

Frequently Asked Questions (FAQs) related to Pathogen-Reduced Apheresis Platelets & Use in Pediatric and Neonatal Patients

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KEY Points – Use of Pathogen-Reduced Platelets for Pediatric Patients

- Labeling of the PR platelet will include actual platelet yield of unit.
- PR platelets can be ordered with empty aliquot bags attached or as a neonatal PR aliquot. Check with Hospital Relations Specialist for availability in your region.
- PR platelets can be transfused to infants undergoing phototherapy.
- PR platelets do not need to be irradiated. No adverse effects have been noted if a PR platelet is irradiated inadvertently.
- When creating aliquots at the hospital, a sterile connecting device can be used. Follow site-specific policies for preparing aliquots and minimum volume that needs to remain for the “mother bag” to maintain the original expiration date.
- The container for INTERCEPT® PR platelets cannot be centrifuged. Transfer the contents of the PR platelet to another container (transfer bag) for centrifugation.

PATHOGEN-REDUCED (PR) PLATELETS FOR PEDIATRIC & NEONATAL PATIENTS***Are there any contraindications for use of pathogen reduced (PR) platelets in neonates who may need phototherapy?***

- Per the package insert,¹ pathogen-reduced platelets (psoralen-treated) should not be used in neonatal patients treated with phototherapy devices that emit a peak energy wavelength of less than 425 nm or have a lower emission bandwidth less than 375 nm. The concern is based on a theoretical risk that exposure to these wavelengths may result in development of skin rashes from interaction of ultraviolet light and amotosalen (type of psoralen).
- However, the risk of such an adverse event in a neonate undergoing phototherapy appears to be quite low given the following:
 - For the treatment of hyperbilirubinemia in neonates, the American Academy of Pediatrics- (AAP) guidelines recommends phototherapy devices emit between 430-490 nm (blue-green visible light) wavelengths for intensive phototherapy.²
 - All neonatal phototherapy devices currently marketed in the US are compliant with the AAP recommendation.²
 - UVA illumination (320–400 nm wavelengths) used in the PR process is less than that recommended by AAP for phototherapy devices.¹
 - To date, no photosensitivity reactions in neonates undergoing phototherapy have been reported.^{3,4}

Are pathogen-reduced (PR) platelets DEHP-free?

- Di(2-ethylhexyl)phthalate (DEHP) is known to be released from PVC medical devices, and increased leaching can occur with extended storage or increased surface area contact. The fear is that in infants and children the exposure to high doses of DEHP may affect normal growth development. As a result, most medical device (e.g. IV bags and tubing) are now DEHP-free.⁵
- Per the package insert,¹ the tubing components and container ports of the INTERCEPT® Blood System contain polyvinyl chloride (PVC). However, the platelet product is only in contact with the PVC for a brief period (approximately 15 minutes) during processing. The final bag that the PR platelets are stored in for distribution to the hospitals is DEHP-free.

Will pathogen-reduced (PR) platelets be labeled with the actual platelet yield?

- Yes. Both PR and LVDS platelets will be labeled with the actual platelet yield. This will allow hospital transfusion service staff to determine the amount of platelets in an aliquot for a neonate and calculate the remaining platelet count of the “mother” bag after making the aliquot(s).

Can pathogen-reduced (PR) platelets be volume-reduced?

- The final storage container for the INTERCEPT® Blood System has not been validated for withstanding centrifugal force and the manufacturer does not recommend centrifuging the PR platelet container. Therefore, if volume reduction is needed (e.g. removal of plasma due to ABO incompatibility or prevention of circulatory overload), the PR platelets should be transferred to an appropriate size transfer bag that can be centrifuged.⁶

- With the platelet-filled transfer bag affixed to the now empty Intercept® PR platelet bag, the INTERCEPT® PR bag can be used for removal of the plasma after centrifugation. As long as the INTERCEPT® bag is not receiving the force of centrifugation at the bottom of the centrifuge cup, it can be used for transfer of the plasma in such situations.
 - It is recommended that the hospital follows the same policy for residual plasma in the final product (to resuspend the platelets) as when volume-reducing conventional platelets. Follow site-specific policies for labeling and expiration of the volume-reduced PR platelet. As a guide, expiration of the final platelet product after volume-reduction would be 4 hours.
- If at any point during the volume reduction process damage to the INTERCEPT® PR bag occurs by pinching, tearing or excess pressure and/or creation of an “open system” (e.g., transfer bag attached by spiking the port of the INTERCEPT® PR bag), there is the risk of bacterial contamination of the PR platelet.

Can pathogen-reduced (PR) platelets be ordered volume-reduced from Versiti?

- Yes, PR platelets may be ordered volume-reduced. The component modification is done in an “open” system (PR bag is spiked) and final product would have a “4 hour” expiration from time of preparation.

Will pathogen-reduced (PR) platelets be received from Versiti in a double-bag configuration?

- A PR platelet may be stored in two (2) containers when the platelet count is greater than 5.3×10^{11} but not enough to manufacture 2 separate platelet products. The two containers are used to provide sufficient surface area for optimal gas exchange during storage and maintain the platelet quality and potency. From recent manufacturing data at Versiti, frequency of a double-bag PR platelet is anticipated to be about 0.5% or 1 in every 200 PR platelets distributed.
- If a hospital transfusion service desires to combine the two containers this should be done just prior to issue for transfusion. After combining the containers, it is acceptable to label the final product with a 24 hour outdate or original product expiration (whichever is sooner).

Are there any contraindications to irradiating a pathogen-reduced (PR) platelet?

- While irradiation of an INTERCEPT® PR platelet is not needed or recommended since PR technology inactivates the donor lymphocytes, irradiating a PR platelet is not contraindicated. If the PR platelet is accidentally irradiated, it will not impact the quality or potency of the product.
 - INTERCEPT® PR platelets were irradiated in the clinical trials submitted for approval in advance of the FDA approving pathogen reduction technology in place of irradiation. These platelets were transfused to study subjects with no adverse effect on bleeding outcomes.^{1,6}
- At Versiti, PR platelets cannot be ordered “irradiated”. Pathogen reduced technology is comparable to irradiation for inactivating donor lymphocytes and prevention of TA-GVHD, and the additional modification to the product incurs an unnecessary cost without clinical benefit.
- If a hospital irradiates blood products on site and opts to irradiate a PR platelet, ISBT codes that include the irradiation component modification are available for relabeling the platelet product. Refer to the ICCBA site (www.iccba.org) or contact your Hospital Relations Specialist.

PREPARATION OF PEDIATRIC ALIQUOTS FROM A PATHOGEN-REDUCED (PR) PLATELET

Can pathogen-reduced (PR) platelets be ordered from Versiti with empty aliquot bags attached?

- Yes

Can pathogen-reduced (PR) platelets be ordered from Versiti as a filled neonatal aliquot (aliquot bag already filled with PR platelets)?

- Only orderable at certain Versiti Blood Centers. Contact your Hospital Relations Specialist for availability in your region.
- Where available, neonatal aliquots of PR platelets may be ordered as either 25 mL or 40 mL. Both will have a 4-hour expiration.

Can a sterile connecting device be used with pathogen-reduced (PR) platelets to prepare aliquots for neonates or infants?

- Yes – follow your site-specific policy and procedures

Do pathogen-reduced (PR) platelets have an adequate number of platelets to prepare an aliquot for transfusion for a neonate?

- Despite having a slightly larger volume, a PR platelet can be used for preparing neonatal aliquots. The concentration of the platelets in the aliquot will be sufficient to raise the infant's platelet count.
- Neonates and infants require approximately $9-10 \times 10^9$ platelet per kg to raise the platelet count by $100-125 \times 10^3/\mu\text{L}$, assuming post-transfusion recovery of 60% (some platelets will be lost to the spleen).⁷
- As an example:
 - The Transfusion Service has a PR platelet containing 3.0×10^{11} platelets in a total volume of 300 mL. The concentration would then be approximately $1.0 \times 10^9/\text{mL}$.
 - An aliquot is created for the baby at a dose of 10mL/kg, which would result in a final dose of 10×10^9 platelets/kg and sufficient to raise the baby's platelet count.

Are there limitations for making aliquots from a PR platelet?

- There are no specific limitations. When preparing aliquots from PR platelet, it is recommended that a hospital follow the same site-specific policies as when preparing aliquots from conventional platelets.
- Per the manufacturer, the INTERCEPT® PR bag is intentionally made larger to increase the oxygen exchange to maximize the stability of the platelets. The manufacturer, Cerus, is not able to make any claims as to the minimum volume that must remain in the bag following aliquot removal to maintain the original expiration date of the “mother” bag. The manufacturer's recommendation is to follow the same policy for minimum volumes and corresponding expiration dates for PR platelets that a hospital may currently have in place for conventional platelets.⁸

Where can I find additional information on pathogen-reduced (PR) platelets?

- For more information on proper handling, storage and implementation of pathogen-reduced (PR) platelets for your facility, visit Cerus website at either <https://hcp.intercept-usa.com/hcp-resources/implementation> or <https://transfusionsafetyonline.com/programs/intercept-hospital-implementation/>

References:

1. INTERCEPT Blood System for Platelets (Package Insert) Cerus Corporation, May 28, 2019 (available at <https://hcp.intercept-usa.com/hcp-resources/package-inserts>)
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