



# Ask the FDA and CMS/CLIA

**2018 AABBB Annual Meeting**

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

**The following Regulatory Affairs Staff have no financial disclosures:**

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# Objectives

- Apply a regulatory strategy for regulations recently issued by Food and Drug Administration (FDA).
- Apply FDA's recommendations in recently issued guidance to industry.
- Describe FDA's approach for blood and Human Cells, Tissues, and Tissue-Based Products (HCT/P's) policies, regulations and inspection programs.

# Thank you

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

We also appreciate the support of both FDA and Centers for Medicare & Medicaid Services (CMS).

## **Our FDA attendees:**

Orieji Illoh, Director, DBCD/OBRR

Wendy Paul, Deputy Director, DBCD/OBRR

Anne Eder, Acting Deputy Director, DETTD/OBRR

Camilla Smith, CSO, DBCD/OBRR

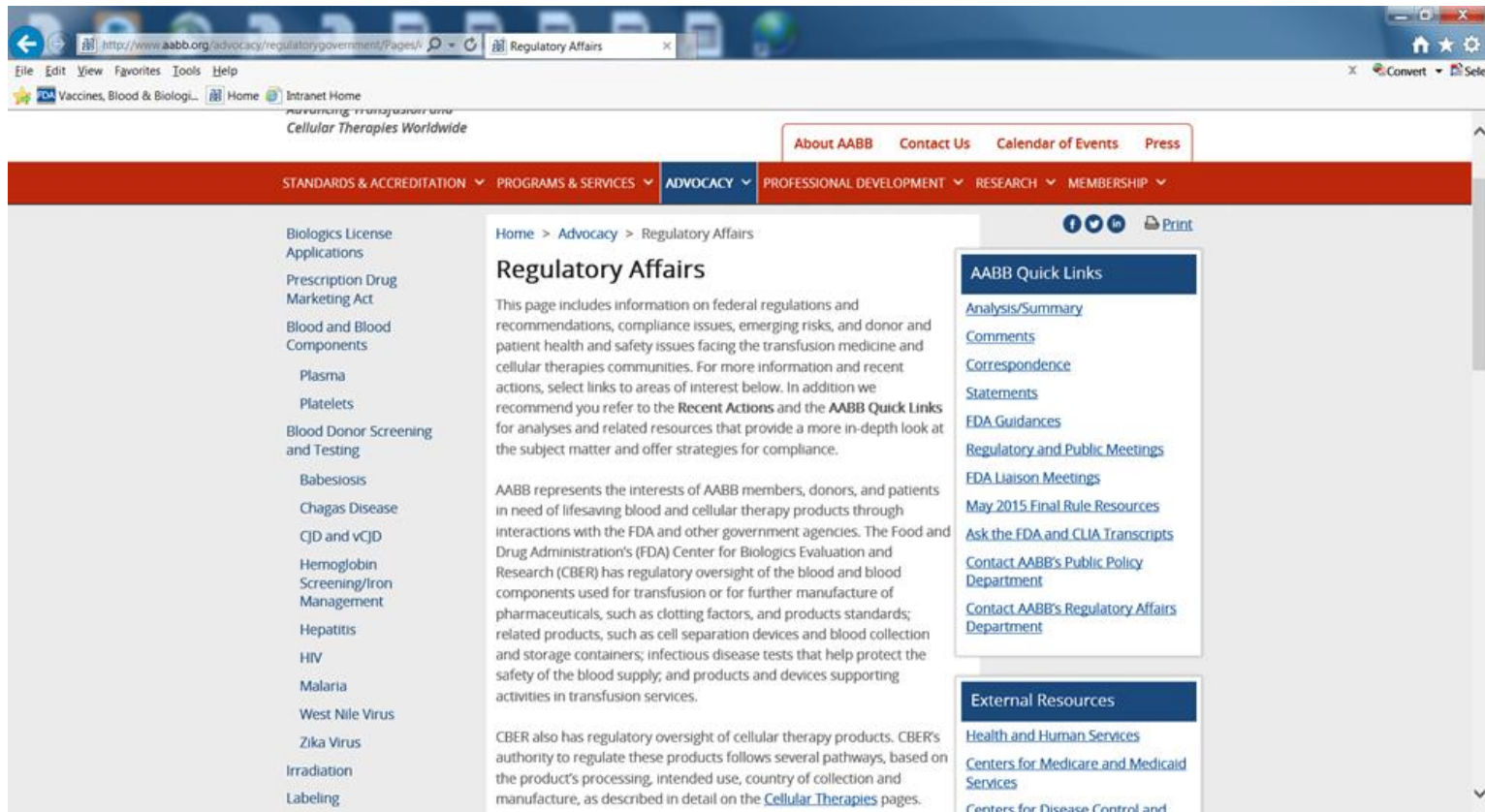
Kanaeko Ravenell, CSO, DBCD/OBRR

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Lisa Harlan, Director, Investigations Branch, ORA/OBPO

# You can find these slides and the transcript!



The screenshot shows a web browser window displaying the ABB Regulatory Affairs page. The address bar shows the URL: <http://www.aabb.org/advocacy/regulatorygovernment/Pages/RegulatoryAffairs>. The page features a navigation menu with categories: STANDARDS & ACCREDITATION, PROGRAMS & SERVICES, ADVOCACY (selected), PROFESSIONAL DEVELOPMENT, RESEARCH, and MEMBERSHIP. The main content area is titled "Regulatory Affairs" and includes a breadcrumb trail: Home > Advocacy > Regulatory Affairs. The page text discusses federal regulations, compliance issues, and provides links to "Recent Actions" and "AABB Quick Links". A sidebar on the left lists various biological products and conditions, including Babesiosis, Chagas Disease, CJD and vCJD, Hemoglobin Screening/Iron Management, Hepatitis, HIV, Malaria, West Nile Virus, Zika Virus, Irradiation, and Labeling. A right sidebar contains "AABB Quick Links" and "External Resources".

Home > Advocacy > Regulatory Affairs

## Regulatory Affairs

This page includes information on federal regulations and recommendations, compliance issues, emerging risks, and donor and patient health and safety issues facing the transfusion medicine and cellular therapies communities. For more information and recent actions, select links to areas of interest below. In addition we recommend you refer to the **Recent Actions** and the **AABB Quick Links** for analyses and related resources that provide a more in-depth look at the subject matter and offer strategies for compliance.

AABB represents the interests of AABB members, donors, and patients in need of lifesaving blood and cellular therapy products through interactions with the FDA and other government agencies. The Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research (CBER) has regulatory oversight of the blood and blood components used for transfusion or for further manufacture of pharmaceuticals, such as clotting factors, and products standards; related products, such as cell separation devices and blood collection and storage containers; infectious disease tests that help protect the safety of the blood supply; and products and devices supporting activities in transfusion services.

CBER also has regulatory oversight of cellular therapy products. CBER's authority to regulate these products follows several pathways, based on the product's processing, intended use, country of collection and manufacture, as described in detail on the [Cellular Therapies](#) pages.

**AABB Quick Links**

- [Analysis/Summary](#)
- [Comments](#)
- [Correspondence](#)
- [Statements](#)
- [FDA Guidances](#)
- [Regulatory and Public Meetings](#)
- [FDA Liaison Meetings](#)
- [May 2015 Final Rule Resources](#)
- [Ask the FDA and CLIA Transcripts](#)
- [Contact AABB's Public Policy Department](#)
- [Contact AABB's Regulatory Affairs Department](#)

**External Resources**

- [Health and Human Services](#)
- [Centers for Medicare and Medicaid Services](#)
- [Centers for Disease Control and](#)

**Watch for Regulatory Updates  
EVERY FRIDAY!!**

**We will notify you when the slides and responses are posted.**



# Ask the FDA

## Blood and Blood Components



## Definition of Distributed

**Background:** Some products are manipulated after issue from the transfusion service.  
**FDA regulations at [21 CFR 606.3\(k\)](#) state:**

*Distributed means: (1) The blood or blood components have left the control of the licensed manufacturer, unlicensed registered blood establishment, or transfusion service; and in [§606.3\(l\)](#) Control means having responsibility for maintaining the continued safety, purity, and potency of the product and for compliance with applicable product and establishment standards, and for compliance with current good manufacturing practices.*

**Example:** A blood product is issued by the transfusion service. At the bedside, the Red Blood Cells (RBC's) or platelet product is transferred from the original bag into a syringe or other container, either as part of a “push-pull exchange transfusion” or infusion pump.

## Definition of Distributed (cont'd)

### **Question:**

1) Would the medical director of the transfusion service be responsible for this manipulation of the blood product at bedside or is that considered “clinical practice?”

**FDA RESPONSE:** “There are no specific FDA requirements that address such manipulations or administration procedures at the bedside for blood and blood components. The transfusion service’s responsible physician, however, should be aware of their hospital’s policies and procedures for administration of blood and blood components.”

## Licensing of Microbiology Departments Performing Secondary Safety Testing of Platelets

**Background:** Some transfusion services use the facility's microbiology laboratory for testing. Under [§607.3\(c\)](#):

*Establishment means a place of business under one management at one general physical location. The term includes, among others, human blood and plasma donor centers, blood banks, transfusion services, other blood product manufacturers and independent laboratories that engage in quality control and testing for registered blood product establishments.*

**Example:** A hospital transfusion service that does not perform manufacturing steps, and is not registered with FDA, has implemented secondary safety measure testing of apheresis platelet components necessary to extend dating to day 6 and 7. A positive test is obtained on one of these components. A sample of the component is sent to the hospital's microbiology laboratory for confirmation and bacterial identification per existing Standard Operating Procedures (SOPs). The blood supplier is notified of the results of the culture performed by the hospital's microbiology laboratory, also per existing SOP.

## Licensing of Microbiology Departments Performing Secondary Safety Testing of Platelets (cont'd)



Visual inspection,  
anyone???

### Questions:

2) In this example, does FDA require the hospital-based microbiology department to register as a testing facility?

**FDA Response:** “Our current thinking is that the implementation of a bacterial detection device used to extend platelet expiration to 6 or 7 days is a manufacturing step that would require the transfusion service to register. The microbiology department would not be required to register.”

## Licensing of Microbiology Departments Performing Secondary Safety Testing of Platelets (cont'd)

3) Is the medical director of the microbiology laboratory or the medical director of the transfusion service required to send the culture results to the blood supplier's responsible physician?

**FDA Response:** “§606.145(c) states that the transfusion service is responsible. The transfusion service must notify the blood collection establishment of the species identified or advise the collection establishment that the species cannot be identified.”

4) If future FDA guidance provides for a culture-based option to extend dating to day-6 and day-7, would the hospital-based microbiology department performing the test be required to register with FDA?

**FDA Response:** “No, the microbiology department would not register with the FDA. Registration applies to the blood establishment performing the activities of extending the expiration date and relabeling the product.”

## Scope of FDA's Authority

**Background:** FDA's website states:

"FDA is responsible for protecting the public health by assuring that foods (except for meat from livestock, poultry and some egg products...are safe, wholesome, sanitary and properly labeled; ensuring that human and veterinary drugs, and vaccines and other biological products and medical devices intended for human use are safe and effective."

We hear about "***unusual applications***" for blood - such as:

"I am currently setting up a large scale blood donation project based in another country that will take blood from volunteers in several cities around the world, including xxxx and possibly xxx. [all in the US]. The blood we take will not be for human use, but for creative use by an artist. In the UK the MHRA have stated that we do not need to become an official blood establishment as the blood is not for human use, and as such there are no specific regulations we need to follow. Does this also apply to the USA as well? I am having some difficulty finding out about blood regulations in the USA as there are potentially any different regulatory bodies so any help would be very much appreciated."

## Scope of FDA's Authority (cont'd)

### Question:

5) Is it acceptable for blood collected in the US from volunteer donors, not intended for transfusion, to be shipped out of the country for “artistic creative use” such as painting, and are there regulations for donor safety? Please direct us to the other federal agencies with oversight in this area.



## Scope of FDA's Authority (cont'd)

**FDA RESPONSE:** “Our regulatory framework as FDA, governing blood establishments, would not apply to this activity. So, we recommend that the blood establishment’s responsible physician exercise prudent medical judgement when collecting this material. It’s really up to the medical director or the responsible physician to decide how to handle the donor and the product. We don’t have a lot of federal agencies to give you in terms of oversight, but you should note that the Department of Transportation also has requirements for the shipping of biological material.”



## Use of a Prepopulated Donor History Questionnaire (DHQ)

**Background:** Blood centers are always looking for ways to improve donor satisfaction.

**Regulations at [§630.10\(c\) state:](#)**

*You must determine donor eligibility on the day of donation, and before collection.*

**Example:** Donors often make requests to expedite the donation process. In the spirit of customer service, a blood collector considered the use of a prepopulated DHQ that would be provided to the donor on the day of donation.

- The DHQ would be prepopulated with information from the donor's most recent donation, but only if the donor had donated in the prior 6 months.
- If returning to donate within 6 months, the donor would review the prepopulated DHQ, and either approve it if accurate, or update it as needed.
- On the day of donation, the donor screener would “still go through all the questions and answers with donor one more time before accepting the donor.”

## Use of a Prepopulated Donor History Questionnaire (DHQ) (cont'd)

### Question:

6) Would such a practice be acceptable to FDA?

**FDA RESPONSE:** “There are no FDA regulations or requirements that prohibit you from providing the donor with his or her prior responses at the time of their return, but we do have some concerns about this process. First, FDA has recognized and accepted the AABB DHQ materials, including the User Brochure. The current User Brochure does not include this process. Second, the donor may not pay the same attention to the questions compared to answering each question individually. Lastly, we have not previously reviewed this process. The process should be validated to ensure the eligibility of the donor and to make sure it is determined in a manner consistent with the regulations and found acceptable by FDA. If you intend to use this process, please contact the FDA and ask to speak to your consumer safety officer.”

## Dental Implants

**Background: General donor eligibility requirements at [§630.10\(e\)\(1\)](#) state:**

*How do you assess the donor's medical history?... Your assessment must include each of the following factors:*

*(1) Factors that make the donor ineligible to donate because of an increased risk for, or evidence of, a relevant transfusion-transmitted infection... including (ii) Receipt of blood or blood components or other medical treatments and procedures associated with possible exposure to a relevant transfusion-transmitted infection.*

**Question:**

**7) Is a one-year deferral required for a donor with a dental implant using allograft demineralized bone matrix?**



## Dental Implants (cont'd)

**FDA RESPONSE:** “One of themes that you will notice here is that we are going to be asking the blood centers or the responsible physician to make some determinations, so you will keep on hearing this over and over again. For this question, FDA does not have specific deferral requirements for blood donors who present with a history of dental implants using allograft demineralized bone matrix. Generally, demineralized bone is a collagen matrix of allograft bone that after extensive processing contains no blood, cells, and minerals. Typically, the preparation of such grafts entails a detailed donor screening, recovery and disinfection processes. Therefore, it is our thinking that in most cases, there is an unlikely risk of an Relevant Transfusion Transmitted Infection (RTTI) transmission. Despite this, I think the blood establishment’s responsible physician should evaluate the source of the graft to determine the eligibility of the donor.”

## Ebola - Countries with Widespread Transmission

**Background:** We hear about Ebola outbreaks in the news. As blood establishments review SOPs to stay prepared for an Ebola outbreak, there is some confusion about where to find the necessary information from Centers for Disease Control and Prevention (CDC).

In the January 2017 Guidance, [Recommendations for Assessment of Blood Donor Eligibility, Donor Deferral and Blood Product Management in Response to Ebola Virus](#), Section III. states:

“The recommendations in section III.A.2. and III.B. should be implemented when the CDC has classified one or more countries as having **widespread transmission** of Ebola virus. We recommend that you continue to follow the recommendations for 4 weeks after the date CDC classifies the last affected country as a country with **former widespread transmission**... (See <http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/distribution-map.html> for CDC’s classification of countries with reported Ebola cases and for the specific dates when a country is classified as a country with former widespread transmission of Ebola virus.)”



## **Ebola - Countries with Widespread Transmission (cont'd)**

**Example:** Throughout the guidance, FDA refers to a CDC webpage that now has the title of [2014-2016 Ebola Outbreak Distribution in West Africa](#) yet the webpage contains no recent information. In addition, the webpage [Current Outbreaks](#) provides more recent information but nothing on widespread transmission. Our quality approach drives us to try to verify the absence of widespread transmission.

### **Questions:**

8) Did CDC change the webpage content or titles?

9) In the absence of a change, what is the best way to confirm that CDC still has not identified widespread transmission of Ebola?

**FDA Response:** “FDA worked closely with CDC to develop the Ebola guidance and as Sharon explained, the guidance states that the recommendations should be implemented when the CDC has classified one or more countries as having widespread transmission

## **Ebola - Countries with Widespread Transmission (cont'd)**

of Ebola virus. CDC provided that specific link for us to include in the guidance. So, FDA confirmed with CDC that they intend to post the information (if there is widespread transmission) on that webpage listed in the guidance. So, that is the webpage to check. Currently, there are Ebola cases in the Democratic Republic of Congo, but the situation is not considered widespread transmission, so there is no information posted. No news is good news. If CDC makes the determination that there is widespread transmission of Ebola, FDA will work with CDC to assure that the information is posted on that webpage, given in the guidance document, and will make efforts to make the appropriate announcements through the regular channels.”

## Non-English-Speaking Donors

### Background: Regulations at [§630.10\(b\)](#) state:

*You must provide educational material concerning relevant transfusion-transmitted infections to donors before donation... You must present educational material in an appropriate form, such as oral, written or multimedia, and in a manner designed to be understood by the donor.*



### Questions:

10) What are FDA's expectations for collecting from a non-English speaking donor?

**FDA Response:** "FDA's expectation is that the educational material is presented in a manner where the donor understands, and this can include ensuring the materials are in the donor's language."



## Non-English-Speaking Donors (cont'd)

11) Should a translation of the DHQ be “certified”?

**FDA Response:** “There are no FDA requirements for a certified translation.”

12) Should all information and educational materials presented to the donor be in the form of a validated translation or could a fluent family member or staff member perform this translation?

**FDA Response:** “There are no FDA requirements for a validated translation. We have the following concerns about using a family member to translate the materials used for donor screening. First, the family member may not understand the terms in the materials and therefore not provide an accurate translation. Second, the employee present during the process may not be fluent in that language and will not be able to assess if the translation is correct. Third, as you know, the DHQ asks the donor about high-risk behaviors. It is possible, that the donor may not feel comfortable providing truthful information about any high-risk behavior when a family member is present. There are other methods that may be more reliable, such as translated materials, bilingual employees, or a translation service.”

## A Beer with Lunch

**Background:** We hear a lot of things from our donors and then have to determine what to do!! **Regulations at [§630.10\(e\)\(2\)](#) present *other factors* that make the donor ineligible:**

*(vi) Whether, in the opinion of the interviewer, the donor appears to be under the influence of any drug, alcohol or for any reason does not appear to be providing reliable answers to medical history questions.*

**Example:** A blood drive is held at a Renaissance Festival. A donor presents to donate and asks if he can donate if he had two beers with his lunch a short while ago. He does not appear to be intoxicated.



### **Question:**

**13)** How would a donor center determine if the donor is “under the influence” if all observations do not suggest a problem?

## A Beer with Lunch (cont'd)

**FDA RESPONSE:** “The regulation states ‘in the opinion of the interviewer.’ Your responsible physician may describe how to handle these situations and should describe these procedures in your SOPs. If you have additional questions, you may always contact your consumer safety officer.”

## **MD Signature for Emergency Release of Blood Products**

**Background:** Questions arise regarding certified registered nurse practitioners and the authority of a physician.

**Regulations at [§606.151\(e\)](#) describe *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.*

**Regulations at [§606.160\(b\)\(3\)\(v\)](#) provide requirements to maintain storage and distribution records for:**

*Emergency release of blood, including signature of requesting physician obtained before or after release.*

AABB Standard 5.27.5 is consistent with the referenced regulations.



## MD Signature for Emergency Release of Blood Products (cont'd)

**FDA RESPONSE:** “Our regulations require a physician’s signature for the emergency release form. This can not be delegated, but do note under [§606.160](#), the signature can be obtained before or after the release of the blood component. Therefore, the Certified Registered Nurse Practitioner as described may still request for blood components in an emergency and subsequently have a physician sign the emergency request. Now if you have this procedure, we recommend that you have procedures in place to determine how long you want a period to elapse before getting a signature from the physician, because my experience is that this happens in emergencies rapidly and that there’s no follow-up to close out the circle. So, it will be nice to have a procedure just to make sure you close the loop.”

## FDA Inspections and Inspection Intervals



**Background:** We have noticed that the interval between inspection varies.

**Regulations at [§600.21](#), Time of inspection, state:**

*An inspection of each licensed establishment and its additional location(s) shall be made at least once every 2 years.*

**Regulations at [§600.22\(a\)](#), Duties of inspector, state:**

*The inspector shall: (a) Call upon the active head of the establishment, stating the object of his visit.*

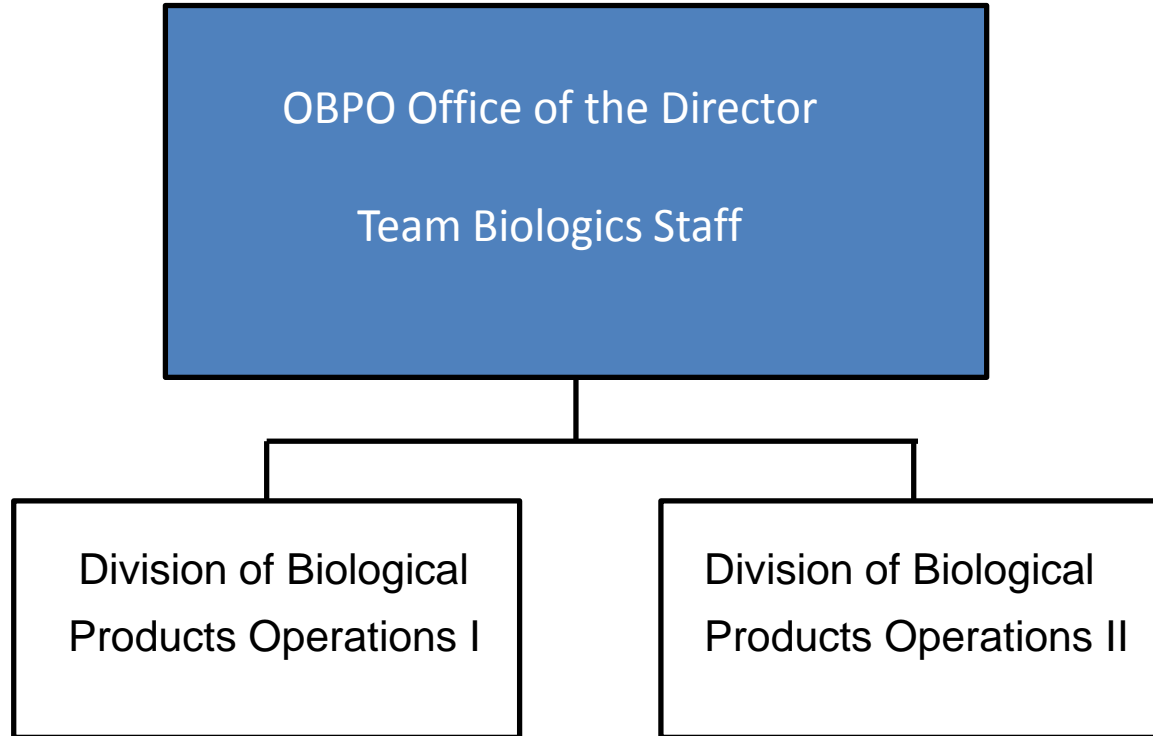
Also, in January 2018, FDA issued a Direct Final Rule (and companion proposed rule) that would have, among other things, eliminated the requirement for a two-year inspection cycle and removed the longstanding requirement to call on the active head of the establishment. It was withdrawn, presumably based on substantive comments. FDA inspections are very rigorous and we would like tools that could be used as we try to ensure our quality system is adequate. There are a variety of questions about FDA inspections.

## 2013 FDA Program Alignment Charge:

*“...Modernize and strengthen the FDA workforce to improve public health response.”*



# Office of Biological Products Operations



# Office of Biological Products Operations



**Biologics Program Divisions**

- Division 1 (ATL, BLT, CIN, FLA, NOL, NWE, NWJ, NYK, PHI, SJJ)
- Division 2 (DAL, DEN, DET, KAN, CHI, LOS, MIN, SAN, SEA)
- FDA Current District Boundaries



# Program Alignment – Why now?

## Context:

- Increasing complexity of products
- Innovation in manufacturing methods/technologies
- Ever-evolving regulatory framework

## Program alignment produced:

- Focused product jurisdiction
- Vertical and horizontal specialization
- Continuity of oversight

# Impacts of Program Alignment - External

- Interactions with one management team nationwide
- Continuity of expertise

## **Various enhancements to:**

- Risk-based selection of facilities for inspection
- Investigator assignments
- Consistency of inspections
- Consistency of compliance recommendations

# Who do I contact following my FDA inspection?

- **E-mail your inspection-related correspondence to:**  
[orabioinspectionalcorrespondence@fda.hhs.gov](mailto:orabioinspectionalcorrespondence@fda.hhs.gov)
- **You can e-mail files under 100 megabytes to:**  
[orabioinspectionalcorrespondence@fda.hhs.gov](mailto:orabioinspectionalcorrespondence@fda.hhs.gov)  
Files larger than 100 megabytes can be submitted as smaller files in separate emails or you can send an FTP link and password for file transfer.
- **Hard copy responses** can be sent to the address of your firm's home district as listed on your FDA-482.

# What other contact information do I need to know?

## OFFICE DIRECTOR

Ginette Michaud – [ginette.michaud@fda.hhs.gov](mailto:ginette.michaud@fda.hhs.gov)

## OFFICE DEPUTY DIRECTOR

Susan Turcovski – [susan.turcovski@fda.hhs.gov](mailto:susan.turcovski@fda.hhs.gov)

## FDA Inspections and Inspection Intervals (cont'd)

### Questions:

15) Why do the FDA inspection intervals at my facility vary from 2 to 3 years and does FDA still have plans to remove the requirement for inspections every 2 years?

**FDA Response:** “FDA inspections are conducted on a risk-based schedule, as outlined in the [‘Food and Drug Administration’s Safety and Innovation Act,’ Section 705](#), which replaces the biannual inspection requirement. The risk-based inspection schedules vary based on the compliance history of the establishment and other factors, so you can refer to the [‘Compliance Program Guidance Manual 7342.001; Inspection of License and Unlicensed Blood Banks, Brokers, Reference Laboratories, and Contractors’ Part IID, ‘Frequency of Scheduling of Inspections.’](#)”

## FDA Inspections and Inspection Intervals (cont'd)

**16)** For some organizations, FDA continues to “strike fear” in the hearts of those who are inspected – Is there a checklist that could be used to help a facility prepare for FDA inspections and, more importantly, to ensure policies and procedures comply with FDA requirements?

**17)** With “many oversight organizations” moving to a “more transparent format of assessing a facility,” does FDA have plans to create tools with consolidated information to assist those who are inspected?

**FDA Response:** “Obviously, the whole point of our inspections is not to ‘strike fear’ in anyone. We put our pants on one leg at a time just like all of you do. That being said, obviously there are differences in personality and certainly some differences in approach with each investigator as to how they conduct their inspection; just as we all have different personalities in this room. We understand that the audit process is difficult and



## FDA Inspections and Inspection Intervals (cont'd)

very stressful for many people. We are all audited ourselves, so we have been on the other side of that. Basically, the whole purpose of us being there is to make sure that you are complying with the federal regulations. That's the endpoint for every inspection. As far as a checklist or a tool with consolidated information, we don't really have such a thing. However, we do use the 'Compliance Program' to conduct our inspections. Probably, the easiest way you can find that is if you just Google '[Compliance Program](#).' For blood it's [7342.001](#). For plasma it's [7342.002](#). The compliance programs will come right up. In that document, you'll see what we do during an inspection, what we look at, systems that we cover."

**18)** What is the scope of an FDA inspection of a Transfusion Service currently performing cell washing, post storage leukoreduction, and/or irradiation?

## FDA Inspections and Inspection Intervals (cont'd)

19) And will that inspection focus solely on those procedures or will it also include processes like QC, inventory management, transfusion reactions, and crossmatch?

**FDA Response:** “If you are a transfusion service and maybe you do some cell-washing that requires you to register, or you irradiate something that triggers you to have to register, we will come and do an inspection at your facility and we will do a comprehensive inspection. Again, just referring to the ‘[Compliance Program](#),’ it shows you all the areas that we cover during our systems-based inspections. We will cover the areas that apply to you, so if you’re doing cell-washing, we won’t just look at your cell-washing process. We will look at all of the applicable systems that you have at your site.”

## Maximum Red Cell Volume Loss

**Background:** Blood establishments must accurately determine red blood cell loss.

**Donor eligibility requirements in [§630.15\(a\)](#) specific to Whole Blood, Red Blood Cells and Plasma collected by apheresis state:**

*(a) What additional donor eligibility requirements apply when you, an establishment that collects blood or blood components, collect Whole Blood or Red Blood Cells by apheresis?*

*(1) Donation frequency must be consistent with protecting the health of the donor.*

*(i) For a collection resulting in a single unit of Whole Blood or Red Blood Cells collected by apheresis, donation frequency must be no more than once in 8 weeks, and for apheresis collections resulting in two units of Red Blood Cells, the donor must not donate more than once in 16 weeks.*

## **Maximum Red Cell Volume Loss (cont'd)**

In FDA's December 2007 [Guidance for Industry and FDA Review Staff: Collection of Platelets by Automated Methods](#), Section VII.B.3. describes donor monitoring and red cell loss:

*Under 21 CFR 640.3(b), a person may not serve as a source of Whole Blood more than once in 8 weeks. In any such assessment, and in assessing a donor's RBC loss during the past rolling 12-month period, the RBC loss associated with the collection of Platelets, Pheresis, and including any other donation type (i.e., Whole Blood, RBC by apheresis), should also be considered.*

Questions arise regarding donor safety.

### **Questions:**

**20)** If a donor only donates whole blood, do I need to track RBC and plasma losses for that donor? And if the donor decides to “cross-over to apheresis” for double red cell donations, do I need to track their RBC and plasma losses to ensure the maximum loss limits for RBCs is not exceeded?

## Maximum Red Cell Volume Loss (cont'd)

**FDA Response:** “If a donor donates only whole blood, tracking the interval of donation is sufficient. If a donor decides to cross-over to apheresis for double red cell donations, monitoring the interval of donation is also sufficient, as addressed in the regulations at [§630.15](#).”

**21)** Is there a defined maximum of red cell volume loss for all collections in a rolling 12-month period, or is red cell loss only controlled by regulations concerning donation intervals and pre-donation requirements?

**FDA Response:** “The regulations do not define a maximum red cell volume loss for all collections in a rolling 12-month period. Each establishment should have written SOPs consistent with the regulations for the appropriate donation intervals, donation frequency, and maximum allowable red cell loss per donation. The regulations assessing donor deferral due to red cell loss associated with donation of whole blood, red cells, and

## Maximum Red Cell Volume Loss (cont'd)

plasma by apheresis are found at [§630.15\(b\)\(6\)](#). Regulations addressing deferral of plateletpheresis donor due to red cell loss are found at [§640.21\(f\)](#).”

22) The volume of red cells lost during an apheresis collection can be obtained from the instrument but how would you go about recording the red cell loss from a whole blood collection?



## Maximum Red Cell Volume Loss (cont'd)

**23)** Should it be calculated to capture the difference for each donor based on their hematocrit, collection volume/type, etc.?

**FDA Response:** “Red cell loss due to whole blood donation is managed with donation interval, but in response to these specific questions, I will add that FDA does not have any requirements or recommendations for methods to calculate or record the volume of red blood cell loss from any donation. The methods used for tracking red cell loss may be determined by the individual blood establishment in a manner that is feasible for the establishment’s operations and consistent with the regulations. Each establishment must maintain written procedures that explain how calculation and monitoring of red blood cell loss is performed.”

## Red Cell Loss for Apheresis Platelet Donation

**Background:** Donors must also be protected by limiting unexpected red cell loss as a result of plateletpheresis.

**Platelet donor eligibility requirements at [§640.21\(f\)\(3\)](#) state:**

*Deferral of plateletpheresis donors due to red blood cell loss.*

*(3) You must defer a donor for 8 weeks or more if the cumulative red blood cell loss in any 8-week period could adversely affect donor health.*

Refer to Table 2, page 18, of the 2007 Guidance, Collection of Platelets by Automated Methods:

<b>Donor's <u>Initial</u> packed RBC loss</b>	<b>Donor's <u>Second</u> packed RBC loss <u>within 8 weeks</u></b>	<b>Eligibility</b>
Less than 200 mL	No donation or total from initial and second loss less than 200 mL	No deferral of donor for packed RBC loss; frequency of donation of Platelets, Pheresis as discussed in section III.B.2
Less than 200 mL	More than 200 mL but less than 300 mL total	Donor is not eligible to donate for 8 weeks from 2nd loss
More than 200 mL but less than 300 mL	NA	Donor is not eligible to donate for 8 weeks from initial loss
Less than 200 mL	Total loss from initial and second loss of more than 300 mL	Donor is not eligible to donate for 16 weeks from the 2nd loss
300 mL or more	NA	Donor is not eligible to donate for 16 weeks from initial loss.



## Red Cell Loss for Apheresis Platelet Donation (cont'd)

### Question:

24) Does this indicate that our center must establish an 8-week RBC loss limit for successful donations for all apheresis donors, OR does this apply only to scenarios where there is a procedure without rinseback?

**FDA Response:** “Table 2 in the 2007 Guidance [Collection of Platelets by Automated Methods](#) provides guidance for deferrals based on red cell loss for all apheresis collection procedures. This includes procedures that are considered successful, meaning those where rinseback was given and those where rinseback was not given. Deferral of plateletpheresis donors is based on the cumulative red cell loss. As noted in the question, it’s found at [§640.21\(f\)\(3\)](#), which states that you must defer a donor for 8 weeks or more, if the cumulative red blood cell loss in any 8-week period could adversely effect donor health. So, the specific answer to this question is yes. The blood establishment should have written procedures establishing an 8-week red blood cell loss limit for plateletpheresis donors.”

## **Apheresis Platelet Quality Control**

**Background:** In the 2007 Guidance for Industry, [Collection of Platelets by Automated Methods](#), Section X. provides information on submission of a CBE-30: *CBE-30:*

*We recommend two months of QC data for actual platelet yield and volume, pH, and residual WBC count (if requesting approval for Leukocytes Reduced platelets).*

### **Question:**

**25)** For the purposes of meeting the time frame of “two months,” does the FDA consider 30 consecutive days as equivalent to a month, or should this be calculated from the 1st of a month to last day of the month?

**FDA Response:** “Your facility can decide how you want to define a month in your SOPs and your facility should be following those SOPs. The FDA does not have regulations regarding this.”

## Blood Establishment Computer Systems (BECS) and Duplicate Records

**Background: Compatibility testing requirements in [§606.151\(a\)](#) state:**

*Standard operating procedures for compatibility testing shall include the following: A method of collecting and identifying the blood samples of recipients to ensure positive identification.*

**Example 1:** Unresolved duplicate patient records that are not merged in the Blood Establishment Computer System (BECS).

**Questions:**

**26)** What are the requirements for duplicate patient record checking in the BECS?

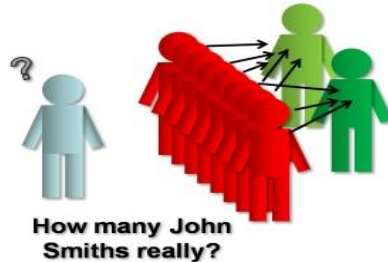
**FDA Response:** “FDA does not have software requirements for duplicate patient record checking for transfusion services. The April 2013 [Guidance for Industry Blood Establishment Computer System Validation in the User’s Facility](#), discusses the initial

## Blood Establishment Computer Systems (BECS) and Duplicate Records

validation of your BECS to include instances to prevent duplicate donor records and deferral codes when converting from a legacy system.”

27) Is it acceptable to leave potential duplicate patient records unmerged in our BECS if we cannot determine with certainty that both records are for the same patient? If yes, what is the recommended procedure?

**FDA Response:** “We do not have specific requirements on when it is acceptable to merge duplicate patient records. We agree that you should not merge patient records that are not verified to be from the same patient. Your facility should have a validated process in place to check for duplicate records on a routine basis and verify which record contains the correct information.”



## BECS and Additional 510(k) Cleared Software

**Background:** To determine donor eligibility, we utilize:

- Our BECS for all donor eligibility determination (whole blood, apheresis, etc.).
- And another 510(k) cleared software system for our apheresis donors that interfaces directly with our apheresis collection devices.

This 510(k) cleared software system that interfaces directly with the collection device:

- Makes more specific calculations for “actual volume loss” based on the prospective collection – which differs from our BECS which utilizes conservative estimates to calculate prospective loss volumes for a collection.
- Counts the actually number of days within a rolling calendar year – which differs from our BECS which calculates based upon today’s date plus 12 months.

As a result, we sometimes encounter a donor that is eligible within the 510(k) cleared software system, but not in the BECS. However, we have validated and documented that utilizing the 510(k) cleared system’s donor eligibility criteria for donation interval, frequency, annual loss limits, etc. would defer a donor who should not be collected and would not put the donor at risk for collection.

## **BECS and Additional 510(k) Cleared Software (cont'd)**

**28)** Based on the example, can that 510(k) cleared system be used to determine the donor's eligibility for donation that day rather than the BECS?

**FDA Response:** “From the information provided, the 510(k) cleared software system appears to be a BECS, since it determines donor eligibility. If you have validated the 510(k) cleared software system to determine eligibility and it is part of your standard operating procedure, then the 510(k) cleared software system can be used to determine the donor eligibility on the day of donation.”

## Donor Notification

**Background:** Some donor centers work with the State Public Health Department for the donor notification process.

**Regulations at [§630.40\(a\)](#) state that a blood establishment:**

*...must make reasonable attempts to notify any donor...who has been deferred based on the results of tests for evidence of infection with a relevant transfusion-transmitted infection(s),... you must also notify a deferred donor of the results of the further testing.*

**Example:** As part of the donor notification process, a donor center provides a donor notification letter (from the donor center's medical director to the donor) to be delivered to the donor at the time of a visit by a state public health official, per the department's policy. This qualified, trained public health representative performs the notification on behalf of both the donor center and state health department to ensure timely and accurate notification, which is the preference of the state health department. All steps are documented by the donor center. The state confirms the notification has been completed.

## Donor Notification (cont'd)

29) Is this an acceptable notification process under [§630.40\(a\)](#) OR must the donor center contact the donor directly by letter?

**FDA Response:** “This is a broad question and I’ll attempt to provide a general response that highlights the specifics of the regulation. The regulation at [§630.40\(a\)](#) addresses the requirements for donor notification of deferral, based on the results of tests for evidence of an infection with an RTTI. FDA’s interpretation of this regulation is that the blood establishment is ultimately responsible for donor notification of deferral. The regulation states that an establishment must make reasonable attempts to notify any such deferred donor and then outlines the following specifics regarding the content of that notification under [§630.40\(b\)](#). The notification should inform the donor that they are deferred from donating and the reason for that decision. The notification should also include the types of blood or blood components that the donor is ineligible to donate. It should include the results of the test that are the basis for the decision to defer and it should provide



## Donor Notification (cont'd)

information from medical follow-up and counseling where applicable. In addition, [§630.40\(c\)](#) states that an establishment should make reasonable attempts at notifying deferred donors within eight weeks after the determining that the donor is deferred or determined not to be eligible for donation. It also states that you must document that you have successfully notified the donor or when you are unsuccessful, that you have made reasonable attempts to notify the donor. To summarize, the regulations are not specific about the method of delivery of donor notification, but a blood establishment may determine the mode of delivery that is feasible for their operations. Ultimately, each blood establishment is responsible for having written procedures in place that will ensure that notification occurs during the required time period, that the notification contains the required content, and that documentation of successful notification is maintained.”

## Therapeutic Phlebotomy for Testosterone Therapy

**Background:** Proper labeling is required for therapeutic collections.

**Regulations regarding therapeutic phlebotomy at [§630.15\(a\)\(2\)](#) state:**

*...under a prescription to promote the donor's health, you may collect from the donor more frequently than once in 8 weeks for collections resulting in a single unit of Whole Blood or Red Blood Cells, or once in 16 weeks for apheresis collections resulting in two units of Red Blood Cells, provided that the container label conspicuously states the disease or condition of the donor that necessitated phlebotomy.*

*However, no labeling for the disease or condition is required under this section if:*

- (i) The donor meets all eligibility criteria;*
- (ii) The donor undergoes a therapeutic phlebotomy as prescribed by a licensed health care provider treating the donor for:
  - (A) Hereditary hemochromatosis; **or****



## Therapeutic Phlebotomy for Testosterone Therapy (cont'd)

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

### **Questions:**

**30)** Does part (ii) (B), “in accordance with a procedure that has been found acceptable for this purpose by FDA” mean that blood collectors must have an Approved Variance for collection from donors on testosterone therapy?

**Example:** Some centers would like to use collections from a donor needing phlebotomy to treat erythrocytosis due to high elevation or smoking, if the donor meets all eligibility requirements and there is a written prescription from a licensed health care provider.

## Therapeutic Phlebotomy for Testosterone Therapy (cont'd)

**FDA Response:** “When we reviewed this question, we felt that we need to clarify, first of all, what we mean by a variance and also clarify the regulation [§630.15](#). Just to clarify the definition of a variance, under [§640.120](#), blood establishments must submit a request for an exemption or alternative procedure to the requirements in 600 to 680 of the regulations. So basically, if we have a regulation in place and you choose to do something different from the regulation, then you request a variance. I think the confusion here comes from our previous regulation and then our new regulation. As many of you remember, in the past we had §640.3(d) which actually doesn't exist anymore. That regulation basically required you to put special labeling on a blood product if it was collected from a donor in order to treat them, so a therapeutic phlebotomy. In that case, when we had that regulation, if you wanted to collect from a donor with hereditary hemochromatosis for example, and use that component for transfusion, you had to request a variance of §640.3(d). Now, in place of §640.3(d), we have a revised

## Therapeutic Phlebotomy for Testosterone Therapy (cont'd)

regulation, [§630.15](#) and I'm going to focus more on a(2). This regulation outlines requirements for collections performed to promote a donor's health. So, e.g. a therapeutic phlebotomy for which you want to use the blood for transfusion. In addition, compared to the old regulation where we said you must label, if you wanted to not label, you had to request a variance. This one kind of provides accommodations for not labeling. In addition, this regulation provides conditions for when no labeling for the disease or condition is required. So, we have part A, which is your hereditary hemochromatosis, and then we have part B, which lists another disease or condition. Now, there are conditions for part B. Under [§630.15\(a\)2\(ii\)\(B\)](#), if a blood establishment intends to collect blood from a donor, in order to promote their health, the blood establishment must submit a procedure to FDA for review and can implement this procedure when the FDA finds this procedure acceptable for this purpose. As stated in the regulation, FDA's considerations for this procedure would be that the health of the

## Therapeutic Phlebotomy for Testosterone Therapy (cont'd)

donor with that disease or condition would not be adversely affected by donating and the donor's disease or condition would not adversely affect the safety, purity, and potency of the blood and blood components or any products manufactured from there. So, these are the things we will look at when you submit your request to FDA, and then we'll decide to approve. Bottomline, you have to submit a request or procedure to FDA, so that FDA can determine that these procedures are acceptable. This is not a request for a variance. You're just trying to comply with [§630.15\(a\)\(2\)\(ii\)\(B\)](#) in this case. So, consistent with [§601.12](#), if you are a licensed blood establishment, you can submit this as a prior approval supplement for FDA review. Back to question 30. For therapeutic phlebotomy donors on testosterone therapy, a variance is not required, but you must submit your procedure to FDA for review and can implement this procedure when FDA finds the procedure acceptable.”

## Therapeutic Phlebotomy for Testosterone Therapy (cont'd)

31) Would elevation or smoking be considered “another disease or condition” that would not “adversely affect the safety, purity, and potency” of the donated components and therefore not require an Approved Variance?

**FDA Response:** “Once again, I hope I’ve clarified that in this case, you will not be submitting a variance. You will be submitting a request or a procedure to FDA to review and approve. So, just remember, as I talked about [§630.15\(a\)\(2\)\(ii\)\(B\)](#), this applies to disease conditions for which the blood is being collected to promote the donor’s health. In this situation, you’re describing a donor who has a prescription from a physician for a therapy phlebotomy, so that is to promote their health. If a physician determines that an individual has a condition for which a therapeutic phlebotomy is necessary to promote their health, then yes, such a donor would fall under this regulation and the blood establishment would need to submit their procedure for FDA approval. FDA will then

## Therapeutic Phlebotomy for Testosterone Therapy (cont'd)

determine whether this procedure is acceptable, looking at the donor health impact and also the product safety, purity and potency to make this decision. So now, we talked about this internally. I don't know how often this happens. I'm assuming there will be different situations and different scenarios. So, once again, if you do encounter this and you want to establish a program to collect routinely from a donor who has erythrocytosis because of smoking, although there are other things that you can do to treat that situation, if you do want to establish such a program, please do contact FDA. Contact your CSO and we can provide additional advice.”





# Ask the FDA

Cellular Therapy (CT)

TUESDAY, OCTOBER 16

## Use of Unproven Cellular Therapies

### **Background:**

There are several facilities and clinics in the United States that are advertising cellular therapies for unproven or experimental indications.

**32)** What enforcement actions and future plans does the FDA have to aid in stopping the proliferation of these clinics?

**FDA Response:** “Information about the agency’s inspection and surveillance activities including whether the agency is considering action is generally not made available to the public unless and until compliance action is taken. We encourage patients and healthcare providers to report adverse events or any other concerns associated with the cellular therapies to FDA. When FDA has learned of information about clinics offering unproven stem cell treatments, the agency has been and remains actively engaged. FDA is committed to ensuring that patients have access to safe and effective regenerative medicine products within the framework of FDA regulation.”

## Sample Collection and Sample Separation

**Background:** Cord blood units are collected and shipped to the cord blood bank, along with maternal whole blood samples for donor testing. The bank receives the product and samples and then sends the donor testing samples to the testing facility.

NAT package inserts allow sample separation and refrigeration within 72-hours. This generally takes place after shipment of the product and samples to the bank as outlined above. The entire kit (cord blood and samples) are shipped at 15-25 C.

### **An example of the problem:**

The manufacturer's (Abbott) package insert for the following infectious disease testing kits states that the sample requirements are (serum or plasma) at 2 – 8 C for up to 14 days:

- Treponema pallidum, HBsAg, HBcAb, HTLV I/II, HCV
- However the facility process is to store and ship the maternal samples at 15 – 25 C. The samples are accepted at the cord blood bank within 48 hours and the samples are then

## Sample Collection and Sample Separation (cont'd)

sent to the testing laboratory where they are usually received (separated & refrigerated if necessary) and tested within another 24 hours approximately. No documentation is available from the manufacturer or testing lab to confirm this process is acceptable.

**33)** Can the FDA provide clarification on how facilities should address the period between sample collection and sample separation if no guidance is given in the test manufacturer's package insert?

**FDA Response:** “Before I address the question regarding sample collection, I just wanted to clarify that first statement – ‘cord blood units are collected and shipped to the cord blood bank, along with maternal whole blood samples for donor testing.’ Just wanted to clarify that in the cord blood donation setting, the baby is the donor and not the mom. While we understand that you are referring to the samples that will be used for testing for relevant communicable disease agents and diseases, we just want to emphasize

## Sample Collection and Sample Separation (cont'd)

that the baby is the donor, not the birth mother. So, going onto the question, according to the [§1271](#) regulations, donor testing for relevant communicable diseases must be performed in a CLIA-certified laboratory using appropriate FDA licensed, approved, or cleared donor screening tests in accordance with the manufacturer's instructions. You can find this requirement in [§1271.80\(c\)](#). We did pull the package inserts and the package inserts for each of the donor screening assays that were referenced include instructions for specimen collection and preparation. So, the appropriate donor specimen storage and shipping conditions are described in the package insert of each test. If there is a question about the instructions of a specific infectious disease assay, you may contact the manufacturer of the assay for more information. We also noted that there was a question referring to infectious disease testing for treponema pallidum / syphilis manufactured by Abbott, but the name of the assay was not specified, so we are not sure which assay this is referring to. Please be advised that you must use a licensed,

## Sample Collection and Sample Separation (cont'd)

approved or cleared donor screening test. The use of diagnostic tests is not acceptable for testing of HCT/P donors. So, because this question relates to the use of contract testing laboratories, it is important to also discuss the requirements related to the manufacturing agreements under [§1271.150\(c\)](#). When an HCT/P establishment, such as a cord blood bank, engages another establishment, for example a donor testing laboratory, under an agreement or contract to perform a manufacturing step for them, each establishment must comply with those requirements applicable to the operation that they perform. Also, before entering into to a contract you must ensure that the contact establishment is in compliance with the applicable regulations. The current good tissue practices guidance document includes recommendations about the ways the manufacturers can ensure that their contractors are in compliance with the regulations. For example, for the scenario described in the question, the cord blood bank and the testing laboratory would need to ensure responsibilities are listed in the contract and

## **Sample Collection and Sample Separation (cont'd)**

understood. The cord blood bank may review the package insert of tests that are used by the testing laboratory to ensure that they are storing and shipping the specimens in accordance with the manufacturer's instructions. The contract testing laboratory is also responsible for ensuring specimens for testing are stored and prepared in accordance with the manufacturer's instructions. Some testing laboratories provide instructions to their clients regarding the sample requirements. These are some of the key points to consider and address before you enter into the contract for a manufacturing agreement.”

## Cellular Therapy Requests for Research-Related Purposes or Further Manufacture

### **Background:**

Cellular therapy facilities may receive requests for waste products for research-related purposes. Additionally, cord blood units may be requested for use for “further manufacture.”

### **Questions:**

**34)** What factors does FDA recommend cellular therapy facilities to consider for release?

**35)** How is the FDA addressing the acquisition of umbilical cord blood units from either established cord blood banks or cord blood/tissue collectors by firms that “further manufacture” these units into “stem cell” therapy products that are distributed nationally and internationally?

**36)** Same question as above – substitute “stem cells” from cord tissue, Wharton’s Jelly, placental tissue, etc., for umbilical cord blood.



## Cellular Therapy Requests for Research-Related Purposes or Further Manufacture (cont'd)

**FDA Response:** “I’m going to answer all three questions at once, and the answer is going to be divided into two parts. First, regarding the waste products for research related purposes. We’re understanding that you mean that this is not for human use, so not for human infusion. So, if the HCT/Ps are intended for non-clinical research use, they’re accepted from the requirements of [§1271](#). You can find this exception in [§1271.15\(a\)](#), so if you’re not going to do anything for human use and its totally for research, you can follow your institutional policies for release and you’re exempt from the 1271’s, but you must look at the exceptions in [§1271.15\(a\)](#). Now, if the HCT/P was originally intended for clinical use, but because the donor was determined to be ineligible or does not meet other criteria, you intend to make that HCT/P available for non-clinical purposes, in such cases, you must label the HCT/P for non-clinical use only and with the biohazard legend. These rules are in the [§1271.65\(c\)](#). You may also want to refer to some of the state

## Cellular Therapy Requests for Research-Related Purposes or Further Manufacture (cont'd)

requirements for use of human cells or tissues for research. Again, not for human use. For example, some states may have requirements for obtaining donor consent or authorization if donor cells or tissues are used for non-clinical research and the FDA is not able to provide any advice regarding the state requirements. The second part of the question has to do with further manufacture. Further manufacture is a very broad term and without more specifics, it's going to be difficult for us to respond. As many of you heard, some of the sessions in the past few days, biologics can be a drug, it can be a device. So, for any HCT/P, you need to consider the regulatory framework in the 1271's. If your HCT/P meets all the requirements in [§1271.10\(a\)](#), it is regulated solely under section 361 of the PHS, or Public Health Service Act and 1271 or 21 CFR Part 1271. So, the 361 HCT/Ps are not subject to premarket review. The HCT/Ps that don't meet all the four criteria in [§1271.10\(a\)](#), again, they're regulated as drugs, devices, or biological

## Cellular Therapy Requests for Research-Related Purposes or Further Manufacture (cont'd)

products and they're subject to the premarket review requirements. So, manufacturers of this HCT/P must comply with the 1271's, including the requirements for CT and the Good Tissue Practices as well as the Good Manufacturing Practices and the device Quality System Regulations, or whatever's applicable. So, again, depending on what the further manufacture is, different sets of rules apply."

## List of BSE-Affected Countries Applicable to Donor Deferral

### **Background:**

The list of BSE-affected countries applicable to donor deferral can be found in the August 2007 guidance document, [Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products \(HCT/Ps\)](#). There could be an event of a breakup of a country. For example, Yugoslavia is on the BSE-affected countries list. However, Yugoslavia is now divided into Serbia and Montenegro.

**37)** What does FDA recommend regarding donor screening of Bovine Spongiform Encephalopathy (BSE) affected countries in countries that no longer exist and have formed into “new” countries?

**FDA Response:** “We really appreciate this question and we thank you. It will be considered in any future guidance updates and it actually gives me the opportunity to read a lot about the geography of Yugoslavia, which is great. The risk for variant CJD and exposure to bovine transmissible spongiform encephalopathy are assessed based on geographic areas of risk, as you’re aware. According to the [2007 CT guidance](#), persons who spend five years or

## List of BSE-Affected Countries Applicable to Donor Deferral (cont'd)

more cumulatively in Europe from 1980 until the present are considered to have risk factors for variant CJD and should be determined ineligible. Now, in the appendix 5 of that CT guidance, it provides a list of the CT countries, which includes Yugoslavia, for assessing donors based on geographic risk of BSE. So, although Yugoslavia is now divided into two countries, Serbia and Montenegro, they're still in the same geographic area within Europe. So, in your donor screening procedures, you may include an updated list that includes all three, meaning the former Federal Republic of Yugoslavia, Serbia, and Montenegro. So, if your donor answers a question depending on the year, all of your areas are covered.”

## Donor Screening – Incarceration

### **Background:**

In the August 2007 guidance document, [Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products \(HCT/P\)](#), risk factors and conditions are specified for screening a donor. Specifically, “8. Persons who have been in juvenile detention, lock up, jail or prison for more than 72 consecutive hours in the preceding 12 months (Refs. 29, 67, and 68) (risk factor for HIV, Hepatitis B and Hepatitis C).”

**38)** Is there any reason to exclude a donation if the donor’s partner or person with whom they live has had a recent history of incarceration?

**FDA Response:** “The 2007 CT guidance includes the list of conditions related to risk factors for HIV, Hep B, and Hep C as referenced in the question. As it was described in the questions, these conditions are related to the time spent in incarceration, so its not so much incarceration as it’s the risk exposure. Specifically, according to the CT guidance,

## Donor Screening – Incarceration (cont'd)

an HCT/P donor who has been in juvenile detention, lock-up, jail or prison for more than 72 consecutive hours in the preceding 12 months, should be determined ineligible because of the risk factors of HIV, Hep B, and Hep C. However, this does not extend to the donor's partner or person with whom the donor has lived, even if the partner or person with whom they've lived has a recent history of incarceration.”



# ASK CMS/CLIA

TUESDAY, OCTOBER 16



## Competency Assessment Responsibility-Laboratory Director

### **Background:**

According to Clinical Laboratory Improvement Amendment (CLIA) Brochure #10:

*Documented competency assessment is required for individuals fulfilling the following personnel responsibilities outlined in Subpart M of the CLIA regulations: clinical consultant (CC), technical consultant (TC), technical supervisor (TS), general supervisor (GS) and testing personnel (TP).*

### **Requirements at [42 CFR 493.1235](#) state:**

*As specified in the personnel requirements in subpart M, the laboratory must establish and follow written policies and procedures to assess employee and, if applicable, consultant competency.*

## Competency Assessment Responsibility-Laboratory Director (cont'd)

According to a CMS presentation “*The Why’s & Wherefore’s of CLIA Competency Evaluation:*”

*...a Laboratory Director serving as TC, CC, TS &/or GS isn’t subject to competency requirements.*

In the “COLA Meaningful Competency Assessments” (2015) the following was provided:

*Q: Who evaluates competency of LD or Clinical Consultant?*

*A: Competency assessment is not required for the Lab Director. The Lab Director responsibilities will be evaluated in detail at the time of survey. If the Clinical Consultant and the Lab Director are the same person, competency assessment is not required. If they are two different people, then competency assessment is required for the Clinical Consultant. This should be done by the Lab Director and is simply a review to determine if the CLIA responsibilities of the position are being met.*

## Competency Assessment Responsibility-Laboratory Director (cont'd)

**CMS Response:** “The CMS presentation *‘The Why’s & Wherefore’s of CLIA Competency Evaluation’* predates CLIA Brochure #10 – *‘What do I Need to Assess Personnel Competency?’* which was published in 2013.

- Brochure #10 reflects the current interpretation of the competency assessment requirements, which is that a competency assessment must be performed on the individual(s) serving as the CC, TC, TS, and/or GS based upon their regulatory responsibilities.
- However, if any of these individuals is performing testing or reporting patient test results, the six procedures of competency assessment also apply.
- If there’s a sole practitioner, the sole practitioner must establish a minimal level of proficiency in order to demonstrate competency.
- This could be accomplished via testing of proficiency testing samples or another entity reviewing the work to determine competency.
- With regards to the ‘COLA Meaningful Competency Assessments,’ please ask COLA to explain their work.”

## Competency Assessment Responsibility-Laboratory Director (cont'd)

**Example:** Laboratory Director 1, who is qualified as a Laboratory Director under [§493.1235](#), contracts (delegates) with Laboratory Director 2, to perform the non-testing responsibilities for the CLIA roles of Technical Supervisor, Clinical Consultant, Technical Consultant and General Supervisor in his laboratory. Laboratory Director 2 is qualified in their own laboratory as a Laboratory Director under [§493.1235](#) but under a different CLIA certificate.

### **Question:**

**40)** Is Laboratory Director 1 responsible for performing competency assessment for Laboratory Director 2, even though they are currently qualified in their own laboratory and are routinely assessed through their own laboratory accreditation?

## **Competency Assessment Responsibility-Laboratory Director (cont'd)**

**CMS Response:** “The CLIA qualifications for Laboratory Director are at [§493.1405](#) for moderate complexity laboratory director and [§493.1445](#) for high complexity laboratory director.

The CLIA requirements at [§493.1235](#) are that the laboratory must establish and follow written policies and procedures to assess employee and, if applicable consultant competency.

The Interpretive Guidelines (IGs) for [§493.1235](#) (provided below) state that documented competency assessment is required for the TC, CC, TS and GS.

### **Competency Assessment Guidelines**

Technical consultant, clinical consultant, technical supervisor, general supervisor  
Documented competency assessment is required for the following named positions on the Form 209: technical consultant, clinical consultant, technical supervisor, general

## **Competency Assessment Responsibility-Laboratory Director (cont'd)**

supervisor. The laboratory must have policies and procedures to assess competency based on the position responsibilities listed in Subpart M and these assessments must be performed at a frequency determined by the laboratory. Cite D5209 ([§493.1235](#)). If these people perform testing on patient specimens, they are required to have the six required procedures in their competency assessment in addition to a competency assessment based on their federal regulatory responsibilities (see [§493.1413\(b\)\(8\)](#) / [§493.1451\(b\)\(8\)](#)). In the example provided, since Laboratory Director 2 is serving as the TC, CC, TS and GS in Laboratory Director 1's laboratory, then 'YES' Laboratory Director 1 is responsible for performing the competency assessment on Laboratory Director 2 based on the regulatory responsibilities of the CC, TC, TS and GS."

## Competency Assessment Responsibility and Intervals

### **Background:**

Requirements at [§493.1413\(b\)\(9\)](#) and [§493.1451\(b\)\(9\)](#) address the Technical Consultant (TC) and Technical Supervisor (TS) Responsibilities, including evaluating and documenting the performance of individuals responsible for moderate complexity testing at least semiannually during the first year the individual tests patient specimens and at least annually thereafter.

### **Questions:**

**41)** For competency assessment: What does “annually thereafter” mean? Is it 12 months from a specific date (identify whether initial or last competency in the 1st year) or is it the next calendar year from 1 January through 31 December?

**CMS Response:** “The laboratory must follow its own policy for determining when the year begins. The laboratory may coordinate the competency assessment with its routine practices and procedures to minimize impact on workload.”

## Competency Assessment Responsibility and Intervals (cont'd)

42) Does the technical supervisor have to sign off initial training and competency of new staff; or can that be delegated to the general supervisor based on [§493.1463 \(b\)\(4\)](#) which lists the responsibilities of the General Supervisor (GS) as: “Annually evaluating and documenting the performance of all testing personnel.”

**CMS Response:** “If the TS delegates, in writing, the responsibility for performing and documenting competency assessments to the GS, then it’s the GS’s written responsibility to perform and document the competency assessment.”



## CLIA Certification Requirements for Donor Centers

### Background:

#### Requirements at [§493.15](#) state:

*Laboratories performing waived tests. (c) Certificate of waiver tests. A laboratory may qualify for a certificate of waiver under section 353 of the PHS Act if it restricts the tests that it performs to one or more of the following tests or examinations (or additional tests added to this list as provided under paragraph (d) of this section) and no others: (9) Hemoglobin by single analyte instruments with self-contained or component features to perform specimen/reagent interaction, providing direct measurement and readout.*

### Question:

**43)** Do donor centers, whether they do infectious disease testing or simply hemoglobin/hematocrit testing, require CLIA certification?

## CLIA Certification Requirements for Donor Centers (cont'd)

**CMS Response:** “The CLIA definition of a laboratory (provided below) is found at [§493.2](#):

*‘Laboratory’ means a facility for the biological, microbiological, serological, chemical, immunohematological, hematological, biophysical, cytological, pathological, or other examination of materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings. These examinations also include procedures to determine, measure, or otherwise describe the presence or absence of various substances or organisms in the body. Facilities only collecting or preparing specimens (or both) or only serving as a mailing service and not performing testing are not considered laboratories.*

Donor centers that simply perform hemoglobin/hematocrit as well as donor centers that do infectious disease testing are performing testing that meets the CLIA definition of a laboratory, so ‘YES’ a CLIA certificate is required.”

## CLIA Certification for Bacterial Testing

**Background:** Our establishment is currently using the BacTAlert System for initial platelet bacterial detection to qualify our apheresis platelets to day-5. We are performing Proficiency Testing (PT) for this assay purchased through CAP. BacTAlert is only performed on platelet products and a positive test result would not be reported to the donor's physician to act upon. It would only be reported to the recipient's physician as a positive test. CLIA provided us the following explanation for determining if a test is regulated by CLIA: "If the results of the test do not go to a medical provider to use in diagnosis, monitoring or prevention of disease, then it is not a CLIA regulated test."

### **Question:**

44) Does the BacTAlert testing we perform qualify as a CLIA test?

**AABB Response:** "It is important to note that assumption is incorrect in this statement, 'If the results of the test do not go to a medical provider to use in diagnosis, monitoring or prevention of disease, then it is not a CLIA regulated test' based on the regulations in

## CLIA Certification for Bacterial Testing (cont'd)

### 21 CFR 606.145 Control of bacterial contamination of platelets which state:

*...The transfusion service must take appropriate steps to identify the organism... The transfusion service must further notify the blood collection establishment either by providing information about the species of the contaminating organism when the transfusion service has been able to identify it, or by advising the blood collection establishment when the transfusion service has determined that the species cannot be identified.*

**AND CFR 630.40(a)**. The May 2015 final rule discusses the importance on notifying platelet donors based tests to identify the organism, stating:

*'We have finalized the donor notification provisions in §630.40. Consistent with the proposed rule, §630.40(a) requires establishments to notify donors whose platelet component has tested positive for a bacterial contamination that is likely due to an*

## CLIA Certification for Bacterial Testing (cont'd)

*infection endogenous to the bloodstream of the donor, such as Streptococcus bovis. Identification of this bacterium indicates that the donor may have a serious health condition such as colon cancer.”*

**CMS Response:** “Facilities that perform BacTAlert testing on platelets and report the test result(s) to the platelet recipient’s physician, for the purpose of providing the physician information for the recipient’s health care/management, would need to obtain a CLIA certificate.”

**Again, we refer you to the AABB response that begins on slide 91** and corrects the assumption in the question. AABB is highlighting the fact that the results of the positive culture on a platelet product and further testing to identify the organism are required (by FDA and AABB) to protect to health of the both the donor and potential recipient(s). This information will help determine if the presence of certain bacteria indicates “that the donor may have a serious health condition, such as colon cancer” as highlighted above. The donor must be notified.

## CLIA Certification for Bacterial Testing (cont'd)

45) If it does qualify as a CLIA test, does our microbiology department need to perform PT, given that per [§493.801](#) PT is required for only the test system, assay, or examination used as the primary method for patient testing during the PT event?

**CMS Response:** “The BacTAlert testing performed on platelets as a CLIA test is subject to proficiency testing (PT). This test, however, is not found in Subpart I of the CLIA regulations so the laboratory must meet the CLIA requirements at [§493.1236 \(c\)\(1\)](#), provided below:

***§493.1236 Standard: Evaluation of proficiency testing performance.***

*(c) At least twice annually, the laboratory must verify the accuracy of the following:*

*(1) Any test or procedure it performs that is not included in subpart I of this part.*

## CLIA Certification for Bacterial Testing (cont'd)

### **Refer to subpart I, Proficiency Testing Programs for Nonwaived Testing.**

Subpart I includes those specialties, subspecialties, analytes and tests that are considered regulated tests. For those tests not listed in subpart I (not regulated), the laboratory must verify the accuracy of the test or procedure twice annually, including the accuracy of calculated results, if applicable.

For those tests not listed under Subpart I, the laboratory may enroll in a PT program to verify the accuracy of their test or procedure. However, under no circumstances may these PT samples be referred (or results communicated) to another laboratory for any reason prior to the PT testing event cut-off date. The PT referral consequences (loss of certificate and bar on owner/operator) apply equally to all PT testing samples and results. (See D2013).”

## CLIA Certification for Verax testing to Extend Platelet Dating

**Background:** This past summer we began performing Verax rapid bacterial testing to extend the shelf life of our platelets to day-6 and day-7.

### **Question:**

**46)** Is this test covered under CLIA for which we would have to perform proficiency testing and full competency assessment?

**CMS Response:** “The purpose for performing the test determines whether or not the test is subject to CLIA. Testing that is not performed for purposes of clinical treatment, medical diagnosis, health assessment or disease prevention is not subject to CLIA. If the results of the Verax rapid bacterial testing are reported then the testing is subject to CLIA.”



# THANK YOU

Contact Regulatory Affairs  
at

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