

Stored Red Blood Cells¹

Rejuvenated Red Blood Cells¹

When RBC quality matters

- ✔ **FACT** In the US, someone needs blood every 2 seconds.²
- ✔ **FACT** As red blood cells (RBCs) are stored, their quality may degrade, a term called “Storage Lesion”.³
- ✔ **FACT** Biochemical 2,3-DPG in RBCs, associated with the delivery of oxygen, is drastically reduced by 14th day of storage.⁴
- ✔ **FACT** The average age of blood that is transfused in the US is 18 days.⁵
- ✔ **FACT** rejuvesol (red blood cell processing) Solution is the only FDA-approved product for the rejuvenation of stored red blood cells, and restores 2,3-DPG and ATP to levels equal to or greater than those in fresh blood.⁶



To learn more about rejuvesol Solution and blood quality, please visit www.zbinetwork.com.

Important Safety Information: For in vitro processing of RBCs. Not for injection. Rx use only.

1. Unpublished data from bench research at University of Pennsylvania, School of Medicine, Philadelphia, PA. August 2014.
1. SEM (Scanning Electron Microscope) picture of Fresh (EDTA whole blood); 2. SEM picture of RBCs in Image #2 that were treated on day 42 with a rejuvenating solution (50 mL), incubated for 60 minutes at 37 °C, washed and re-suspended.
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REJUVESOL® RED BLOOD CELL PROCESSING SOLUTION FOR USE IN THE EXTRACORPOREAL REJUVENATION OF RED BLOOD CELLS

DESCRIPTION Rejuvesol® Red Blood Cell Processing Solution (rejuvesol® Solution) is a sterile, non-pyrogenic solution intended only for use in the extracorporeal rejuvenation of a unit of red blood cell concentrate (RBC). Each 50 mL of rejuvesol® Solution contains sodium pyruvate 0.550 g, inosine 1.34 g, adenine 0.034 g, dibasic sodium phosphate (heptahydrate) 0.730 g, and monobasic sodium phosphate (monohydrate) 0.311 g, in water for injection, pH 6.7-7.4.

CLINICAL PHARMACOLOGY A gradual depletion of RBC adenosine triphosphate (ATP) and 2,3 diphosphoglycerate (2,3-DPG) occurs with storage of RBC at 1-6 °C.¹ The level of 2,3-DPG in RBC stored for greater than 14 days is less than 10% of normal¹⁻³. Rejuvenation of RBC with rejuvesol® Solution increases the levels of ATP and 2,3-DPG.^{1,3,5,6,8,11} An in vitro loss of RBCs occurs with the preservation and processing of RBC. Thus, the effectiveness of a transfusion is influenced by both the total number of RBCs transfused and the number of those cells which remain in circulation. Therefore, the “dose” of a transfusion is defined as the percentage of pre-transfusion recovered RBCs multiplied by the 24 hour post-transfusion survival value. Rejuvenation is accomplished by incubating the rejuvesol® Solution with RBC (prepared from up to 550 mL of whole blood) for sixty (60) minutes at 37 °C. Citra recommends that the entire 50 mL of rejuvesol® Solution be added to RBC when the net packed cell weight is > 110 grams.^{1,7}

INDICATION AND USAGE Rejuvesol® Solution is intended only for in vitro rejuvenation of RBC. RBC may be rejuvenated in CPD (non-leukocyte reduced), CPDA-1, (non-leukocyte reduced) or CPD/ADSOL® (CPD/AS-1 leukocyte reduced). The final concentration of ATP and 2,3-DPG achieved after rejuvenation will vary depending on the number of days of liquid storage at 1-6 °C prior to rejuvenation. Citra Labs, LLC, recommends that rejuvenation of RBC be performed after 14 days or longer of liquid storage.

Rejuvenation of CPD or CPDA-1 RBC for Immediate use or for Cryopreservation: RBC which have been collected and stored in CPD or CPDA-1 anticoagulant may be rejuvenated up to three days after the expiration date of the RBC, as long as storage at 1-6 °C is not interrupted.^{8,9} After rejuvenation, RBC (CPD and CPDA-1) must be either washed and stored at 1-6 °C for up to 24 hours prior to transfusion or glycerolized and frozen at -80 °C (below -65 °C). RBC Frozen Rejuvenated with were collected and stored in CPD or CPDA-1 may be stored frozen up to 10 years.¹⁰

Rejuvenation of CPD/AS-1 RBC: Rejuvesol® Solution has not been approved for the rejuvenation of RBC stored in any additive systems other than AS-1. RBC stored in CPD/AS-1 at 1-6 °C may be rejuvenated up to, but not exceeding, 42 days of storage as long as storage at 1-6 °C is not interrupted. Rejuvenated CPD/AS-1 RBC must be either washed and stored at 1-6 °C for up to 24 hours prior to transfusion or glycerolized and frozen at -80 °C. RBCs Frozen Rejuvenated which were collected and stored in CPD/AS-1 may be stored for up to 3 years. Unlike rejuvenated CPD, CPDA-1 and CPD/AS-1 RBC, rejuvenated RBCs collected and stored in any other anticoagulant/additive solution combination have not been approved to be immediately washed and transfused.

– Rejuvenation of CPD/AS-1 RBC for cryopreservation: When CPD/AS-1 RBC are rejuvenated at 42 days of liquid storage, frozen, deglycerolized, and stored for 24 hours, the concentration of 2,3-DPG and ATP increases to above normal. In a limited study, the average 24 hour post-transfusion survival value of these cells was statistically higher than the reported² survival value of CPD/AS-1 red blood cell concentrates which are stored for 42 days prior to transfusion. The “dose” may be equivalent for a CPD/AS-1 RBC whether the unit is stored for 42 days prior to transfusion or stored for 42 days, rejuvenated, frozen, deglycerolized, and stored for 24 hours prior to transfusion.

– Rejuvenation of CPD/AS-1 RBC for Immediate Use: When CPD/AS-1 RBC are rejuvenated at 42 days of liquid storage, washed, and stored for 24 hours, the concentration ATP increases to fresh values. For 2,3-DPG rejuvenation of RBCs stored in CPD/AS-1 for 42 days, the range of 2,3 DPG relative to day 0 value was 46%-172% with a mean of 98% ± 29%. For 66% of the RBC units (44/67, 33/33) in Site A and 11/34 in Site B) the 2,3-DPG reached at least 80% of the day 0 value in Site A and 11/34 in Site B) the 2,3-DPG reached at least 80% of the day 0 value.

WARNING AND CONTRAINDICATIONS Rejuvesol® Solution is intended only for the extracorporeal rejuvenation of a RBC. It should never be directly administered to humans. Rejuvesol® Solution must not be added to whole blood because the additional plasma may reduce the effectiveness of the rejuvenation process. Immediately after rejuvenation, RBC must either be washed via an approved protocol prior to transfusion or glycerolized and frozen. RBC which have been rejuvenated, glycerolized, and frozen must be deglycerolized via an approved protocol prior to transfusion. RBC rejuvenated before 6 days of storage may achieve 2,3-DPG levels in excess of 2 times normal and ATP levels in excess of 1.5 times normal.^{11,12} In patients with reduced arterial blood pO₂ of less than 40 torr, the use of RBC rejuvenated before 6 days of storage are contraindicated because their high 2,3-DPG levels and low oxygen affinity may impair proper oxygenation of the red blood cells in the lung.¹³ Rejuvenated RBC are further processed prior to transfusion to remove the un-used portion of rejuvesol® Solution, by-products of the rejuvenation process, and any other potential storage related impurities in rejuvesol® Solution.

PRECAUTIONS Aseptic technique must be maintained at all times. Do not use unless solution is clear/colorless and seal is intact. Product that exhibits a slight yellow color should not be used. Product instability has been observed after continuous exposure at high temperature (after 6 months at 40 °C and after 9 months at >30 °C). This product contains no bacteriostatic or antimicrobial agents and is intended for single use only. Rx Only - Federal (USA) law prohibits dispensing without prescription.

STORAGE It is recommended that the product be stored at 15 - 25 °C (59 - 77 °F). Protect from freezing.

HOW SUPPLIED PN 7012: 50 mL vial; 12 vials per case

For details see Package Insert, call 1-800-299-3411 or visit <http://www.rejuvesol.com>. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch4 or call 1-800-FDA-1088. Rejuvesol® Solution is a registered trademark of Citra Labs, LLC, a Biomet Biologics Company. Manufactured for Citra Labs, LLC, 55 Messina Drive, Braintree, MA 02184, USA.

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