Carter BloodCare
SPECIALTY SERVICES

Blood Matters

September/October 2021

News for Blood Bank Medical Directors, Physicians and the Lab

Blood Matters is a quarterly news *outlet with important medical information for you, our customers and colleagues, from Carter BloodCare. We hope you will share it with others interested in the work we do together.*

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HOT TOPICS

New "Cold-Stored Platelet" (CSP) Variance for Carter BloodCare Approved by the FDA

Frances Compton, MD

As of July 14, 2021, the FDA has approved Carter BloodCare's request to produce "cold-stored platelets". The approved variance states that these platelets can be stored "at 1-6°C for up to 14 days without agitation" and that the cold-stored platelets "are approved for the treatment of actively bleeding patients through day 14 of storage when conventional platelet products are unavailable or their use is not practical."

Carter BloodCare plans to start distributing these products to hospitals in **January 2022.**

See Carter BloodCare's FDA approved Circular of Information insert for cold-stored platelets:

APHERESIS PLATELETS LEUKOCYTES REDUCED, COLD STORED

Storage: Product is stored at 1-6°C without agitation.

Shelf Life: 14 days.

Reconstitution/Stability: After resuspension, inspect the product for aggregates prior to infusion. If aggregates are present, allow product to rest at room temperature and gently rock to disperse aggregates. Discard if aggregates do not disperse after 30 minutes.

Indications: For the treatment of actively bleeding patients through day 14 of storage when conventional platelet products are unavailable or their use is not practical.

Bacterial Risk: This product must be continuously refrigerated at 1-6 °C

Some Background Information on CSPs:

Data show that cold-stored platelets have benefits beyond the logistics of longer storage time and no need for agitation in the blood bank. While cold storage preserves platelet metabolic function and prevents bacterial growth, cold-induced platelet activation can, in fact, contribute to an increased hemostatic potential in bleeding patients.[1] Early data showed that cold-stored platelets actually improved bleeding times better than room temperature-stored platelets.[2] Other early studies showed that cold-stored platelets have decreased post-transfusion *in vivo* lifespan compared to room temperature-stored platelets.[3] These phenomena of platelet activation and subsequent increased clearance after refrigeration are actually the main reasons why platelets have been, historically, stored at room temperature as the industry standard for years - in order to improve the post-transfusion lifespan of transfused platelets.

Recently, the importance of cold-stored platelet activation has become more appreciated as we better understand how it promotes clot formation.[4] Numerous *in vitro* studies (ROTEM, TEG, etc.) have shown that clot formation is significantly better in cold-stored platelets compared to room temperature-stored platelets.[1] Animal studies have shown that labeled, cold-stored platelets (in whole blood) contribute to clot formation on pathologic assessment.[5] Furthermore, a randomized clinical trial in Norway showed that the use of cold-stored platelets results in less post-operative chest tube bleeding than the use of room temperature-stored platelets.[6]

Implementation of the Use of CSPs:

Cold-stored platelets are intended to be used, as described by the FDA, only in bleeding patients. Non-bleeding, thrombocytopenic patients who require prophylactic transfusion should continue to receive the standard, room temperature-stored platelets in order to maximize post-transfusion platelet lifespan.

This is an ideal product for smaller hospitals that keep platelets in-house for potentially bleeding patients, but do not have a frequent need for platelet transfusion (minimal prophylactic transfusion). This use of CSPs is beneficial in this setting for both the logistical and clinical advantages of the product. It is also advantageous to use CSPs in an ED/Trauma refrigerator or for MTP/OR purposes, where bleeding patients could benefit from pre-activated platelets. It is important for these larger trauma/surgical facilities to plan for a dual platelet inventory so that the right type of platelet (cold vs room temperature) is transfused to each patient appropriately. Carter BloodCare looks forward to working with our community hospitals in order to ensure these exciting new products are used to their full potential for the benefit of our community.

References:

1. Reddoch-Cardenas KM, Bynum JA, Meledeo MA et al. Cold-stored platelets: A product with function optimized for hemorrhage control. *Transfusion and Apheresis Science.* 2019; 58: 16-22.

2. Becker GA, Tuccelli M, Kunicki T et al. Studies of platelet concentrates stored at 22-C and 4-C. *Transfusion.* 1973; 13: 61–8.

3. Murphy S, Gardner FH. Platelet preservation - effect of storage temperature on maintenance of platelet viability - deleterious effect of refrigerated storage. *New England Journal of Medicine.* 1969; 280: 1094-1098.

4. Getz TM. Physiology of cold-stored platelets. *Transfusion and Apheresis Science.* 2019; 58: 12-15.

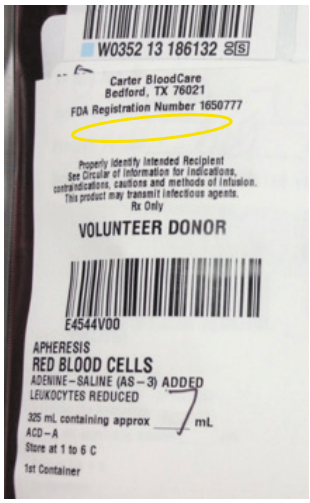
5. Wu X, Darlington DN, Montgomery RK et al. Platelets derived from fresh and cold-stored whole blood participate in clot formation in rats with acute traumatic coagulopathy. *Br J Haematol* 2017; 179: 802–10.

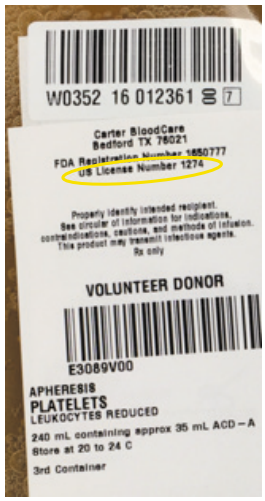
6. Strandenes G, Kristoffersen EK, Bjerkvig CK *et al.* Cold stored platelets for treatment of postoperative bleeding in cardiothoracic surgery. Orlando, FL: American Association of Blood Banks, 2016.

Should it Mean Anything to My Hospital Blood Bank if a Blood Product is Licensed or Not?

Laurie J Sutor, MD, MBA

The label on blood components is required to carry a blood collectors' Food and Drug Administration (FDA) registration number. It may or may not also carry an FDA license number for the collector. Both of these are displayed below the donor identification number (DIN) and facility name:





Your transfusing facility currently gets a mix of licensed and unlicensed components from Carter BloodCare. So, what does this mean to you, if anything?

Carter BloodCare has a facility license from the FDA (the number you see on the blood bag), but must also receive permission from the FDA to put that number on individual components. Component licensure is based on the data we submit to the FDA about the collection process and quality of each type of component made. So, individual components are licensed, as well as our overall facility.

FDA licensure is only required to send blood components over state lines for reimbursement - in other words, for interstate commerce. Therefore, it does not directly have anything to do with the quality or safety of components we make and provide to customers within our state. It does signify the FDA has performed oversight of the products we export out of state, in that regard. For licensure of each product, Carter BloodCare must submit to the FDA rigorous quality control data about each component, its SOPs, and the equipment used in its manufacture. Because of the incredible amount of data that must be submitted for licensure, Carter BloodCare deliberately does not license all components - only those we know we might be shipping out of Texas on occasion. Thus, those components that are most often in periodic excess or danger of outdate, such as red cells and apheresis platelets. (Note: I realize, as I write this, we haven't had any inventory to ship out of state in quite a while now because of our extreme blood shortage.)

However, all components are collected by the same processes and procedures at Carter BloodCare, licensed or not. There is no safety difference in the products you are receiving. One apheresis platelet you get may not be licensed yet because it was collected at a relatively new donor center location that we just opened, and we are in the process of gathering and submitting data to the FDA for licensure, or waiting to hear back from them on the approval status. Another example may be that if we ship you irradiated products, those will not be licensed. We rarely have a need to ship irradiated components to other states; therefore, we did not apply for FDA licensure for irradiated components.

Also, at the time of this article, the current 7-day platelets are not yet FDA licensed because we had to resubmit all the production data on platelets to the FDA after changing bacterial sampling methods from a 24-hour wait to a 48-hour wait before sampling and culturing on the same instrumentation. This change increases patient safety, yet the product will be unlicensed until we hear back from the FDA that they approve our new procedures.

In summary, you should not be concerned if some of the blood components you receive are not FDA licensed. There is no difference in the care, quality, and safety we provide for the preparation of these products. The lack of a license number on a blood bag means that we have not gone through (or yet completed) the lengthy FDA submission process to receive licensure for that particular component. It is a process only needed for interstate shipping.

FDA Platelet Bacterial Detection Guidance Implementation Update

Todd Nishimoto, MD

Two months have passed since implementation of the seven-day; large-volume delayed sampling (LVDS) portion of the FDA guidance for industry "Bacterial Risk Control Strategies for Blood Collection Establishment and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion" or Guidance. In anticipation of losing the number of doses made from one platelet donation by the LVDS process, many departments met in preparation to educate staff and hospitals, to recruit more donors, prepare for the increase in workload, and to plan for the purchasing of equipment and consumables for testing and servicing our customers.

On March 1, 2021, in preparation of the June 22nd LVDS implementation date, Carter BloodCare began converting whole blood donors to platelet donations and recruiting new donors - knowing that not all donors would become long-term platelet donors. Given the preparation requirements and the need to plan for more donors, the Donor Center management team met with Terumo, developer of the Trima apheresis technology, to adjust the volume and the platelet target range to account for the platelets lost due to bacterial testing and quality control testing.

The Hematology Services (HS) department performs a majority of the quality control testing for all blood components, which also includes the bacterial testing on all platelet products. Two full-time employees were hired for the additional work, such as managing all the daughter bags on the platelet rotators, inoculating up to six culture bottles under a biosafety cabinet, responding to bacterial testing alarms, and managing the aerobic and anaerobic culture bottles that are required to be incubating for seven days. HS management analyzed the platelet unit split criteria (depending on the yield, a single donation may be split into a daughter bag defined as a double, or up to a triple dose) and adjusted the yield requirements to higher numbers.

From June 22, 2020 to August 30, 2020, the HS department inoculated 4,750 aerobic culture bottles with a split rate of 91%. One year later, from June 22, 2021 to August 2021, the HS department inoculated 25,000 aerobic and anaerobic culture bottles with split rate of 99%.

Collaborating with Terumo on fine tuning the volume and platelet target range, along with increasing the split criteria for single, double and triple platelet units have been effective in increasing our split rate to 99%. However, from June 22 to the end of July, our data shows a small decrease in our triple platelets and a slight increase in our double platelets. This is due to the fact that the FDA is requiring added sample anaerobic bottles and added testing of daughter bags. However, we are confident that Carter BloodCare will continue to meet our patients' needs in our community.

HOT TOPICS Continued

You may be wondering if we have seen a change in the raw number of positive results based on this process modification which was required by the FDA to improve patient safety. Carter BloodCare's experience shows an increase in the positivity rate which was expected due to the increased sensitivity.

POSITIVITY RATE	False Positives	True Positives	Total Positives
January 1 – June 21, 2021	9	5	14
June 22, 2021 – September 7, 2021 (post-LVDS)	11	13	24

Reference:

1. Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Trans http://www.fda.gov/media/123448/download

MEDICAL MINDS

What topics would you like to see in a future issue of Blood Matters?

Click **here** to submit your choice.

PHYSICIAN RESOURCES

Download updates

- Blood Bulletin Vol. 21, No. 1: Transfusing O-Negative Blood: Good Stewardship of a Precious Resource
- AABB Weekly National Blood Supply Report