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Toolkit for Transfusion Services: FDA Registration Requirements when Extending Platelet Expiration to Day-6 or Day-7 as Described in the December 2020 Platelet Bacterial Risk Control Guidance

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TABLE OF CONTENTS:

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I. OVERVIEW/QUESTIONS & ANSWERS

Skip ahead to the Instructions in Section II unless you have questions…

- **The information provided in this section comes from the December 2020 Platelet Bacterial Risk Control Guidance, Section V. TRANSFUSION SERVICES—REGISTRATION AND BLOOD PRODUCT LISTING, page 13:**

Which activities require Transfusion Service registration with FDA?

- The implementation of a bacterial detection device that is used to re-label a platelet product with a **6 or 7-day expiration date**, thereby extending the dating of the platelet product, is a **manufacturing procedure requiring registration** and blood product listing, as described in 21 CFR 607.3(d).
- If you are a transfusion service that is currently exempt from registration and blood product listing under the provisions of 21 CFR 607.65(f), and you implement a bacterial detection test to determine the suitability of platelet products to be released on day 6 or day 7 after collection, 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.

Which activities do not require Transfusion Service registration with FDA?

- Transfusion services that implement secondary testing on platelets with a **5-day expiration date are not required to register** and list because they are not extending the dating period of platelets.

- **The information provided in this section comes from the following FDA webpages:**

- Blood Establishment Registration and Product Listing
- Blood Establishment Registration - Frequently Asked Questions
- BER Instructions for Completing the Electronic Blood Establishment Registration and Product Listing Form

When must I register?

- Establishments must be registered, and products listed **within 5 days of beginning operation**, and **annually between October 1 and December 31**. Blood product listings must be updated every June and December.

An Establishment DUNS Number is required to submit a registration. What is a DUNS Number and how do I obtain one?

- The DUNS Number is a unique nine-digit identifier for businesses which is generated by Dun & Bradstreet. DUNS number is the required Unique Facility Identifier in accordance with the system specified under section 510 of the Federal Food, Drug, and Cosmetic Act (see 21 CFR 607.25(a)).

- For more information on DUNS Numbers, including methods for obtaining a DUNS, please visit the Dun & Bradstreet website.

- **AABB NOTE:** Most hospital systems have a preexisting DUNS number. Search the DUN and Bradstreet database using the DUNS Number Lookup tool or contact your administration or financial department prior to beginning a new application.

How do I register?

- Electronic submission of blood establishment and product listing information is now required under 21 CFR 607.22, unless waived in certain circumstances. Blood establishments that must register and list

electronically under 21 CFR part 607 should use the electronic blood establishment registration (eBER) system to meet the requirement for electronic submission of establishment registration and product listing.

What happens after I register?

- Once you submit your initial registration to us, we will send a copy of the summary report to your local district office. The Blood Registration Monitor in the district office will contact you to confirm that you are in operation and are registering appropriately. The Monitor will assign your establishment an FEI, and will notify us of your FEI. We will print a summary report and email it to you to keep for your records.
  We will inspect your blood manufacturing operations periodically to ensure that you are following applicable regulations and recommendations. Refer to Title 21 of the Code of Federal Regulations (21 CFR), parts 600 through 660 for regulations related to manufacturing blood products. Our recommendations are available on the Internet at https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/blood-guidances**.**

I have always registered as a Hospital Transfusion Service. Now my summary report says I'm a Hospital Blood Bank. Why has it changed?

- If your product listing includes **manufacturing processes** or irradiating blood components that require you to register, we changed your establishment type from Hospital Transfusion Service to Hospital Blood Bank.
- Section V of the guidance, page 13, specifically states:
  Except as provided in 21 CFR 607.65, all owners and operators of blood establishments that engage in the manufacture of blood products must register with FDA and list the blood products they manufacture, pursuant to section 510 of the Federal Food, Drug, and Cosmetic Act and the implementing regulations under 21 CFR 607.7. The implementation of a bacterial detection device that is used to re-label a platelet product with a 6 or 7-day expiration date, thereby extending the dating of the platelet product, is a manufacturing procedure requiring registration and blood product listing, as described in 21 CFR 607.3(d).
- If you are a transfusion service that is currently exempt from registration and blood product listing under the provisions of 21 CFR 607.65(f), and you implement a bacterial detection test to determine the suitability of platelet products to be released on day 6 or day 7 after collection, 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.

What establishment registration type do I select?

- Review the definitions provided by FDA in eBER before making your decision.
- It is likely you will be a **Hospital Blood Bank** which is defined FDA as:
  "A hospital (or establishment located within a hospital) that routinely collects or processes Whole Blood or blood components. A Hospital Blood Bank may collect components by apheresis or prepare them from Whole Blood. Processing includes freezing, deglycerolizing, washing, irradiating, rejuvenating, or leukocyte-reducing Red Blood Cells. We include hospitals that perform autologous or directed collections in this category. Hospital Blood Banks usually perform product testing (such as blood grouping and hepatitis testing), as well as compatibility testing. We consider hospitals that solely prepare Red Blood Cells or Recovered Plasma, pool Platelets or Cryoprecipitated AHF for ease of transfusion, or issue bedside leukocyte-reduction filters with blood components to be Hospital Transfusion Services. A hospital that collects Source Plasma under licensure should also check "Plasmapheresis Center."
- You must register with FDA as a **Hospital Blood Bank** because implementation of a bacterial detection device that is used to re-label a platelet product with a 6 or 7-day expiration date, thereby extending the dating of the platelet product, is a manufacturing procedure requiring registration and blood product listing, as described in 21 CFR 607.3(d).

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What process do I select?

- **Bacterial Testing**: is 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.

➢ **AABB NOTE**: The process definition for bacterial testing has not been updated in the BER instructions to reflect both bacterial testing processes recommended in the December 2020 Platelet Bacterial Risk Guidance. You should use "Bacterial Testing" when completing your registration process. The FDA approved methods are documented on page 2 of the Guidance - "*Secondary testing consists of culture-based or rapid testing methods*," using devices labeled as a *safety measure* to extend dating up to day 7.

What product do I select?

- **Platelets Extended Dating:** Platelets that have been tested for bacteria using an FDA-cleared bacterial detection device labeled as a "safety measure", following testing with a growth-based quality control test cleared by the FDA for platelet components, that can support extending the expiration date of platelets past 5 days. Platelets shall be stored in a container that is approved or cleared to store platelets up to 7 days.

II. INSTRUCTIONS FOR ELECTRONIC SUBMISSION OF AN FDA REGISTRATION

➢ **The information provided in this section comes from the following FDA webpages:**

- Blood Establishment Registration and Product Listing
- Blood Establishment Registration - Frequently Asked Questions
- BER Instructions for Completing the Electronic Blood Establishment Registration and Product Listing Form

Information for Returning Users, editing your User Establishment Profile and Annual Registration activites has been omitted.

Before you begin, read the General Instructions, Navigation and Saving Information sections: BER Instructions for Completing the Electronic Blood Establishment Registration and Product Listing Form

1. On the Internet, go to the FDA Blood Establishment Registration and Product Listing page.
2. Scroll down and click on the link titled "CBER On-Line: Establishment Registration" This will take you to the Login page for CBER On-Line.
3. On the Login page, **if it is the first time you have used CBER On-Line, you will need to create a new account.** Click on the "Create a New Account" link, and follow the on-screen instructions to enter information such as your name, e-mail address, and a username. After you submit your account request, the electronic blood establishment registration (eBER) system will send you separate e-mails with your username and a system-generated password.
4. When you have your user name and password, enter them on the Login page. Click on "Enter CBER On Line." User Name and Password fields are case sensitive. The eBER will prompt you to change your password on initial login (brand new user) or if you have not changed your password in the last 90 days.
5. Click on the Blood Establishment Registration link. **First time users please go directly to instruction number 6, "Initial Registration".**

6. The first time you use eBER, you need to add your establishments to your account. Click on Edit User Establishments Profile. Enter the registration number (FEI) and validated date (located in the top right corner of your last validated registration summary report, "Validated by FDA:") for each establishment, and then click "Add This Establishment." If you cannot locate your last validated summary report, or if eBER does not accept the date you are entering, email the Blood Registration Coordinator. **If your establishment has never submitted an FDA registration, please select "Initial Registration" and begin entering information for a new establishment.**

7. **Legal Name/Location page** – provide the legal name (not the "doing-business-as" or other name, street address, and telephone number of the actual location. Note: The Other Names Used at this location tab allows you to provide any other name by which your facility is commonly known.

8. **Reporting Official page**– enter the Reporting Official's name, institution name if applicable, street address, e-mail address, and telephone number.

9. **U.S. Agent page**– if applicable, enter the U.S. agent name, institution name if applicable, street address, e-mail address, and telephone number. Note: U.S. Agent information is required for non-U.S. establishments.

10. **Owner Type page**– enter the type of ownership under which your establishment operates.

11. **Establishment Type page** – enter your establishment type.

    AABB NOTE: When registering because you are a hospital transfusion service that is **no longer considered exempt because you are engaging in blood product manufacturing** under 21 CFR 607.3(d), you should register as a **"Hospital Blood Bank".**

12. Products/Process page– on the displayed grid, check off the products you manufacture (**Platelets Extended Dating/Bacterial Testing)**

13. On the report screen, verify that your information is correct. From this screen you may:

    - Use the tabs near the top of the page to go to previous screens to make changes
    - Submit your registration. To submit your registration, you must click on the **Submit to FDA for Review** button at the bottom of the Report page. The eBER will display a message that you submitted your information, provide you with a confirmation number, and give you an opportunity to print a report.
    - If you would like to save your registration without submitting. The eBER system will hold your registration information for 30 days before deleting. Write down your pre-confirmation number so that you may access your information later.
    - Print a report with your information

14. If, after you submit the form, you determine that you need to make changes, contact us (FDA) and we will provide instructions.

15. Log out by clicking on the log out link near the top of the page.

III. ADDITIONAL REQUIREMENTS FOR REGISTERED BLOOD ESTABLISHMENTS EXTENDING EXPIRATION TO DAY-6 OR DAY-7

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- **Circular of Information**
  Update your October 2017 Circular of Information to include language consistent with the **December 2020 FDA recommendations** to control the risk of bacterial contamination in platelets stored at room temperature, at the time you implement these recommendations. Acceptable language may be found on AABB's Circular Of Information For the Use Of Human Blood And Blood Components web page.
- **Annual Reporting:**
  21 CFR 607. 21 Times for establishment registration and blood product listing provides the Annual Reporting requirements for registered establishments:
  "The owner or operator of an establishment entering into an operation defined in §607.3(d) shall register such establishment within 5 days after the beginning of such operation and submit a list of every blood product in commercial distribution at the time. If the owner or operator of the establishment has not previously entered into such operation (defined in §607.3(d) of this chapter) for which a license is required, registration shall follow within 5 days after the submission of a biologics license application in order to manufacture blood products. ***Owners or operators of all establishments so engaged must register annually between October 1 and December 31*** *and must update their blood product listing every June and December."*

IV. ADDITIONAL REGULATORY RESOURCES

- Refer to AABB's Comprehensive List of Regulatory Resources for Platelets
  Including links to the AABB Association Bulletin #21-02, AABB Bacterial Risk Reference Sheets a Flowchart for Timelines for Testing Strategies for Apheresis Platelets, Commonly use platelet codes to proactively update your computer system for imported products, ICCBBA's "TB-015 Bacterial testing strategies for Platelets"

- **FDA Links:**
  - FDA's Blood Establishment Registration and Product Listing
  - FDA's Blood Establishment Registration and Product Listing On-Line Contact Form

V. CHECKLIST - FDA REGISTRATION OF A TRANSFUSION SERVICE PERFORMING EXTENSION OF PLATELET EXPIRATION DATING TO DAY-6 OR DAY-7

____ Read Section V, Transfusion Services – Registration and Product Listing, on page 13 of FDA's 2020 Guidance
____ DUNS Number for your facility is established [refer to the DUNS question, page 2 above]
    ____ Determine if your hospital has a preexisting DUNS number using the Dun and Bradstreet DUNS Number Lookup tool.
    ____ Request a DUNS Number if no current DUNS number is identified
____ Navigate to the CBER On-Line: Establishment Registration screen
____ If this is the first time you have used CBER On-Line, you will need to create a new account. Select the "Create a New Account" link, and follow the on-screen instructions to enter information. [refer to #3 above]
____ Once logged in, select "Initial Registration" to begin entering information if your establishment . You will need your establishment DUNS Number on this first screen.
____ Complete the information on each subsequent page:
    ____ Legal Name/Location [refer to #7 above]
    ____ Reporting Official page [refer to #8 above]
    ____ U.S. Agent page [U.S. Agent information is required for non-U.S. establishments – refer to #9 above]

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____ Owner Type page [refer to #10 above]

____ Establishment Type page (Hospital Blood Bank) [refer to #11 above]

____ Products/Process page (Platelets Extended Dating/Bacterial Testing) [refer to #12 above]

____ Report page – verify your information is correct [refer to #14 above]

____ Submit your registration for FDA review OR Save your registration - The eBER system will hold your saved registration information for 30 days before deleting. [refer to #13 above]

____ Print a report

____ Update your October 2017 Circular of Information [refer to Section III above]

____ Register with FDA annually between October 1 and December 31 [refer to Section III above]