establishments that manufacture reproductive HCT/Ps described in [§1271.10](#) and regulated solely under section 361 of the PHS Act ([§1271.150\(c\)\(3\)](#)).

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CELLULAR THERAPY (cont'd)

FDA/OTAT Hanh Khuu Q39: (cont'd)

For supplies, reagents or other components used for manufacturing HCT/Ps that are also regulated as drugs, devices and/or biological products and subject to premarket review requirements, manufacturers must comply with the current good manufacture practice regulations under [parts 210](#) and [211](#) or quality system regulations in [part 820](#), as applicable.”

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Advancing

Ask CMS/CLIA

TECHNICAL CONSULTANT RESPONSIBILITIES (Laboratories Performing Moderate Complexity Testing)

Background: [42 CFR 493.1413](#) Standard; Technical consultant responsibilities.

(b) The technical consultant 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;

...

(iv) Direct observation of performance of instrument maintenance and function checks;

TECHNICAL CONSULTANT RESPONSIBILITIES (Laboratories Performing Moderate Complexity Testing) (cont'd)

Question 40: Are there recommendations in regard to CLIA Testing Personnel direct observation for Competency Assessment? How can establishments maintain social distancing when performing direct observations? Are zoom, skype, or video recordings acceptable to perform observations?

CMS Response Q40:

“We understand the challenges of the ongoing public health emergency and are discussing this issue at CMS Baltimore.”

Question 41: Does FDA consider direct observation of cleaning as a required activity for CLIA Testing Personnel competency assessment of performance of instrument maintenance and function checks?

TECHNICAL CONSULTANT RESPONSIBILITIES (Laboratories Performing Moderate Complexity Testing) (cont'd)

CMS Response Q41:

“The Food and Drug Administration (FDA) has the responsibility for the CLIA test categorization. CMS has the responsibility for laboratory oversight. CMS publishes CLIA rules and regulations to include the regulations for instrument maintenance, function checks and testing personnel competency assessment.

The FDA’s CLIA website is provided below for your information and convenience.

<https://www.fda.gov/medical-devices/ivd-regulatory-assistance/clinical-laboratory-improvement-amendments-clia>”

Question 42: Could FDA provide examples of instrument maintenance and function checks that would require direct observation?

TECHNICAL CONSULTANT RESPONSIBILITIES (Laboratories Performing Moderate Complexity Testing) (cont'd)

CMS Response Q42:

“See the response to Question 41. The manufacturer’s instructions for all tests that have been approved, cleared or authorized by the FDA must be followed. If there are specific instructions related to maintenance and function checks, then those instructions must be followed. The CLIA regulations for maintenance and function checks are at [42 CFR §493.1254](#), and the interpretive guidelines at [§493.1254](#) provide examples. You may access the CLIA interpretive guidelines at https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/som107ap_c_lab.pdf.”

GENERAL SUPERVISOR RESPONSIBILITIES (Laboratories Performing High Complexity Testing)

Background: [42 CFR 493.1463](#) Standard: General supervisor responsibilities.

The general supervisor is responsible for day-to-day supervision or oversight of the laboratory operation and personnel performing testing and reporting test results.

(b) The director or technical supervisor may delegate to the general supervisor the responsibility for—

(1) Assuring that all remedial actions are taken whenever test systems deviate from the laboratory's established performance specifications;

(2) Ensuring that patient test results are not reported until all corrective actions have been taken and the test system is properly functioning;

GENERAL SUPERVISOR RESPONSIBILITIES (Laboratories Performing High Complexity Testing) (cont'd)

(3) Providing orientation to all testing personnel; and

(4) Annually evaluating and documenting the performance of all testing personnel.

Question 43: Can the CLIA General Supervisor delegate some duties to another person who qualifies as a General Supervisor?

CMS Response Q43:

“CLIA, at [42 CFR §493.1463](#), states that the laboratory director or the technical supervisor may delegate responsibilities to the general supervisor or staff who meet the general supervisor qualifications.”

GENERAL SUPERVISOR RESPONSIBILITIES (Laboratories Performing High Complexity Testing) (cont'd)

Question 44: Are delegations limited so only the Director and/or Technical Supervisor can delegate duties to staff who qualify as General Supervisor?

CMS Response Q44:

“Yes – see the response to Question 43.”

NOTIFICATION REQUIREMENTS

Background: Recently during a review of [42 CFR 493.63](#) *Notification requirements for laboratories issued a **certificate of accreditation** (Rev. 140, Issued: 05-29-15, Effective: 05-29-15, Implementation: 05-29-15)* it was discovered that section §6016 of the [State Operations Manual](#) (SOM) was revised for reporting of changes for the Certificate of Accreditation. These revisions are not included in [42 CFR 493.63](#) and does not include that the Personnel - Technical Supervisor change must be reported as indicated in the SOM. The SOM section number is only referenced in the Interpretative guidelines document.

Question 45: How can a facility be held accountable for changes to the SOM when the regulations are not updated to reflect the changes?

CMS Response Q45:

“CLIA requirements are minimal requirements. You must follow all the standards of your accreditation organization (AO), which may be more stringent than the CLIA regulations. The [State Operations Manual](#) (SOM) provides guidance to assist laboratories in complying with the CLIA regulations.”

NOTIFICATION REQUIREMENTS (cont'd)

Question 46: How were facilities notified of a revision to the SOM that impacts the regulations?

CMS Response Q46:

“CMS notifies the AO point of contact in writing of any changes to the SOM, policy letter updates and regulatory changes.

Laboratories can sign up to receive CMS-CLIA email communications. We provided the helpful link to the CLIA Listserv:

https://public.govdelivery.com/accounts/USCMS/subscriber/new?topic_id=USCMS_12461

Individuals can sign up to receive email updates directly from CMS-CLIA by submitting their email addresses to this icon at the bottom of the CMS-CLIA homepage.

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NOTIFICATION REQUIREMENTS (cont'd)

CMS Response Q46 (cont'd):

https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Interpretive_Guidelines_for_Laboratories



CMS-CLIA also updates the public at the Clinical Laboratory Improvement Advisory Committee (CLIAAC) meetings which are hosted by the CDC. Any information about CLIAAC to include transcripts of past CLIAAC meetings is at this website:

<https://www.cdc.gov/cliac/index.html>”

NOTIFICATION REQUIREMENTS (cont'd)

Question 47: In addition, it is noted that a new document titled [Laboratory Quick Start Guide to CMS CLIA Certification](#) was added to the [CMS website](#) under the heading on [How to Apply for a CLIA Certificate, Including International Laboratories](#). The document contains the information from the revised SOM. How are facilities notified when new documents are added to the CMS website that affect the regulations?

CMS Response Q47:

“See the response to Question 46.”

Question 48: It is our understanding that the agency who has deemed status to assess a facility against [42 CFR 493](#) cannot cite a facility against the Interpretative guidelines document if the language in [42 CFR 493](#) does not contain the same information. Is this accurate?

NOTIFICATION REQUIREMENTS (cont'd)

CMS Response Q48:

“CLIA-certified facilities are surveyed (inspected, assessed) for compliance with the **CLIA regulations**. The interpretive guidelines (IGs) clarify and/or explain the CLIA requirements to laboratories.

Accreditation organizations are awarded deemed status by CMS because CMS-CLIA has determined that the AO's standards are equivalent to or more stringent than the CLIA requirements. When the AOs assess facilities for compliance with the AO standards, the AOs **are also** assessing compliance with the CLIA regulations.”

TEST CATEGORIZATION

Background: The organization recently began using a manufacturer that provides a kit for Hgb S testing. The manufacturer is approved by the FDA. However, the test has not been categorized by the FDA and is not listed in the FDA CLIA database. The manufacturer has been in contact with the FDA for several months and FDA has indicated there will be a delay in evaluating the categorization for this test due to other priorities.

The uncategorized test has the same methodology as the previous manufacturer based on review of manufacturer instructions; for the previous manufacturer, the test is categorized as moderate complexity testing.

Specifically, [42 CFR 493.17](#) indicates a test is considered high complexity until categorized.

TEST CATEGORIZATION (cont'd)

[42 CFR 493.17](#) **Test categorization** states the following:

(c) Process for device/test categorization utilizing the scoring system under [§493.17\(a\)](#).

(4) If a laboratory test system, assay or examination does not appear on the lists of tests in the Federal Register notices, it is considered to be a test of high complexity until PHS, upon request, reviews the matter and notifies the applicant of its decision. Test categorization is effective as of the notification to the applicant.

An uncategorized test that must be considered high complexity because of a delay in test complexity categorization causes staffing challenges across the organization.

Question 49: Is there another process the manufacturer can use to get the test categorized?



TEST CATEGORIZATION (cont'd)

CMS Response Q49:

“The FDA’s Center for Devices and Radiological Health (CDRH) is responsible for CLIA Test Categorization. The FDA categorizes diagnostic tests by their complexity—from the least to the most complex: waived tests, moderate complexity tests, and high complexity test. CLIA categorization is determined after the FDA has cleared or approved a marketing submission, or upon request for legally marketed devices, as described in the FDA guidance [Administrative Procedures for CLIA Categorization](#). Tests that are waived by regulation under [42 CFR 493.15\(c\)](#), or cleared or approved for home use, are categorized as waived. Otherwise, the FDA determines the test’s complexity by reviewing the package insert test instructions, and using a criteria “[scorecard](#)” to categorize a test as moderate or high complexity ([42 CFR 493.17](#)). Each test is graded for level of complexity by assigning scores of 1, 2, or 3 for each of the seven criteria on the scorecard.

You may email CDRH directly at CLIA@fda.hhs.gov.

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TEST CATEGORIZATION (cont'd)

CMS Response Q49: (cont'd)

Here is the link to the FDA's CLIA website:

<https://www.fda.gov/medical-devices/ivd-regulatory-assistance/clinical-laboratory-improvement-amendments-clia>

Below is the link to the FDA's searchable database:

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCLIA/search.cfm>”

TEST CATEGORIZATION (cont'd)

Question 50: Can the organization consider the new test as moderate complexity given that the test uses the same methodology and interpretation of results as the comparable moderate complexity test?

CMS Response Q50:

“The FDA assigns CLIA test complexity, and laboratories must follow the FDA’s test complexity assignment. Facilities cannot assign nor assume test complexity. You may contact CDRH directly at CLIA@fda.hhs.gov.

Any tests without an approval/clearance by the FDA defaults to high complexity. In order to do testing without FDA approval/clearance, you must be a CLIA certified laboratory that meets regulatory requirements to perform high complexity testing under §§493.1441 through 493.1495 of the CLIA regulations. In addition, the laboratory must establish performance specification per §493.1253(b)(2) as the FDA Has not

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TEST CATEGORIZATION (cont'd)

CMS Response Q50: (cont'd)

cleared or approved the test system. It is the laboratory director's responsibility to ensure that the procedures used to establish performance specifications are adequate to determine accuracy, precision, and other pertinent performance characteristics of the method (e.g., number of samples), and that the test method has the capability to provide the quality of results required for patient care. You may access the CLIA regulations at:

<https://www.ecfr.gov/current/title-42/chapter-IV/subchapter-G/part-493#sp42.5.493.e>

Below is the link to the FDA's searchable database:

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCLIA/search.cfm>”

COMPATIBILITY TESTING

Background: [42 CFR 493.863](#) provides the proficiency testing requirements for compatibility testing.

A reference laboratory screens donor units prior to shipment to the transfusion service by mixing donor red cells with patient serum but does not issue the blood as crossmatched.

Question 51: Does this mixing of donor cells with patient serum fall under the CLIA definition of compatibility testing?

CMS Response Q51:

“CLIA does not have a definition of compatibility testing but follows the FDA definition. FDA’s definition of compatibility testing is the mixing of donor cells with patient serum. Based on the FDA definition, CLIA considers the mixing of donor cells with patient serum compatibility testing to fall under CLIA.”

COMPATIBILITY TESTING (cont'd)

Question 52: If “Yes,” must the test be listed on the reference laboratory CLIA certificate and proficiency testing be performed?

CMS Response Q52:

“Yes, the mixing of donor cells with patient serum is considered compatibility testing and the laboratory must be appropriately CLIA certified to perform this testing. The CLIA certified laboratory must perform proficiency testing or the twice annual verification of accuracy.”

MULTIPLE SITE EXCEPTIONS UNDER CLIA

Background: The CMS.gov website describes a [Certificate and Regulatory Multiple Sites Exceptions under CLIA](#).

Question 53: What is a multisite exception CLIA certificate and how does a facility obtain one?

CMS Response Q53:

“For each certificate type under the CLIA regulations (42 CFR sections [493.35\(b\)](#), [493.43\(b\)](#) and [493.55\(b\)](#)) there are exceptions that allow a laboratory, in specific circumstances, to apply for a single certificate for multiple testing sites. The Centers for Medicare & Medicaid Services (CMS) is clarifying these requirements by offering examples for each type of exception due to questions and instances where the exceptions are applied to laboratories incorrectly.

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MULTIPLE SITE EXCEPTIONS UNDER CLIA (cont'd)

CMS Response Q53: (cont'd)

Caution should be used when determining if an entity can be issued one certificate for multiple sites. Each exception stands alone and must not be mixed with another exception.

The CLIA multiple site exceptions are identified below. There is a policy memo ([SCLetter12_09.pdf](#)) which provides clarifying information on determining if an entity is eligible for one of the multiple site exceptions. AOs may have similar standards or be more stringent than CLIA. The link to the policy memo is at the end of this response.

EXCEPTION 1 -- Temporary Testing Sites and Mobile Units --493.35 (b)(1); 493.43(b)(1); 493.55(b)(1)

The CLIA regulations for temporary testing sites are as follows:

(b)(1) – Exception. Laboratories that are not at a fixed location, that is, laboratories that move from testing site to testing site, such as mobile units

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MULTIPLE SITE EXCEPTIONS UNDER CLIA (cont'd)

CMS Response Q53: (cont'd)

providing laboratory testing, health screening fairs or other temporary testing locations may be covered under the certificate of the designated primary site or home base, using its address.

EXCEPTION 2 -- Limited Public Health Testing--493.35 (b)(2); 493.43(b)(2); 493.55(b)(2)

The CLIA regulations for limited public health testing are as follows:

(b)(2) – Exception. Not-for-profit or Federal, State, or local government laboratories that engage in limited (not more than a combination of 15 moderately complex or waived tests per certificate) public health testing may file a single application.

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MULTIPLE SITE EXCEPTIONS UNDER CLIA (cont'd)

CMS Response Q53: (cont'd)

EXCEPTION 3 -- Hospital Exception --493.35 (b)(3); 493.43(b)(3); 493.55(b)(3)

The CLIA regulations for hospitals are as follows:

(b)(3) – Exception. Laboratories within a hospital that are located at contiguous buildings on the same campus and under common direction may file a single application or multiple applications for the laboratory sites within the same physical location or street address.

Below is the link to the multiple site exception policy memo S&C 12-09-CLIA.

https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Downloads/SCLetter12_09.pdf

GENERAL QUESTIONS

Question 54: For a donor center that performs non-ABO/Rh antigen typing such as E, C, K, what CLIA category is that reported under?

CMS Response Q54:

“For CLIA certification purposes, those laboratories performing Blood type Ag donors and Blood type RBC antigens, must be certified in the subspecialty of compatibility testing (550) in order to perform antigen typing/antigen confirmations. This conforms with the instructions on the CMS-116.”

Question 55: Do Eluate and Donath-Landsteiner tests require twice annual verification?

CMS Response Q55:

“The preparation of an eluate does not require proficiency testing. However, accreditation organizations may have more stringent requirements than CLIA and laboratories must follow them if they receive their CLIA certification by virtue of accreditation by a

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GENERAL QUESTIONS (cont'd)

CMS Response Q55: (cont'd)

CMS-approved accreditation organization.

The Donath-Landsteiner tests does require the twice annual verification as required at 493.1236(c) and proficiency testing may be used to meet this requirement.”

Question 56: Is there a plan to re-evaluate reimbursement of blood (namely, plasma) in the “pre-hospital” setting (eg, helicopters and ambulances), given the new data on reduction in mortality with earlier transfusion?

CMS/CLIA Response Q56:

“The CMS CLIA program regulates laboratories that perform testing on patient specimens to ensure accurate, reliable and timely results. Your inquiry related to billing and reimbursement is outside the scope of the CLIA program.

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GENERAL QUESTIONS (cont'd)

CMS Response Q56: (cont'd)

Please refer questions regarding billing to: Clinical Laboratory Fee Schedule
CLFS_Inquiries@cms.hhs.gov

If you have further reimbursement questions, you may contact the Medicare Administrative Contractor (MAC) for your facility. Contact information for the MACs is found at:

<https://www.cms.gov/Medicare/Medicare-Contracting/Medicare-Administrative-Contractors/MedicareAdministrativeContractors.html>.

You may also contact the appropriate Medicaid contact with your questions. You may find Medicaid contact information at: <https://www.medicaid.gov/about-us/contact-us/index.html>.”



GENERAL QUESTIONS (cont'd)

Question 57: How are data reviewed to update reimbursement of blood products? For example, we have new information that suggests earlier plasma transfusion is associated for reduced mortality. In order to achieve consistency in pre-hospital transfusions, reimbursement is a key driver to equip ambulances and helicopters with blood products.

CMS Response Q57:

“See the response to #56.”

Question 58: Is there an interest in aligning reimbursement of blood products pre-hospital and in hospital better to reflect costs of blood centers and hospitals to provide blood products?

CMS Response Q58:

“See the response to #56.”

Remember to look for the Weekly Report article announcing that the transcript has been posted on our website:

[Ask the FDA and CLIA Transcripts](#)

Thank You!

Contact AABB's Regulatory Affairs Staff at
regulatory@aab.org