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Hospital Forum Minutes
"*Mad Scientist*"
March 29, 2019

Attendees:

Guests: Krista Roberts, Texas Health Arlington Memorial Hospital; Tanya Robohm, Texas Health Dallas; Patti Calcote, UT Health Tyler; Ashley Flores, Cook Children's Medical Center; Rick Melman, BSW All Saints Medical Center; Suzanne Moore, Medical City Dallas; Julia Blackburn, Texas Health HEB; Jessica Gandy, Texas Health Southwest; Tess Attard, Texas Health Southwest; Brian Gibson Methodist Hospital Southlake; David Hanna, Texas Health Presbyterian Rockwall; Janelle Theibaud, Texas Health Harris Methodist Stephenville; Julia Maxwell, Methodist Dallas Medical Center; Jessica Weesner, BSW Sunnyvale; Simeonette Ballesteros, Methodist Dallas Medical Center; Kathy Price, Hunt ER Commerce; Mary Sue Devorss, Hunt Regional Medical Center; Kenni Monk, UT Health Quitman; Robin Mosley, UT Health Pittsburg; Ron Pundt, Coryell Health; Dionne Cook, Central Texas VA; James Burner, MD, UTSW; Josh Combs, Children's Health Dallas; Patricia Tennery, Dallas Medical Center; Liang Shen, THR Fort Worth; Catrina Donnelly, THR Fort Worth; Greg Cusano, MD, THR Fort Worth; Jessica Milne, THR Denton; Cindy Yarborough, THR Fort Worth; Chris Webber, Medical City Lewisville; Candy Schaper, Methodist Hospital for Surgery; Carol Barker, North Texas Medical Center; Dawn Webber, BSW Carrollton; Ann Tabor, Methodist Mansfield Medical Center; Barbara McComas, BSW Carrollton, Frances Compton, MD, UTSW; Kele Crouch, BSW Hillcrest

Carter BloodCare: Dr. Merlyn Sayers, Lavetta Kennedy, Pam Boyd, Judy Thornburg, Dr. Todd Nishimoto, Sandy Wortman, Josey Keep, Marla Boren, B.J. Smith, Dr. Laurie Sutor, Dr. Geeta Paranjape, Fernando Lerma, Clint McCoy, Linda Goelzer, Mike Newhouse, Marie Becerra, Veronica Moore

Maternal Designation for Level of Care – New Texas Law, Laurie Sutor, MD, MBA, Vice President of Medical and Technical Services, Carter BloodCare

- ✓ Presentation handouts attached, review for comprehensive information shared.
  - o Dr. Sutor prompted the group for discussion.

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- Is it worth looking into getting this changed? Can we get some advocacy group to help support possibly making some changes to the requirements?
- Hospital comments:
  - We are one of the hospitals that has implemented and therefore are required to maintain a platelet on site; however, the chances are minimal that we will transfuse.
  - Believe it is more relevant to have cryo on site for maternal hemorrhage
  - It is a requirement to have MTP drills on all shifts
  - It is a requirement to have/participate in a multi-disciplinary meeting
  - Recently had a maternal hemorrhage and the patient used seven platelets in a very short time frame. On that point, what is one platelet going to do?
  - Possible that the intent of the requirement to maintain one platelet on site is to stabilize the patient and transport to a higher level of care.

Supercalifragilisticexpialidocious Blood Banker, Julia Maxwell, MLS (ASCP) SBB, Technical Coordinator, Methodist Dallas Medical Center Presentation handouts attached, review for comprehensive information shared.

- Attendee Questions/Comments
  - Q1: Can you share the cost associated with the SBB program (based on your experience)?
    - Approximately $3-$5,000 per semester dependent on whether this is in-state or out of state tuition.
  - Q2: Do you feel it is very burdensome to meet your continuing education hours?
    - I personally do not feel that it is burdensome.
  - Q3: We put together a 'home grown' study session to challenge the SBB and take the test. Each of us passed.
  - I think it is important to give thought to what each individual's learning style is and this will help you decide if challenging and taking the SBB exam or enrolling into an SBB program is the route to follow.

Molecular Updates, Pam Boyd, BB(ASCP), Manager of Reference and Transfusion, Carter BloodCare

- ✓ Presentation handouts attached, review for comprehensive information shared
  - Attendee Questions/Comments
    - Q1: Now that the test is FDA approved, will there be a different CPT code for billing?

- No, the code is the same.

2018 Customer Satisfaction Survey Summary, **Veronica Moore, MBA, MT(ASCP), Director of Hospital Relations, Carter BloodCare**

- ✓ Presentation handouts attached, review for comprehensive information shared.
  - o Attendee Questions/Comments
    - A client noticed that platelet orders were being automatically cancelled, is this part of the process?
      - Please review the memorandum sent in December 2017 for details regarding the back order process.

Since many of you had concerns regarding our management of product backorders, we distributed a survey asking for your feedback on how to improve this process. As a result, we will be changing backorders for routine stock orders.

Effective **Monday, January 8, 2018**, Carter BloodCare will begin cancelling all routine stock orders not filled by 2359 each day. This means there will be no backorders for stock orders carried over to the next day helping reduce the number of duplicate orders.

This change will not apply to specialty products, Rh negative platelets, or standing orders. This process change should help simplify your ordering. We will evaluate the effectiveness of the change and modify as necessary.

We sincerely appreciate your understanding in helping us manage the community's blood supply. If you have any questions about this new process, please do not hesitate to contact us.

Open Discussion

- ✓ FDA Draft Bacterial Guidance published December 2018 provided in handouts.

A most sincere thank you to the presenters – this program exists because of your generosity to share your knowledge and experiences with the group.

And of course, thank you to all the attendees!

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Maternal Designation for Level of Care – New Texas Law

Laurie J Sutor, MD, MBA
Vice President of Medical and Technical Services

Overview

Background
Impact on blood banking
Future actions

Background

- **Subchapter H of the Health and Safety Code, Chapter 241, Hospitals**
- **Section 241.182 Level of Care Designations**
  - To be able to receive reimbursement through the Medicaid program for maternal services
  - Assigned for maternal and neonatal care services separately
  - Will be minimum criteria to qualify
  - Not related to size of hospital/number of patients
  - Reviewed every three years
  - Starts Sept 1, 2020

Minimum Criteria for Each Level

- **Established by a Perinatal Advisory Council**
- **19 members appointed by the executive commissioner of the Health and Human Services Commission:**
  - 4 physicians specializing in neonatology
  - One physician practicing general pediatrics
  - Two physicians specializing in OB-Gyn
  - Two physicians specializing in Maternal fetal health
  - Two physicians practicing family medicine who do OB in a rural community
  - One RN with expertise in Maternal health care
  - One RN with Expertise in perinatal health care
  - One representative from a childrens' hospital
  - One representative from a hospital with a Level II neonatal intensive care unit
  - Two representatives from a rural hospital
  - One representative from a general hospital
  - One ex officio member for the office of the medical director of the HHS Commission

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Definition of Levels of Service

- **Level I = Basic Care**
  - Lowest level of care
  - Generally healthy patients, no significant risk of maternal morbidity or mortality
  - Blood bank services available on a 24 hour basis
    - Guidelines for massive transfusion
    - Emergency release of components
    - Management of multiple component therapy
  - Written protocols for massive hemorrhage and transfusion of the pregnant or postpartum patient in coordination of the blood bank, including management of unanticipated hemorrhage and/or coagulopathy.

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- **Level II**
  - "Specialty Care"
  - Low to moderate risk of maternal morbidity or mortality
  - Blood bank capable of:
    - providing ABO-Rh specific or O-Rh negative blood, fresh frozen plasma and/or cryoprecipitate, and platelet products on-site at all times
    - Implementing a massive transfusion protocol
    - Ensuring guidelines for emergency release of blood components
    - Managing multiple blood component therapy

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- **Level III**
  - "Subspecialty care"
  - Patients with from low to high risk of maternal morbidity or mortality; complex medical, surgical and/or obstetrical underlying conditions
- **Level IV**
  - "Comprehensive care"
  - The most complex underlying conditions with low to high risk of maternal morbidity or mortality; includes care of fetus
- **Same blood bank services as level II**

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Concerns

- **In the DFW area, many hospitals are applying for this who never stocked platelets before**
- **This is already having a big impact on the local platelet inventory**
- **Most of these hospitals will never use the platelets and they will probably expire**
- **Is there anything we can do to get this law changed?**
- **Any other comments?**

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SUPERCALIFRAGILISTICEXPIALDOCIOUS BLOOD BANKER

Julia Maxwell
MLS(ASCP)SBB
Technical Coordinator
Methodist Dallas Medical Center

Objectives

- My facility, blood bank, and myself
- SBB eligibility and programs
- Reasons to pursue SBB
- Lessons learned and recommendations

Methodist Dallas Medical Center

- 1927
- 585 beds
- Level 1 Trauma
- 20 OR suites
- Transplant Institute
- Level III Neonatal ICU
- Heart Center
- Neuro ICU
- CareFlite

Dallas Blood Bank

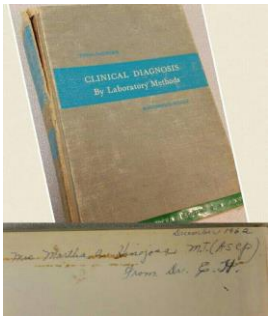
- Hospital system
- 11 Full-time/3 PRN
- No tissues or albumin
- 16000 Transfusions
- Reference testing

Test Menu

ABO/RH
Antibody screen
Antigen typing
Antibody ID
Elution
REST
Titer
FMS
Sickle

Julia Maxwell

- Anatomic Pathology
- CLS
- Generalist
- Blood Bank
- Technical Coordinator



SBB

WHY?	WHY NOT?
• Career advancement	• Family
• Transfusion knowledge	• Cost
• Teach	• Health
• Marketability	• Experience

SBB Eligibility

- ROUTE 1 – SBB program
- ROUTE 2
- ROUTE 3
- ROUTE 4

Degree and Experience

- ROUTE 5
- ROUTE 6

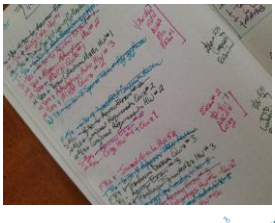
Educator

SBB Programs

- 68% Pass rate
- Curriculum delivery
- Graduate credit
- Certificate
- Student or Employee

Challenges

- Information
- Scheduling
- Organization



What has it done for me?

- Career Advancement
- Respect of peers
- Confidence
- Networking
- Knowledge

Lessons Learned and Recommendations

- Persistence
- Confidence
- SBB is not the end
- Comfortable with distance learning
- Work/school/life balance
- Schedule exam ASAP
- Utilize others

Thank You

- https://www.ascp.org/content/docs/default-source/boc-pdfs/boc_statistical_reports/exam-stats-2017.pdf?sfvrsn=14
- https://www.ascp.org/content/docs/default-source/boc-pdfs/exam-content-outlines/ascp-boc-us-procedures-book-web.pdf
- http://www.aabb.org/development/specialist/Pages/sbbdirectory.aspx

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Molecular Updates

Pam Boyd, BB (ASCP)
Manager of Reference and Transfusion
Carter BloodCare

Molecular Testing Laboratory Updates

- The Molecular Testing lab has moved to Bedford!
- What will change?

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Molecular Testing Laboratory Updates

AABB
Accredited MT Lab

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Molecular Testing Laboratory Updates

- No change on testing frequency

- Molecular Testing will continue to be performed 3 times per week:
  - Approximately Mondays, Wednesday, Fridays

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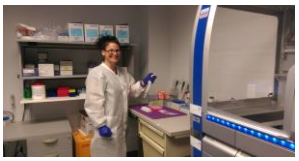
Molecular Testing Laboratory Updates

- Two expert Medical Technologist will be performing the Molecular Testing: **Fernando Lerma & Ami Richards**



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Molecular Testing Laboratory Updates

- MT Kit Changes-
  - Grifols ID Core^{XT} is now FDA Approved

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Molecular Testing Laboratory Updates

- MT Kit Changes-
  - Grifols ID Core^{XT} is now FDA Approved:
    - Software upgrades & Training completed
    - Validation is in progress
    - Projected go live date: **May 1st**
    - No changes will be made to the molecular testing current pricing at this time

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Molecular Testing Laboratory Updates

- MT Kit Changes-
  - Previously on the reports:

This test has not been cleared by or approved by the Federal Drug Administration.

This test uses reagents or kits labeled by the manufacturer as "Research Use Only".

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Molecular Testing Laboratory Updates

- MT Kit Changes-
  - Previously on the reports:

This test has not been cleared by or approved by the Federal Drug Administration.

This test uses reagents or kits labeled by the manufacturer as "Research Use Only".

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Molecular Testing Laboratory Updates

Mark Your Calendar!!

Carter BloodCare Immunohematology & Molecular Symposium

WHEN: Friday, September 13, 8AM – 4PM
WHERE: Texas Star Golf Course, Euless, TX

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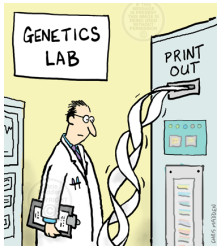
Molecular Testing Laboratory Updates

- Questions?



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Customer Satisfaction Survey

- Hospital Services
- IRL
- Finance
- Hospital Relations/iWeBB
- Special Donations
- Medical Services

HOSPITAL SERVICES

59% Always satisfied with updates: short-dated inventory & substitutes

48% Not always satisfied with updates regarding shipping of back orders

89% Routine
70% ASAP
48% STAT

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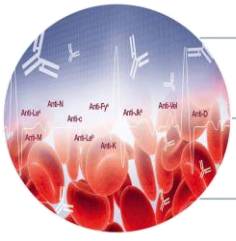
Immunohematology Reference lab



54% Always satisfied with updates

41% Not always satisfied with receipt of final report

75% Always meet TAT for ABID

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Finance
Hospital Relations

Always receive a prompt response

Invoices are always accurate

Incident/inquiry response timely

Contacts/visits satisfactory

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Medical Services & Special Donations

- Consultation
- In-services
- Autologous/directed
- Special programs

Survey feedback

- Too many questions
- Not asking for relevant feedback
- Performance improvement

Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion

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Draft Guidance for Industry

This guidance document is for comment purposes only.

Submit one set of either electronic or written comments on this draft guidance by the date provided in the *Federal Register* notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov/. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
December 2018

Table of Contents

Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion

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Draft Guidance for Industry

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

We, FDA, are issuing this guidance document to provide you, blood collection establishments and transfusion services, with recommendations to control the risk of bacterial contamination of room temperature stored platelets intended for transfusion. The recommendations in this guidance apply to all platelet products, including platelets manufactured by automated methods (apheresis platelets), whole blood derived (WBD) platelets, pooled platelets (pre-storage and post-storage) and platelets stored in additive solutions.

Additionally, this guidance provides licensed blood establishments with recommendations on how to report implementation of manufacturing and labeling changes under 21 CFR 601.12. This draft guidance replaces the draft guidance of the same title dated March 2016.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Room temperature stored platelets are associated with a higher risk of sepsis and related fatality than any other transfusable blood component. The risk of bacterial contamination of platelets is a leading risk of infection from blood transfusion. Bacterial residual risk per transfused unit on the day of transfusion is 1/2300 (Ref. 1), and fatal transfusion reactions from undetected

contaminated platelet collections continue to occur (Ref. 2). This risk has persisted despite numerous interventions, including the widely used method of primary culture to test platelets prior to transfusion (Refs. 3, 4, 5, 6).

The reported rates of septic transfusion reactions from platelets vary from 1/100,000 by passive surveillance to 1/10,000 by active surveillance when testing with primary culture alone (Refs. 1, 7). Surveillance data on platelets stored up to 5 days have shown that 95-100% of platelet transfusion-related septic reactions (Refs. 3, 4, 8) and 100% of associated fatalities have occurred with transfusion of day 4 and day 5 stored platelets (Ref. 8).

FDA has established regulations to address the control of bacterial contamination of platelets. Under 21 CFR 606.145(a), blood establishments and transfusion services must assure that the risk of bacterial contamination of platelets is adequately controlled using FDA approved or cleared devices, or other adequate and appropriate methods found acceptable for this purpose by FDA.

Currently, this risk can be controlled by bacterial testing or pathogen reduction methods. Bacterial testing includes the use of culture-based or rapid detection tests.[1] While primary testing is typically performed by culture and within 24 hours of collection, secondary testing is performed at later times of storage prior to transfusion. Pathogen reduction is performed shortly after platelet collection.

Under 21 CFR 610.53(b), the dating period for platelets with a storage temperature between 20 and 24 degrees Celsius is 5 days from the date of collection, unless a different dating period is specified in the instructions for use by the blood collection, processing and storage system approved or cleared for such use by FDA. Accordingly, implementation of the recommendations in this guidance on extension of platelet dating beyond day 5 is contingent on the use of cleared or approved and suitably labeled platelet storage containers, bacterial detection tests and pathogen reduction devices.[2] The current maximum dating period (expiration date) for platelets in the United States (U.S.) is up to 7 days in the cleared storage containers.

Most recently, FDA convened a Blood Products Advisory Committee (BPAC) meeting in July 2018 (Ref. 9) to discuss bacterial contamination of platelets and strategies to control the risk. At this meeting, BPAC considered the scientific evidence and operational considerations of all available strategies to control the risk of bacterial contamination of platelets with 5-day and 7-day dating, including bacterial testing strategies using culture-based devices, rapid bacterial

[1] Bacterial tests are labeled as a "safety measure" when clinical studies have shown benefit for detection of bacterial contamination not revealed by previous bacterial testing or have analytical sensitivity at least equivalent to a previously cleared "safety measure" device or qualify by other methods found acceptable to FDA.

[2] Currently, storage systems that ensure platelet efficacy past 5 days of storage, and up to 7 days of storage, of platelets treated by pathogen reduction technology (PRT) are not available. Extended dating past 5 days based on pathogen reduction of apheresis platelets may not be implemented until such technologies are approved for use in this blood component (21 CFR 606.65(e)).

detection devices, and the implementation of pathogen reduction technology. The data presented and BPAC's discussion at the July 2018 meeting provided the foundation for the recommendations in this guidance.

III. RECOMMENDATIONS FOR THE CONTROL OF BACTERIAL CONTAMINATION OF PLATELETS

Table 1 summarizes recommended strategies for 5-day platelet storage and 7-day platelet storage.

Table 1. Summary Table of FDA's Recommendations

Recommendations to control the risk of bacterial contamination in platelets		
Dating	Method	Applicable components
5-day storage	Primary culture + secondary culture (no earlier than Day 3)	• Apheresis • Pre-storage pools
	Primary culture + secondary rapid testing	• Apheresis • Pre-storage pools
	Pathogen Reduction Technology	• Apheresis[3]
7-day storage	Primary culture + secondary culture (no earlier than Day 4)	• Apheresis
	Primary culture + secondary rapid testing	• Apheresis
	Large volume delayed sampling[4]	• Apheresis

A. General Considerations

1. Use FDA-cleared or approved bacterial detection tests, pathogen reduction devices, and platelet storage containers.

2. Bacterial detection testing, pathogen reduction, and the use of platelet storage containers must be performed consistent with the instructions for use of the device (21 CFR 606.65(e)).

[3] This strategy could apply to other platelet products in the future if appropriately labeled devices become available.
[4] The instructions for use of the culture-based device currently labeled as a "safety measure" require a primary culture and secondary test to extend dating of platelets. Therefore, the large volume, delayed sampling strategy cannot be implemented until appropriately labeled devices are available.

3. Blood collection establishments and transfusion services should have in place measures to promptly alert the collection establishment or transfusion service if a distributed platelet product is subsequently identified as positive for bacterial contamination.

B. Primary Culture Testing

This section provides general information pertaining to recommendations for primary culture testing. Primary culture testing is used as one of several strategies discussed in this guidance.

Culture-based primary testing should be performed no sooner than 24 hours after collection. Testing should include methods to identify both aerobic and anaerobic organisms. To maximize the sensitivity of the culture, we recommend use of the upper limit of the sample volume range permitted by the device's instructions for each of the aerobic and anaerobic cultures. If you opt to sample a volume larger than the upper limit of the volume range described in the device's instructions for use for one culture, we recommend that the amount of the sample that is in excess of the upper limit volume recommended for use be inoculated into additional culture.

If the instructions for use of the bacterial detection device specify a minimum incubation period, you should release platelet products consistent with the incubation period specified. If the instructions for use of the bacterial detection device do not specify a minimum incubation period, we recommend a minimum incubation period of 12 hours.

C. 5-Day Platelet Storage

The following strategies apply to platelets with 5-day storage:

1. Primary culture followed by secondary culture performed no earlier than Day 3

This strategy applies to apheresis platelets and pre-storage pools and includes the following steps:

- Initial primary culture (see section III.B of this guidance).
- Secondary culture on Day 3 or Day 4.

Secondary culture:

To maximize the sensitivity of the culture, we recommend use of the upper limit of the sample volume range permitted by the device's instructions for use, taken from the main collection, and inoculating the sample into an aerobic media. Use of an anaerobic culture, in addition to the aerobic culture, should be considered.

If the instructions for use of the bacterial detection device specify a minimum incubation period, you should release platelet products consistent with the incubation period specified. If the instructions for use of the bacterial detection device do not specify a minimum incubation period, we recommend that you establish a minimum incubation time period in your Standard Operating Procedures (SOPs).

2. Primary culture, followed by secondary rapid testing

This strategy applies to apheresis platelets and pre-storage pools, and includes the following steps:

- Initial primary culture (see section III.B. of this guidance).
- Secondary testing with a rapid test.

3. Pathogen reduction

This strategy applies to apheresis platelets.[5,6] Platelets that have been treated by pathogen reduction need no further measures because pathogen reduction technology adequately controls the risk of bacterial contamination of platelets

D. 7-Day Platelet Storage

Storage may be extended beyond 5 days if:

- The platelets are stored in a container cleared or approved by FDA for 7-day storage, and
- Individual platelet units are subsequently tested for bacterial detection using a bacterial detection device cleared by FDA and labeled for use as a "safety measure." [7]

The following strategies are recommended for storage of platelets of up to 7 days:

1. Primary culture, followed by a secondary culture with a device labeled as a "safety measure" performed no earlier than Day 4

This strategy applies to apheresis platelets, and includes the following steps:

[5] This strategy could apply to other platelet products in the future if appropriately labeled pathogen reduction devices and storage systems become available.
[6] See footnote 2.
[7] See footnote 1.

- Initial primary culture (see section III.B. of this guidance).
- Secondary culture no earlier than Day 4, using a device labeled as a "safety measure."

Secondary culture:

To maximize the sensitivity of the culture, we recommend use of the upper limit of the sample volume range permitted by the device's instructions for use, inoculated into both an aerobic culture and an anaerobic culture.

If the instructions for use of the bacterial detection device specify a minimum incubation period, you should release platelet products consistent with the incubation period specified. If the instructions for use of the bacterial detection device do not specify a minimum incubation period, we recommend a minimum incubation period of 12 hours.

2. Primary culture, followed by a secondary rapid test labeled as a "safety measure"

This strategy applies to apheresis platelets, and includes the following steps:

- Initial primary culture (see section III.B of this guidance).
- Secondary testing with a rapid test labeled as a "safety measure."

3. Large volume delayed sampling [8]

This strategy applies to apheresis platelets, and includes the following steps:

- A single culture performed using a culture-based bacterial detection device no sooner than 48 hours after collection with a sampling volume of at least 16 mL, inoculated evenly into an aerobic culture and an anaerobic culture.

- Each apheresis unit should be sampled for culture. If the apheresis product is split, each split product should be sampled.

- If the instructions for use of the bacterial detection device specify a minimum incubation period, you should release platelet products consistent with the incubation period specified. If the instructions for use of the bacterial detection device do not specify a minimum incubation period, we recommend a minimum incubation period of 12 hours.

[8] The instructions for use of the culture-based device currently labeled as a "safety measure" require a primary culture and secondary test to extend dating. Therefore, the large volume, delayed sampling strategy cannot be implemented until appropriately labeled devices are available.

E. Post-Storage Pooled Platelets

Transfusion services should perform a rapid bacterial detection test prior to transfusion on pools of WBD platelets if the constituent single units were not previously tested. Post-storage pooled platelets expire 4 hours from the time of preparation (21 CFR 606.122(l)(2)).

F. Single Units of WBD Platelets

Single units of WBD platelets may be stored for 5 days. For single units of WBD platelets that have not been previously tested and are not intended for pooling, testing should be performed according to either or both of the following strategies:

1. Sample no sooner than 24 hours after collection, the largest practical volume within the range permitted by the device's instructions for use and inoculate into a culture. Use of an aerobic and an anaerobic culture may be considered; and/or

2. Perform testing with a rapid test.

G. Labeling

1. Labels on the Container

   a. The container labels must comply with 21 CFR 606.121 and 21 CFR 610.60. Blood collection establishments and transfusion services, as appropriate, must also follow the general requirements for labeling operations described in 21 CFR 606.120.

   b. The container labels must include the expiration date and time, if applicable, of the product based on bacterial detection testing (21 CFR 606.121(c)(4)(i)).

   c. If secondary testing of platelets is performed consistent with this guidance, and the expiration date is extended to 6 or 7 days based on the bacterial testing performed, the blood establishment or transfusion service that performed the secondary testing must update the container label to reflect the new expiration date (21 CFR 606.121(c)(4)(i)).

2. Circular of Information

You must update your Circular of Information to include appropriate statements regarding bacterial detection testing or pathogen reduction (21 CFR 606.122).

IV. REPORTING IMPLEMENTATION OF MANUFACTURING AND LABELING CHANGES

An establishment that distributes platelet products in interstate commerce must have an approved BLA, in accordance with section 351 of the Public Health Service Act.

Licensed establishments must report changes to their approved biologics license applications (BLA) in accordance with 21 CFR 601.12. The information below is intended to assist you in determining which reporting mechanism is appropriate for a change to your approved BLA, as it applies to the bacterial testing of platelet products and the manufacture of apheresis platelets with a 6 or 7-day dating period. [9] You should prominently label each submission with the reporting category under which you are reporting your change, for example, "Prior Approval Supplement," or "Annual Report."

A. Prior Approval Supplement (PAS)

1. Changes requiring supplement submission and approval prior to distribution of the product made using the change (21 CFR 601.12(b)).

Under 21 CFR 601.12(b), changes that have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product must be reported to FDA in a Prior Approval Supplement (PAS). You must not distribute in interstate commerce blood components made using a new or changed manufacturing process requiring a PAS until you have received our approval of your PAS (21 CFR 601.12(b)(3)).

We believe a PAS submission is appropriate in the following situations:

a. You are currently licensed to manufacture apheresis platelets with a 5-day expiration date and you choose to extend the storage time to a 6-day or 7-day expiration date and distribute these products in interstate commerce.

2. To comply with the requirements in 21 CFR 601.12(b)(3), you must include the following minimum information in your PAS submission:

[9] FDA's recommendations for the implementation of pathogen reduction are addressed in the guidance document titled, "Implementation of Pathogen Reduction Technology in the Manufacture of Blood Components in Blood Establishments: Questions and Answers; Draft Guidance for Industry," dated December 2017. The draft guidance, when finalized, will represent FDA's current thinking on this topic.

a. Form FDA 356h, "Application to Market a New or Abbreviated New Drug or Biologic for Human Use."

b. List of the platelet products involved.

c. Address and registration number of the manufacturing facility/facilities.

d. A detailed description of the manufacturing process. We recommend the submission of written standard operating procedures (SOPs) that include:

    i. Component manufacturing (if these SOPs were previously approved by FDA, include the reference number under which they were reviewed).
    ii. Bacterial detection testing, including the name of the devices(s) used for bacterial detection, when the platelet product is sampled and when the product will be released.
    iii. How to label the platelet product based on the results of the bacterial detection testing and the timeframe after which the negative results are no longer valid.
    iv. Measures to alert the consignee that a distributed platelet product has tested positive for bacterial contamination.
    v. Quarantine and disposition of unsuitable products.
    vi. Investigation of units with positive test results.
    vii. A communication plan to notify your consignees the type of storage container the platelets are stored in, for example, a storage container approved for 5-day storage or for 7-day storage and when the bacterial detection testing was performed.

e. The name, address and registration number, if available, of any contractors who are performing bacterial detection testing of platelet products for you.

f. Validation plan for the bacterial detection testing method and a summary of the validation data.

g. Two consecutive months of quality control data for the pH at expiration or on the date the product is issued for each platelet product type that will have the expiration date extended based on bacterial detection testing.

h. Labeling – include the following in your supplement:

i. Container Labels: A container label for each platelet product, unless previously approved by FDA, that includes the expiration date and time, if applicable, of the platelet product based on bacterial detection testing.

ii. Circular of Information.

3. You may also consider submitting a Comparability Protocol as a PAS under 21 CFR 601.12(e). A Comparability Protocol is not required, but an approved Comparability Protocol may justify a reduced reporting category for manufacturing apheresis platelets with a 6-day or 7-day expiration date in multiple locations. In addition to the content listed in section IV.A. of the guidance, Comparability Protocol (21 CFR 601.12(e)) submissions must also include the plan for implementing the bacterial detection testing at multiple manufacturing sites. The plan should include a description of how you will validate the new procedures.

B. Annual Report

Under 21 CFR 601.12(d), changes in the product, production process, quality controls, equipment, facilities, or responsible personnel that have a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product must be documented in an annual report submitted each year within 60 days of the anniversary date of approval of the BLA.

We believe the following changes may be submitted in an Annual Report[10] noting the date the process was implemented:

1. Implementation of bacterial detection testing as described in this guidance without modification and the expiration date of apheresis, single units of WBD platelets, and pre-storage pooled WBD platelets remains at 5 days.

2. You or your contractor change from one type of FDA cleared bacterial detection device to another type of FDA-cleared bacterial detection device.

NOTE: For assistance in reporting your changes, see FDA's "Changes to an Approved Application: Biological Products: Human Blood and Blood Components Intended for Transfusion or for Further Manufacture; Guidance for Industry" dated December 2014.

[10] See 21 CFR 601.12(a)(3).

The December 2014 guidance represents FDA's current thinking on this topic and can be found on FDA's website at: https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htmn/Guidances/Blood/ucm354559.htm.

V. TRANSFUSION SERVICES—REGISTRATION AND BLOOD PRODUCT LISTING

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). 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.

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.

Instructions on how to register electronically with FDA can be found on FDA's website at: https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/EstablishmentRegistration/BloodEstablishmentRegistration/default.htm.

VI. IMPLEMENTATION

We recommend that you implement the recommendations contained in this guidance within 12 months after the final guidance is issued.

VII. REFERENCES

1. Jacobs MR, Smith D, Heaton WA, et al., Detection of bacterial contamination in prestorage culture-negative apheresis platelets on day of issue with the Pan Genera Detection test, *Transfusion*, 2011; 51(12): 2573-2582.

2. Fatalities Reported to FDA Following Blood Collection and Transfusion Annual Summary. https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/default.htm.

3. Hong H, Xiao W, Lazarus HM, et al., Detection of septic transfusion reactions to platelet transfusions by active and passive surveillance, *Blood*, 2016; 127(4): 496-502.

4. Benjamin RJ, Transfusion-related sepsis: a silent epidemic, *Blood*, 2016; 127(4): 380-381.

5. Fuller AK, Uglik KM, Savage WJ, et al., Bacterial culture reduces but does not eliminate the risk of septic transfusion reactions to single-donor platelets, *Transfusion*, 2009; 49(12): 2588-2593.

6. Horth R, Jones J, Kim J, et al; Fatal sepsis associated with bacterial contamination of platelets – Utah and California, August 2017, *MMWR Morb Mortal Wkly Rep*, 2018; 67(25): 718-722. https://www.cdc.gov/mmwr/volumes/67/wr/mm6725a4.htm

7. Eder AF, Dy BA, DeMerse B, et al; Apheresis technology correlates with bacterial contamination of platelets and reported septic transfusion reactions, *Transfusion*, 2017; 57(12): 2969-2976.

8. Benjamin RJ. Blood Products Advisory Committee, September 21, 2012, transcript accessible at https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/BloodProductsAdvisoryCommittee/ucm552872.htm

9. Blood Product Advisory Committee, July 18, 2018, transcript accessible at https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/BloodProductsAdvisoryCommittee/ucm597841.htm