

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

Guidance for Industry

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Contains Nonbinding Recommendations

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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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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.¹ The recommendations in this guidance apply to all platelet products stored at room temperature in plasma or additive solutions, including platelets manufactured by automated methods (apheresis platelets), and Whole Blood derived (WBD) single and pooled (pre-storage and post-storage) platelets.

Additionally, this guidance provides licensed blood establishments with recommendations on how to report implementation of manufacturing and labeling changes under Title 21 of the Code of Federal Regulations (CFR) 601.12.

This guidance updates the final guidance of the same title dated September 2019. The September 2019 guidance finalized the draft guidance of the same title dated December 2018. We received numerous comments from blood collection establishments requesting an extension of the implementation timeframe because of various unforeseen challenges, including responding to the COVID-19 public health emergency. Consequently, we have extended the recommended implementation timeframe in section VI. of the guidance. In addition, we clarified the recommendations for submission of information in a prior approval supplement submission in section IV.A.2.f. and g. of the guidance. We also removed a footnote regarding the lack of appropriately labeled devices for implementation of the large volume, delayed sampling no sooner than 48 hours strategy for a 7-day dating period in section III.B.1.b. of the guidance because of a recent device clearance.

¹ Cold storage (1 to 6°C) of platelet products as a strategy to control bacterial risk is outside the scope of this guidance document. However cold storage of platelets may be found acceptable by FDA as an approach to assure that the risk of bacterial contamination is adequately controlled. Blood establishments should discuss with FDA methods of preparation and storage of cold-stored platelets.

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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 estimated at about 1/2500 (Ref. 1), and fatal transfusion reactions from undetected contaminated platelet collections continue to occur (Refs. 2, 3). This risk has persisted despite the implementation of numerous interventions, including the commonly used method of a single culture performed no sooner than 24 hours after collection of the platelets (Refs. 1, 3, 4, 5, 6).

The reported rates of septic transfusion reaction from platelets vary from 1/100,000 by passive surveillance to 1/10,000 by active surveillance, following testing with single culture performed no sooner than 24 hours after collection (Refs. 1, 7). Surveillance data on platelets stored up to 5 days have shown that 95 to 100% of platelet transfusion-related septic reactions (Refs. 4, 8) and 100% of associated fatalities (Ref. 8) have occurred with transfusion of day 4 and day 5 stored platelets.

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, the bacterial contamination risk in room temperature stored platelet products can be controlled by bacterial testing or pathogen reduction methods. Pathogen reduction is typically performed shortly after platelet collection.

Bacterial testing is performed using culture-based or rapid detection devices. Primary testing is the initial bacterial detection test, usually by culture methods, performed following collection. Primary testing is typically performed using at least an aerobic culture, with sampling of the platelets occurring no earlier than 24 hours after collection. The use of an additional anaerobic culture can enhance the detection of obligate anaerobic organisms, which have been associated with the occurrence of septic transfusion reactions (Ref. 6), and can shorten time to bacterial detection of certain organisms (Ref. 9). However anaerobic bacterial testing is associated with higher false positive rates (Ref. 10) than with aerobic testing alone. Secondary testing is any additional test of a platelet component to detect bacteria in a unit that showed no bacterial contamination upon primary testing. Secondary testing consists of culture-based or rapid testing methods.

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Under 21 CFR 610.53(b), the dating period (expiration date) 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. Consistent with this requirement, the recommendations in this guidance on extension of platelet dating beyond day 5 may not be implemented absent the use of cleared or approved and suitably labeled platelet storage containers, bacterial detection, and pathogen reduction devices². In the United States (U.S.), the current maximum dating period) for platelets with a storage temperature between 20 and 24 degrees Celsius is up to 7 days in the FDA-cleared or approved storage containers.

Since 2012, FDA has held three Blood Products Advisory Committee (BPAC) meetings to address bacterial risk in platelet products. The most recent BPAC meeting, in July 2018 (Ref. 11), discussed the scientific evidence and operational considerations of 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 and rapid bacterial detection devices) and pathogen reduction technology. Subsequently, FDA published the December 2018 draft guidance. Comments to the published draft guidance documents, as well as the BPAC 2018 proceedings, provided the foundation for the recommendations in this guidance.

III. RECOMMENDATIONS

A. General Considerations

1. The recommendations in this guidance entail the use of FDA-cleared or approved bacterial detection devices, pathogen reduction devices, and platelet storage containers.
2. Bacterial detection testing, pathogen reduction, and storage in platelet containers must be conducted consistent with the instructions for use of the device (21 CFR 606.65(e)).
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.
4. Depending on the recommendation, sampling or testing time in this guidance is expressed in units of hours or days:

² At the time of finalization of this guidance, 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)).

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- a. When timing is expressed in units of hours, it is in reference to the actual hour of collection or sampling. For example, if a platelet product is collected at 9 am (0:900) on January 1st, sampling performed no earlier than 24 hours from time of collection means that sampling should be performed no earlier than 9 am (0:900) on January 2nd; sampling performed no earlier than 36 hours means sampling no earlier than 9 pm (21:00) on January 2nd.
 - b. When timing is expressed in units of days, it is in reference to the day of collection, which is considered day 0. A day is defined as beginning at midnight (00:00) and ending at 23:59. Expiry day refers to 23:59 of the stated day (i.e., prior to midnight). For example, if a platelet is collected on January 1st (day 0) at 9 am (0:900) with a 5-day storage period, it means it will expire at 23:59 on January 6th.
 - c. When sampling is recommended to be conducted on a specific day, it means that sampling can occur at any time on that day prior to midnight, regardless of the time of the initial collection. For example, if a platelet is collected on January 1st at 9 am (day 0), secondary culture performed on day 3 should be performed on January 4th, at any time prior to midnight.
5. Products may be shipped during the recommended culture incubation periods, provided the blood collection establishment establishes procedures to maintain control of the product during the incubation period.
 6. Blood collection establishments and transfusion services must not release for transfusion platelets identified as bacterially contaminated (21 CFR 606.145(b) and (c)).
 7. Following secondary testing, it is not expected that blood collection establishments or transfusion services *retest* units to determine platelet yield.
 8. Blood collection establishments and transfusion services should establish procedures to assure traceability of the bacterial testing status of platelet products in their inventory.

B. Strategies for Apheresis Platelets and/or Pre-Storage Pools of WBD Platelets

The recommended strategies for apheresis platelets and pre-storage pools of WBD platelets are either single-step *or* two-step. Each strategy will include the applicable platelet component and dating period (up to 5 days, or up to 7 days). Please see Appendices A and B to this guidance for summary tables of the strategies described in section III.B. of the guidance. Example timelines for the strategies for apheresis platelets are provided in Appendix D to this guidance.

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1. Single-step Strategies

Implementation of a single-step strategy entails the conduct of one step:

a. Large volume, delayed sampling (LVDS) no sooner than 36 hours

This strategy applies to apheresis platelets and pre-storage pools of WBD platelets, and consists of:

1. A single culture with sampling performed no sooner than 36 hours after collection using a sampling volume of at least 16 mL, inoculated evenly into aerobic and anaerobic culture media.
2. Sampling each apheresis unit or each pre-storage pool of WBD platelets for culture. If the apheresis product will be split, each split unit should be sampled.

We recommend a minimum incubation period of 12 hours prior to release for transfusion.

Dating:

Products should be labeled with a 5-day expiration.

Note: LVDS conducted no sooner than 36 hours may also constitute Step 1 of a 2-Step strategy to extend storage beyond 5 days. See section III.B.2. of this guidance for additional detail.

b. LVDS no sooner than 48 hours

This strategy applies to apheresis platelets and consists of:

1. A single culture performed no sooner than 48 hours after collection using a sampling volume of at least 16 mL, inoculated evenly into aerobic and anaerobic culture media.
2. Sampling each apheresis unit for culture. If the apheresis product will be split, each split unit should be sampled.

We recommend a minimum incubation period of 12 hours prior to release for transfusion.

Dating:

Products should be labeled with an expiration of up to 7 days.

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Note: Bacterial testing to extend dating beyond day 5 and up to day 7 should be performed with devices labeled with LVDS as an acceptable safety measure.³ Platelet storage containers must be cleared or approved by FDA for 7-day storage.

c. Pathogen Reduction

Based on current device labeling, this strategy applies to apheresis platelets. The strategy could apply to other platelet products in the future if appropriately labeled pathogen reduction devices and storage containers become available. Platelets that have been treated by FDA approved pathogen reduction devices according to the device instructions for use need no further measures to control the risk of bacterial contamination of platelets.

Dating:

Pathogen reduced components should be labeled with expiration dates consistent with the instructions for use for the pathogen reduction device, currently 5 days (see section III.A.2. of this guidance).

2. Two-step Strategies

Implementation of a two-step strategy entails the conduct of two successive steps, Steps 1 and 2.

a. Step 1

Step 1 consists of one of the following:

i. Primary culture performed no sooner than 24 hours

This applies to both apheresis platelets and pre-storage pools of WBD platelets, and consists of:

1. A culture performed no sooner than 24 hours after collection with a sampling volume of at least 16 mL, inoculated evenly into aerobic and anaerobic culture media
2. Sampling each apheresis collection or each pre-storage pool of WBD platelets. If the collection will be split into multiple units, either the main collection alone ('mother bag') or split units may be tested.

We recommend a minimum incubation period of 12 hours.

³ Bacterial testing devices are labeled as a "safety measure" under one of the following three conditions: 1) when clinical studies have shown benefit for detection of bacterial contamination not revealed by previous bacterial testing; 2) when the bacterial testing devices have analytical sensitivity at least equivalent to a previously cleared "safety measure" device; or 3) when the bacterial testing devices qualify by other methods found acceptable to FDA.

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Dating:

Products should be labeled with a 5-day expiration. To assure that the risk of bacterial contamination is adequately controlled for transfusion after day 3 of storage, secondary testing should be performed on the product (see Step 2 in section III.B.2.b. of this guidance).

ii. LVDS no sooner than 36 hours

LVDS performed no sooner than 36 hours after collection (see section III.B.1. a. of this guidance) can serve as the initial step of a two-step strategy when storage is intended to be extended beyond 5 days.

b. Step 2

Step 2 consists of one of the following:

i. Secondary culture performed no sooner than Day 3

This applies to apheresis platelets and pre-storage pools of WBD platelets, follows Step 1, and consists of:

- Culture performed no sooner than day 3 of storage using at least an 8 mL sampling volume inoculated into at least an aerobic medium.⁴ If the collection had been split, each split apheresis unit should be sampled for culture.

We recommend that you establish a minimum incubation period in your Standard Operating Procedures (SOPs) for the secondary culture.

During the incubation period of the secondary culture, products remain in-date through their labeled storage period, and removal of products from inventory is not required during any portion of the labeled storage, provided you have developed procedures to 1) identify when secondary testing has been completed, and 2) maintain product control during the incubation period.

⁴ Use of a device labeled as a “safety measure” is not required when secondary testing is performed to adequately control bacterial risk through day 5 of storage (see footnote 3).

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Dating:

Products should be labeled with a 5-day expiration.

ii. Secondary culture performed no sooner than Day 4

This applies to apheresis platelets, follows Step 1, and consists of:

- Culture performed no sooner than day 4 of storage with at least 16 mL total sample volume, inoculated evenly between aerobic and anaerobic culture media. If the collection had been split, each split apheresis unit, should be sampled for culture.

We recommend a minimum incubation period of 12 hours.

During the incubation period of the secondary culture, products remain in-date through their labeled storage period, and do not necessitate removal from inventory during any portion of the labeled storage, provided you have developed procedures to identify when secondary testing has been completed, and maintain product control during the recommended incubation period.

Dating:

Products should be labeled with an expiration of up to 7 days.

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

iii. Secondary rapid testing

This applies to apheresis platelets and pre-storage pools of WBD platelets, follows Step 1, and consists of:

- A secondary rapid test performed in accordance with the rapid testing device labeling.

Dating:

Products may be labeled with an expiration of up to 7 days.

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

⁵ See footnote 3.

⁶ See footnote 3.

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C. Strategies for Single Units and Post-storage Pools of WBD Platelets

The recommended strategies for single units of WBD platelets and post-storage pools of WBD platelets are single-step. Please see Appendices A and C for summary tables of the strategies described in section III.C. of this guidance.

1. Rapid bacterial testing

This applies to single units of WBD platelets and post-storage pools of previously untested WBD platelets and consists of:

- A rapid test performed in accordance with the device labeling.

Dating:

- Single units: Products should be labeled with a 5-day expiration.
- Post-storage pools of WBD platelets: Products expire 4 hours after pooling (21 CFR 606.122(1)(2)).

2. Single culture with sampling performed no sooner than 36 hours after collection

This applies to single units of WBD platelets and consists of the following:

- A single culture performed no sooner than 36 hours after collection. Testing should include inoculation into aerobic culture media. A single unit of WBD platelets represents a relatively small volume. Therefore, the largest practical volume within the range permitted by the bacterial testing device instructions for use should be used for culture.

We recommend a minimum incubation period of 12 hours prior to release for transfusion.

Dating:

Products should be labeled with a 5-day expiration.

3. Single culture with sampling performed no sooner than 24 hours after collection

This applies to single units of WBD platelets and consists of the following:

- A single culture performed no sooner than 24 hours after collection. Testing should include inoculation into aerobic culture media. A single unit of WBD platelets represents a relatively small volume. Therefore, the

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largest practical volume within the range permitted by the bacterial testing device instructions for use should be used for culture.

We recommend a minimum incubation period of 12 hours prior to release for transfusion.

Dating:

Products should be labeled with a 5-day expiration. If the unit is transfused after day 3 of storage, secondary rapid testing (see section III.C.1. of this guidance) may be considered.

D. 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 dating is extended beyond 5 days, 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 information about the tests performed or pathogen reduction used to control the risk of bacterial contamination of platelets (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 biologics license application (BLA), in accordance with section 351 of the Public Health Service Act.

Licensed establishments must report changes to their approved 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-day or 7-day dating

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period.⁷ 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. 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:

- 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:
 - 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 SOPs that include processes for:
 - 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 device(s) used for bacterial detection, when the platelet product is sampled and when the product will be released.

⁷ FDA’s recommendations for the implementation of pathogen reduction are provided 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.

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- iii. Labeling the platelet product based on the bacterial detection testing.
 - iv. Alerting 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. Informing consignees of the type of storage container the platelets are stored in, for example, whether the storage container is approved for 5-day storage or 7-day storage.
- 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 if a new testing method is used.
 - g. Quality control data for the pH at end of storage (7 days) for a minimum of four units prepared from different donors and representing all platelet product types (i.e., singles, doubles, triples) at each manufacturing facility that will have the expiration date extended to 7 days.
 - 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, if applicable, expiration time, of the platelet product.
 - 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 this guidance, Comparability Protocol submissions under 21 CFR 601.12(e) 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. For additional information about submitting Comparability Protocols, please refer to the FDA Guidance for Industry: Changes

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to an Approved Application: Biological Products: Human Blood and Blood Components Intended for Transfusion or for Further Manufacture, dated December 2014. Available at <https://www.fda.gov/media/86137/download>.

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 Report⁸ 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. 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/media/86137/download>.

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

⁸ See 21 CFR 601.12(a)(3).

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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/vaccines-blood-biologics/biologics-establishment-registration/blood-establishment-registration-and-product-listing>.

VI. IMPLEMENTATION

We recognize that some of the recommendations contained in this guidance may take time to implement. We recommend prior to October 1, 2021 as a reasonable timeframe for implementation.

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VII. REFERENCES

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APPENDIX A: BACTERIAL RISK CONTROL STRATEGIES ASSOCIATED WITH SPECIFIC PLATELET STORAGE DURATION AND TYPE OF PLATELET UNIT

Types of Units

Storage duration

	Apheresis	Pre-storage pools of WBD platelets	Single units of WBD platelets	Post-storage pools of WBD
5 days	LVDS \geq 36 hours	LVDS \geq 36 hours	Rapid testing	Rapid testing
	Pathogen reduction	Primary culture \geq 24 hours + secondary culture \geq day 3	Primary culture \geq 24 hours	
	Primary culture \geq 24 hours + secondary culture \geq day 3	Primary culture \geq 24 hours + secondary rapid testing	Primary culture \geq 36 hours	
	Primary culture \geq 24 hours + secondary rapid testing			
7 days	LVDS \geq 48 hours	N/A	N/A	N/A
	LVDS \geq 36 hours + secondary rapid testing			
	LVDS \geq 36 hours + secondary culture \geq day 4			
	Primary culture \geq 24 hours + secondary culture \geq day 4			
	Primary culture \geq 24 hours + secondary rapid testing			

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APPENDIX B: SUMMARY OF BACTERIAL RISK CONTROL STRATEGIES FOR APHERESIS AND PRE-STORAGE POOLS OF WBD DERIVED PLATELETS

Strategy	Applicable Components ¹	Time Performed	Volume Sampled ²	Product to be Sampled	Growth Conditions	Recommended Incubation Period	Expiry	
Single-step Strategies								
LVDS ≥36 hours	Apheresis and pre-storage pools	No sooner than 36 hours from the time of collection	≥16 mL total	Each apheresis split unit or pre-storage pool	Aerobic and anaerobic	Minimum of 12 hours	Day 5 ³	
LVDS ≥48 hours	Apheresis	No sooner than 48 hours from the time of collection	≥16 mL total	Each apheresis split unit	Aerobic and anaerobic	Minimum of 12 hours	Day 7 ⁴	
Pathogen Reduction	Per device instructions for use	Per device instructions for use	N/A	Per device instructions for use	N/A	N/A	Per device instructions for use	
Two-step Strategies								
Step 1	Primary culture ≥24 hours or LVDS ≥36 hours	Apheresis and pre-storage pools	No sooner than 24 hours from time of collection	≥ 16 mL total	Main collection (“mother bag”), each apheresis split unit, or pre-storage pool	Aerobic and anaerobic	Minimum of 12 hours	See note ⁵
		Apheresis and pre-storage pools	No sooner than 36 hours from the time of collection	≥16 mL total	Each apheresis split unit or pre-storage pool	Aerobic and anaerobic	Minimum of 12 hours	Day 5 ⁶
Step 2	Secondary culture	Apheresis and pre-storage pools	No sooner than day 3	≥8 mL	Each split unit or pre-storage pool	At least aerobic	Establish a minimum incubation time period in SOPs	Day 5
		Apheresis	No sooner than day 4	≥16mL total	Each split unit	Aerobic and anaerobic	Minimum of 12 hours	Day 7 ⁷
	Secondary rapid testing	Apheresis and pre-storage pools	Per device instructions for use	Per device instructions for use	Each apheresis split unit or pre-storage pool	N/A	N/A	Per device instructions for use (up to day 7 ⁸)

¹ This table applies only to apheresis platelets and pre-storage pools of whole blood derived (WBD) platelets. For post-storage pooled products and single units of WBD platelets, see section III.C. and Appendix C of the guidance.

² When aerobic and anaerobic cultures are performed, sampled volumes should be split evenly between aerobic and anaerobic culture bottles.

³ The storage of platelets tested by LVDS no sooner than 36 hours may be extended by secondary testing methods. See Step 1 of ‘Two-step strategies’, and footnote 4 of Appendix B.

⁴ Platelets may only be stored beyond day 5 and up to day 7 if each component is tested using a bacterial detection device cleared by FDA and labeled for use as a “safety measure” according to its instructions for use, and if the platelet storage container has been cleared or approved for 7-day storage.

⁵ Following primary culture performed no sooner than 24 hours, apheresis and pre-storage pooled platelet components should not be transfused after day 3 unless appropriate secondary testing (culture or rapid testing) has been performed to assure that the risk of bacterial contamination has been adequately controlled. See section III.B.2. of the guidance for additional details.

⁶ The storage of platelets tested by LVDS no sooner than 36 hours may be extended by secondary testing methods. See footnote 4 of Appendix B.

⁷ See footnote 4 of Appendix B.

⁸ See footnote 4 of Appendix B.

APPENDIX C: SUMMARY OF BACTERIAL RISK CONTROL STRATEGIES FOR SINGLE UNIT WBD PLATELETS AND POST-STORAGE POOLS OF WBD PLATELETS

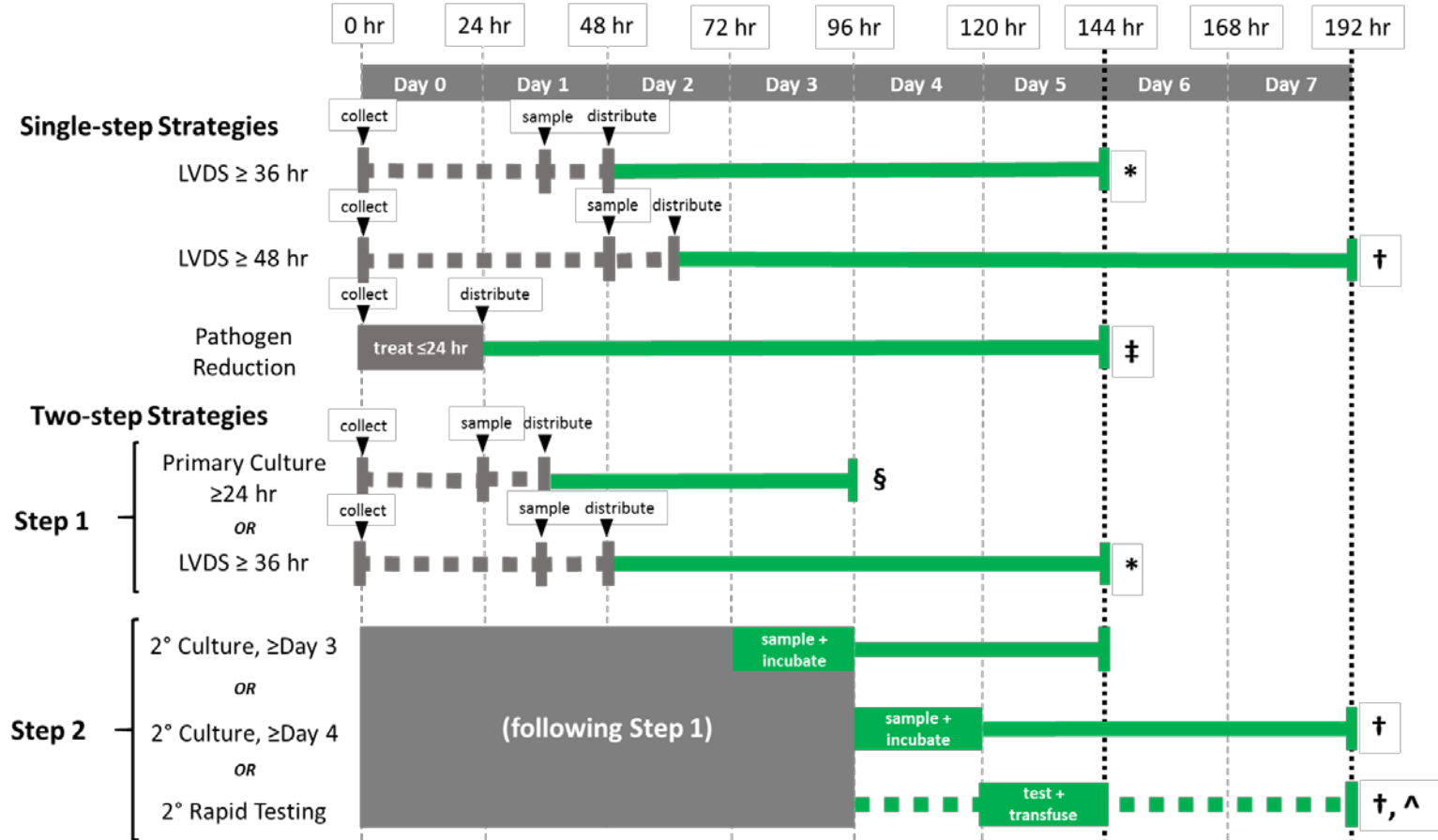
Strategy	Applicable Components	Time Performed	Volume Sampled	Growth Conditions	Recommended Incubation Period	Expiry
Single-step Strategies						
Rapid testing	Single unit or post-storage pool	Per device instructions for use	Per device instructions for use	N/A	N/A	Per device instructions for use (up to day 5) ¹
Single culture	Single unit	No sooner than 36 hours from time of collection or No sooner than 24 hours from time of collection	Largest practical volume within the range permitted by the device instructions for use	At least aerobic	Minimum of 12 hours	Day 5 ²

¹ Based on currently available storage systems, storage of these products is limited to 5 days.

² Following primary culture performed no sooner than 24 hours, for transfusion after day 3 of storage, secondary rapid testing may be considered.

Contains Nonbinding Recommendations

APPENDIX D: EXAMPLE TIMELINES OF BACTERIAL RISK CONTROL STRATEGIES FOR APHERESIS PLATELETS



*The storage of platelets tested by LVDS no sooner than 36 hours may be extended by secondary testing methods. See section III.B.2. of the guidance.

†Platelets may only be stored beyond day 5 and up to day 7 if each component is tested using a bacterial detection device cleared by FDA and labeled for use as a “safety measure” according to its instructions for use, and if the platelet storage container has been cleared or approved for 7-day storage.

‡Pathogen reduced platelet components should be treated and labeled consistent with the device instructions for use. Currently, apheresis platelets treated with approved devices should be treated no later than 24 hours after collection and are limited to 5 days of storage.

§Following primary culture performed no sooner than 24 hours, apheresis platelet components should not be transfused after day 3 unless appropriate secondary testing (culture or rapid testing) has been performed to assure that the risk of bacterial contamination has been adequately controlled. See section III.B.2. of the guidance for additional detail.

^Secondary rapid testing should be performed according to the bacterial testing device instructions for use. Currently, for available cleared or approved devices, platelets should be transfused within 24 hours of a non-reactive test.