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rejuvesol™ is a trademark of Biomet Biologics.
ADSOL® is a registered trademark of Fenwal, Inc.

Manufactured for: Citra Labs, LLC
55 Messina Drive, Braintree, MA 02184 USA
1-800-299-3411 · Fax 781-848-6781
Manufactured by: Grand River Aseptic Manufacturing, Inc.
140 Front Ave SW, Suite 3 Grand Rapids, MI 49504 USA
Introduction
Overview

This rejuvesol™ red blood cell solution Process Development Handbook is a complete package designed for training and implementation by Citra Labs and Biomet Biologics team members for primary institution-based trainers and customers.

Information contained herein may be used for the development of appropriate documentation that includes sample Standard Operating Procedures (SOPs), documents to facilitate staff training and competency and information pertinent to validation when using rejuvesol Solution according to approved indications for use. This document is not intended, and should not be used, to address specific regulatory requirements of any blood establishment.
Indications for Use (IFU)

rejuvesol red blood cell processing solution (PN 7012) for use in the Extracorporeal Rejuvenation of Red Blood Cell (50 mL Glass Vial)

Description
rejuvesol red blood cell processing solution (rejuvesol Solution) is a sterile, non-pyrogenic solution of pyruvate, inosine, adenine, and phosphate in Water for Injection intended only for use in the extracorporeal rejuvenation of a unit of red blood cell (RBC) concentrate. 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 red blood cell adenosine triphosphate (ATP) and 2,3 diphosphoglycerate (2,3-DPG) occurs with storage of RBC at 1-6°C. The level of 2,3-DPG in RBC stored for greater than 14 days is less than 10% of normal. Rejuvenation of RBC with rejuvesol red blood cell processing solution increases the levels of ATP and 2,3-DPG.

An in vitro loss of red blood cells occurs with the preservation and processing of RBC. Thus, the effectiveness of a transfusion is influenced by both the total number of red blood cells 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 red blood cells multiplied by the 24 hour post-transfusion survival value.

Rejuvenation is accomplished by incubating the contents of one 50 mL vial of rejuvesol Solution with one unit of RBC (prepared from up to 550 mL of whole blood) for sixty (60) minutes at 37°C. Citra Labs recommends that the entire 50 mL of rejuvesol Solution be added to “smaller than normal” RBC as long as the pre-rejuvenation net packed cell weight is greater than 110 grams.

Indication and Usage
rejuvesol Solution is intended only to be used as an in vitro processing solution for the rejuvenation of a unit of RBC. RBC may be rejuvenated after 14 days of storage 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.

NOTE: For simplicity, RBC stored in CPD (non-leukocyte reduced), CPDA-1 (non-leukocyte reduced), or CPD/ADSOL® (CPD/AS-1 leukocyte reduced) are referred to hereafter as CPD, CPDA-1, and CPD/AS-1, respectively.

It is at the discretion of the Medical Director when rejuvenation of a RBC should take place. Citra Labs, LLC, recommends that rejuvenation of RBC be performed after 14 days or longer of liquid storage.

RBC (CPD, CPDA-1, and CPD/AS-1) 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. (See Warning and Contraindications).

Rejuvenation of CPD or CPDA-1 RBC
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. 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). Red Blood Cells (Frozen Rejuvenated) which were collected and stored in CPD or CPDA-1 may be stored frozen up to 10 years.

When RBC are rejuvenated after maximum liquid storage, i.e., CPD RBC at 24 days or CPDA-1 RBC at 38 days, the concentrations of 2,3-DPG and ATP increase typically to above normal.

CAUTION: RBC collected in CPD or CPDA-1 cannot be leukocyte reduced prior to rejuvenation.

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 glycerolized and frozen. Red Blood Cells, Frozen Rejuvenated which were collected and stored in CPD/AS-1 may be stored for up to 3 years. Unlike rejuvenated CPD and CPDA-1 RBC, rejuvenated CPD/AS-1 RBC have not been approved to be immediately washed and transfused.

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 reported 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.

Warning and Contraindications
rejuvesol Solution is intended only for the extracorporeal rejuvenation of a RBC. It should not 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. 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.7

Rejuvenated RBC are further processed prior to transfusion to remove the unused portion of rejuvesol Solution, by-products of the rejuvenation process, and any other potential storage related impurities in rejuvesol Solution. Based on the concentration of the residual inosine in rejuvenated, deglycerolized RBC, the average washout of inosine was calculated to be 99.8%. A literature search for potential toxicity associated with the ingredients that comprise rejuvesol Solution, including potential metabolites, was conducted. This report concludes that no theoretical contraindications would be associated with the transfusion of a single unit of unwashed, rejuvenated RBC that would contain amounts of pyruvate, inosine, adenine, phosphate, hypoxanthine, uric acid, and lactate that exceed reference values (excluding lactate) as these substances are naturally metabolized and/or are excreted.

The maximum number of properly processed rejuvenated RBC that can be transfused to a single recipient over their entire lifetime has not been determined.

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. Exposure to temperatures near or below freezing may produce a white precipitate in the solution; this precipitate will dissolve upon brief incubation at room temperature. Alternatively, the product may be warmed at 37°C for up to one hour in a dry air incubator to dissolve the precipitate.

How Supplied
PN 7012: 50 mL vial; 12 vials per case

To Order
Contact Citra Labs Customer Service
e: CitraCS@Biomet.com
p: 800.299.3411 (toll free)
p: 781.848.2174 (MA)
f: 781.848.6781

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch or call 1-800-FDA-1088.
Sample Standard Operating Procedures (SOP)
rejuvesol red blood cell processing solution
Rejuvenation of RBC Prior to Immediate Use
Refer to product labeling for detailed instructions for use

1.0 Introduction
1.1 rejuvesol red blood cell processing solution (rejuvesol Solution) is intended to be used as an in vitro processing solution for the rejuvenation of a unit of red blood cells (RBC). rejuvesol Solution restores 2,3-diphosphoglycerate (2,3-DPG) and adenosine triphosphate (ATP) to fresh levels in treated RBCs. The final concentration of ATP and 2,3-DPG achieved after rejuvenation will vary depending on number of days of liquid storage at 1-6°C prior to rejuvenation.

2.0 Purpose
2.1 This document outlines steps necessary for using rejuvesol Solution to rejuvenate a unit of RBC prior to immediate use.

3.0 Scope
3.1 This procedure may be applied to RBC for rejuvenation prior to immediate use. Immediate use is defined as within the subsequent 24 hours and not cryopreserved.

4.0 Materials and Equipment (As suggested or equivalent)
NOTE: Refer to Appendix A for Materials and Equipment Checklist
4.1 An FDA cleared cell washer/washing system
4.2 Temperature-controlled (circulating) water bath
4.3 Integral tubing sealer
4.4 Sterile alcohol swabs (70%)
4.5 One sterile vial (50 mL) of rejuvesol Solution (Citra PN 7012)
4.6 Y-type Rejuvenation Set (Citra PN 7212) or equivalent
4.7 Two watertight plastic overwrap bags and weights
4.8 Waterproof tape
4.9 Overwrap bag impulse sealer (optional)
4.10 Sterile Docking Device (SCD)

5.0 Procedure
5.1 Combine rejuvesol Solution with RBC
5.1.1 Remove flip-off protective cap from the rejuvesol Solution vial and clean exposed rubber stopper surface with alcohol swab.
5.1.2 Close all slide clamps of Y-type Rejuvenation Set (Citra PN 7212). Heat seal integral tubing between transfer bag and Y connector, detach and discard empty transfer bag.
5.1.3 Aseptically insert vented spike of Y-type Rejuvenation Set into stopper of rejuvesol Solution.
5.1.4 Sterile connect tubing of Y-type Rejuvenation Set to primary collection bag. Alternately, aseptically insert spike of Y-type Rejuvenation Set into one port of primary collection bag.
5.1.5 Elevate rejuvesol Solution vial above primary collection bag.
5.1.6 Squeeze drip chamber to prime and open slide clamp of Y-type Rejuvenation Set.
5.1.7 Allow entire contents of rejuvesol Solution vial to flow into primary collection bag while gently agitating mixture.
5.1.8 After all rejuvesol Solution has been transferred, close slide clamp and heat seal tubing above primary collection bag.
5.1.9 Disconnect at heat seal; discard used tubing and empty rejuvesol Solution vial.
5.1.10 Proceed immediately to Section 5.2.

5.2 Incubate RBC/rejuvesol Solution mixture for 60 minutes at 37°C.\(^\text{1,8,10,12}\)

**NOTE:** Incubation timing is initiated when RBC/rejuvesol Solution mixture is introduced into the water bath. Actual temperature of RBC/rejuvesol Solution mixture does not reach 37°C (the final temperature is usually 29-31°C).

5.2.1 Place primary collection bag containing RBC/rejuvesol Solution mixture into a plastic overwrap bag and remove air.
5.2.2 Seal plastic overwrap bag.
5.2.3 Place sealed overwrapped unit inside second overwrap bag containing weights (to keep the unit submerged during incubation); remove air and seal.
5.2.4 Place overwrapped unit in water bath and secure.
5.2.5 Incubate unit at 37°C for 60 minutes.
5.2.6 Remove unit, blot dry outer overwrap bag and carefully remove overwraps from RBC/rejuvesol Solution mixture.

**NOTE:** Use caution to ensure primary collection bag and mixture are not contaminated with any water.

5.3 Process red blood cell/rejuvesol Solution mixture after incubation.\(^\text{3,10}\)

Use an approved cell washing system and standard operating procedures for that system to wash RBC/rejuvesol Solution mixture.\(^\text{3}\) The rejuvenated, washed RBC may be stored at 1-6°C for up to 24 hours prior to transfusion.\(^\text{3,9,10}\)

**NOTE:** No more than four (4) hours should elapse between the time the unit is removed and returned to the 1-6°C storage environment.\(^\text{10}\)

6.0 Labeling and Documentation

6.1 Ensure appropriate documentation of rejuvenation incubation start time to calculate expiration time. Document product modification per facility protocols.

6.2 Ensure rejuvenated unit is properly labeled according to current guidelines and facility protocols.
Rejuvenation of RBCs: Prior to Immediate Use

1. All clamps are closed.
2. Heat seal the integral tubing. Detach and discard the empty transfer bag.
3. Detach and discard the empty transfer bag.
4. Clamp B is opened and rejuvenesol Solution is transferred. Gently agitate mixture.
5. Bottle is raised 28 in. above RBCs. Squeeze drip chamber to prime.
6. Clamp A is opened and rejuvenesol Solution is transferred. Gently agitate mixture.
7. Close slide clamp. Heat seal the tubing three times. Cut the middle heat seal.
8. Over-wrapped materials are put in circulating water bath 37° C for 60 minutes.
9. Remaining materials are double over-wrapped in plastic.
10. Wash RBCs immediately per operating procedure.
**rejuvesol** red blood cell processing solution
Rejuvenation of RBC Prior to Cryopreservation
Refer to product labeling for detailed instructions for use

1.0 Introduction
1.1 rejuvesol red blood cell processing solution (rejuvesol Solution) is intended only to be used as an in vitro processing solution for the rejuvenation of a unit of red blood cell (RBC). rejuvesol Solution restores 2,3-diphosphoglycerate (2,3-DPG) and adenosine triphosphate (ATP) to fresh levels in treated RBCs. 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.

2.0 Purpose
2.1 This document outlines the procedure necessary for using rejuvesol Solution to rejuvenate a unit of RBC prior to cryopreservation.

3.0 Scope
3.1 This procedure is to be applied to any RBC unit intended for rejuvenation prior to cryopreservation.

4.0 Materials and Equipment (As suggested or equivalent)
**NOTE:** Refer to Appendix A for Materials and Equipment Checklist
4.1 Temperature-controlled (circulating) water bath
4.2 Integral tubing sealer
4.3 Sterile alcohol swabs (70%)
4.4 One sterile vial (50 mL) of rejuvesol Solution (Citra PN 7012)
4.5 Y-type Rejuvenation Set (Citra PN 7212)
4.6 Two watertight plastic overwrap bags and weights
4.7 Waterproof tape
4.8 Overwrap bag impulse sealer (optional)
4.9 Sterile Docking Device (SCD)

5.0 Procedure
5.1 Combine rejuvesol Solution with the RBC
   5.1.1 Remove flip-off protective cap from the rejuvesol Solution vial and clean exposed rubber stopper surface with alcohol swab.
   5.1.2 Close all slide clamps of Y-type Rejuvenation Set (Citra PN 7212).
   5.1.3 Aseptically insert vented spike of the Y-type Rejuvenation Set into the stopper of rejuvesol Solution.
5.1.4 Sterile connect tubing of Y-type Rejuvenation Set to primary collection bag. Alternately, aseptically insert spike of the Y-type Rejuvenation Set into one port of primary collection bag.

5.1.5 Elevate rejuvesol Solution vial above primary collection bag.

5.1.6 Squeeze drip chamber to prime and open slide clamp of the Y-type Rejuvenation Set.

5.1.7 Allow entire contents of rejuvesol Solution vial to flow into primary bag while gently agitation mixture.

5.1.8 After all rejuvesol Solution has been transferred, close slide clamp and heat seal tubing between rejuvesol Solution vial and 3-way connector of Y-type Set.

5.1.9 Disconnect at heat seal and discard empty rejuvesol Solution vial.

5.1.10 Proceed immediately to Section 5.2.

5.2 Incubate RBC/rejuvesol Solution mixture for 60 minutes at 37°C.\(^1,8,10,12\)

**NOTE:** Incubation timing is initiated when RBC/rejuvesol Solution mixture is introduced into the water bath. Actual temperature of RBC/rejuvesol Solution mixture does not reach 37°C (the final temperature is usually 29-31°C).

5.2.1 Place primary collection bag containing RBC/rejuvesol Solution mixture into a plastic overwrap bag and remove air.

5.2.2 Seal plastic overwrap bag.

5.2.3 Place sealed overwrapped unit inside second overwrap bag containing weights (to keep the unit submerged during incubation); remove air and seal.

5.2.4 Place overwrapped unit in water bath and secure.

5.2.5 Incubate unit at 37°C for 60 minutes.

5.2.6 Remove unit, blot dry outer overwrap bag and carefully remove overwraps from RBC/rejuvesol Solution mixture.

**NOTE:** Use caution to ensure primary collection bag and mixture are not contaminated with any water.

5.3 Process RBC/rejuvesol Solution mixture after incubation.\(^1,9,10\)

Complete the glycerolization procedure per Standard Operating Procedure.\(^1,9,10\)

**NOTES:**

i. After incubation, the red blood cell/rejuvesol Solution mixture may need to be concentrated prior to the addition of glycerol solution to insure proper glycerolization.\(^1,8,11,13\) The Y-type Rejuvenation Set contains a transfer bag that may be utilized for this purpose.

ii. No more than four (4) hours should elapse between the time the unit is removed and returned to the 1-6°C storage environment.\(^10\)

6.0 Labeling and Documentation

6.1 Document product modification per facility protocols.

6.2 Ensure rejuvenated unit is properly labeled according to current guidelines and facility protocols.
Rejuvenation of RBCs: Prior to Cryopreservation

All clamps are closed. Bottle & RBC bag are connected to tubing set. Close the slide clamp. Heat seal the tubing three times. Cut the middle heat seal. Remaining materials are double over-wrapped in plastic.

Glycerolize and freeze per standard operating procedure. If required, centrifuge rejuvenated RBC.

Over-wrapped materials are put in circulating water bath 37°C for 60 minutes.

Clamp A Clamp B

Clamp A

Clamp B

Clamp B

Clamp B

Clamp A

Clamp A

All clamps are closed.

Bottle & RBC bag are connected to tubing set.

Squeeze drip chamber to prime. Bottle is raised 28 in. above RBCs.

Mixing

Clamp B is opened and rejuvenesol Solution is transferred. Gently agitate mixture during transfer.

Clamp A Clamp B
Training & Competency Assessment
Objectives of Training Session

NOTE: Refer to Appendix B—Training Presentation for user training materials.

Successful trainees will be able to achieve the following, as evidenced by demonstrated proficiency using rejuvesol Solution to rejuvenate a unit of red blood cells.

- Identify appropriate unit and supplies for rejuvenation.
- Properly use Y-type Rejuvenation Set (or equivalent) for addition of rejuvesol Solution to RBC.
- Incubate unit at appropriate time and temperature.

Training Checklist

By checking, the trainee documents completion of the indicated steps:

Has read and understood:

☐ rejuvesol red blood cell process solution Instructions for Use

☐ Facility SOP for use of rejuvesol Solution

Has successfully demonstrated:

☐ Ability to select appropriate unit for rejuvenation

☐ Proper inspection of rejuvesol Solution and disposable set prior to use

☐ Understanding of use of Y-type Rejuvenation Set

☐ Proper incubation time and temperature for rejuvenation

Trainee's Printed Name

Date

Trainee's Signature

Trainer's Printed Name

Date

Trainer's Signature
Circle the letter of the correct response.

1. rejuvesol red blood cell processing solution (rejuvesol Solution) may be used to improve oxygen delivery capacity of transfused red blood cells.
   a. True
   b. False

2. rejuvesol Solution is supplied in 50 mL glass vials, each vial treats one unit of red blood cells.
   a. True
   b. False

3. rejuvesol Solution contains glycerol.
   a. True
   b. False

4. 2,3-DPG levels decline rapidly within the first 2 weeks, while ATP levels decline steadily during storage of donated red blood cells.
   a. True
   b. False

5. Rejuvenated, frozen CPD/AS-1 red blood cells are approved for up to 3 years of shelf life.
   a. True
   b. False

6. rejuvesol Solution contains the following ingredients:
   a. Phosphate, Adenine, Glycerol, Inosine
   b. Phosphate, Inosine, Pyruvate, Adenine
   c. Pyruvate, Mannitol, Adenine, Glucose
   d. Pyruvate, Inosine, Glucose, Adenine

7. Rejuvenated red blood cells are to be washed with ______________ prior to infusion.
   a. 0.9% Saline (NaCl)/0.2% Dextrose
   b. 0.5% Dextrose
   c. Sterile Water for Injection
   d. Lactated Ringers

8. Rejuvenated red blood cells (for immediate use) should be transfused within:
   a. 24 hours
   b. 42 days

9. rejuvesol Solution is washed off the treated red blood cells prior to infusion. This wash process:
   a. Removes residual rejuvesol solution
   b. Removes by-products of rejuvenation
   c. Removes plasma proteins and other unwanted analytes
   d. All of the above

10. rejuvesol Solution must incubate with the red blood cells at _____ degrees for _____ minutes.
    a. 37°C and 30 minutes
    b. 24°C and 30 minutes
    c. 24°C and 60 minutes
    d. 37°C and 60 minutes

Quiz answers on Page 30
FDA Approval Statement
**rejuvesol** red blood cell processing solution, Part Number: 7012

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| **Original Applicant** | Cytosol Laboratories, Inc.  
55 Messina Drive  
Braintree, MA 02184 US |
| **Current Owner** | Citra Labs, LLC, a Biomet Biologics Company  
55 Messina Drive  
Braintree, MA 02184 US |
| **Type** | New Drug Application (CBER) |

**Y-Type Rejuvenation Set, Part Number: 7212**

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<td>Y-Type Rejuvenation Set</td>
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</table>
| **Original Applicant** | Cytosol Laboratories, Inc.  
55 Messina Drive  
Braintree, MA 02184 US |
| **Current Owner** | Citra Labs, LLC, a Biomet Biologics Company  
55 Messina Drive  
Braintree, MA 02184 US |
| **Type** | 510(k) Traditional |
Process Validation & Control
Process Validation

As is presented elsewhere within this Handbook, Citra Labs has met the US FDA requirements to obtain approval to market rejuvesol red blood processing solution. Data gathered during multicenter trials included pre and post-rejuvenation 2,3-DPG and ATP analysis. Studies confirmed rejuvesol Solution consistently performed as expected when handled according to manufacturer’s instructions.

The objective of process validation for rejuvesol Solution is to generate evidence ensuring each RBC unit, when rejuvenated and processed according to SOP, will consistently yield expected post-rejuvenation results.

The rejuvesol Solution validation process is subjective—organizations may validate the rejuvenation process multiple ways. Sample size may be limited to a small quantity for the purposes of challenging draft standard operating procedures. Validation should, at a minimum, include a walk-through of draft standard operating procedures for rejuvenation prior to immediate transfusion and/or cryopreservation used in tandem with a previously validated washing and/or deglycerolizing process. Validation should also confirm appropriate processes are in place for properly labeling rejuvenated products.

The following tests may be considered for qualitative/quantitative post-rejuvenation data analysis:

**Intent:** Ensure adequate post-rejuvenation wash process:
- Total Protein analysis (dipstick or chemistry)
- Osmolality
- Specific Gravity by refractometer (or equivalent)

**Intent:** Ensure adequate rejuvenation process:
- p50
- 2,3-DPG levels
- ATP levels

Process Control

As with most blood product manufacturing, AABB Standards require ongoing process control as is found below:

**Rejuvenated Deglycerolized Red Blood Cells:**
1. Adequate removal of cryoprotective agents
2. Minimal free hemoglobin in supernatant solution
3. Mean recovery of ≥80% of the preglycerolized red cells

**Rejuvenated Washed Red Blood Cells:**
1. Use of “Method known to ensure that the red cells are washed with a volume of compatible solution that will remove almost all of the plasma”, i.e., ensure standard washed process functions as expected by performing any routine QC prescribed by respective facility.
ISBT Labeling
Blood Product Labeling

As with all blood and blood components, please label in compliance with ISBT 128 Nomenclature.

Washed, Deglycerolized, or Rejuvenated Red Blood Cells*

Neither the anticoagulant nor the nominal collection volume needs to appear on the label. The actual volume shall appear on the label.

Proper Name**

NOTE: Refer to current IFU for approved indications for use.

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<th>Component Class</th>
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Product Codes***

Should be identified using the ICCBBA Product Description Code Database or the Product Description Code Lookup Program found in the Members Only section of the ICCBBA website, ICCBBA.org.

* ICCBBA US Consensus Standard, Version 3.0.0, March 2013 Section 7.8.5  
** ICCBBA US Consensus Standard, Version 3.0.0, March 2013, Section 6.2  
*** ICCBBA US Consensus Standard, Version 3.0.0, March 2013, Sections 4.3 and 8.2
Product Questions
rejuvesol red blood cell processing solution

1. What is rejuvesol Solution?
   It is a sterile, non-pyrogenic solution of pyruvate, inosine, adenine, and phosphate in water for injection and intended only for use in the extracorporeal rejuvenation of a unit of red blood cell (RBC) concentrate.26

2. How does rejuvesol Solution work?
   rejuvesol Solution restores 2,3-DPG and ATP of liquid stored RBCs to “fresh” levels by conversion of the pyruvate, inosine, adenine, and/or phosphate through natural enzymatic pathways within the RBC.26

3. When should rejuvesol Solution be used?
   It is intended for rejuvenation of RBCs stored as CPD, CPDA-1 or CPD/AS-1 prior to cryopreservation. In addition, it is intended for rejuvenation of RBC (CPD or CPDA-1) that are to be washed prior to immediate use.26

4. How is a unit of red blood cells (RBCs) rejuvenated?
   rejuvesol Solution is added to the unit of RBC and the mixture is incubated at 37°C for 60 minutes. Refer to the IFU for more detailed instructions.

5. What is the Y-Type Rejuvenation Set?
   It is a tubing set to assist in the transfer of rejuvesol Solution into the RBCs unit. Its Part Number is PN7212.

6. What equipment can be used to incubate the RBC / rejuvesol Solution mixture?
   Currently, rejuvenation with rejuvesol Solution is approved using a circulating water bath (or equivalent).26

7. Can a 50 mL vial of rejuvesol Solution be used to treat multiple units of RBCs?
   A 50 mL vial of rejuvesol Solution is approved as a single dose to rejuvenate a unit of RBCs.26

8. Does rejuvesol Solution have to be refrigerated after opening?
   The entire contents of the 50 mL vial of rejuvesol Solution is considered a single dose and should be used upon opening.26 Additionally, rejuvesol Solution is to be stored between 15°C and 25°C.

9. Can a unit of rejuvenated RBCs be transfused without further processing?
   The rejuvenated RBCs must be washed (if for immediate transfusion) or cryopreserved (for later use). Refer to the IFU for more detailed instructions.26

10. Can RBCs stored in additive solution AS-1 be rejuvenated after Day 42 of liquid storage?
    RBCs stored in AS-1 can be rejuvenated up to day 42.26

11. Can RBCs be rejuvenated if it has been stored in AS-3 or AS-5?
    No, rejuvesol Solution is currently indicated for rejuvenation of RBCs stored in AS-1.26

12. When RBCs are stored in additive solution AS-1 and rejuvenated, can they be washed for immediate transfusion?
    Refer to current Instructions for Use for detailed indications for use.

13. How can I order rejuvesol red blood cell processing solution and the Y-Type Rejuvenation Set?
    Contact Citra Customer Service at 1-800-299-3411 or via email at CitraCS@Biomet.com. You may also fax purchase orders directly to 781.848.6781.

14. What is the expiration date for rejuvesol red blood cell processing solution?
    Refer to vial labeling (14 months from the date of manufacture).
**Product Questions (cont.)**

15. **What is the expiration date for the Y-Type Rejuvenation Set?**
   Refer to Y-Type Rejuvenation Set labeling (3 years from date of manufacture).

16. **What are rejuvesol Solution contraindications?**
   rejuvesol Solution is intended for extracorporeal rejuvenation of RBCs stored in CPD, CPDA-1 or CPD/ADSOL (CPD/AS-1 leukocyte reduced). It should not be directly administered to humans. Refer to the IFU for more detailed contraindications.26

17. **What is the rejuvesol Solution pregnancy category?**
   Safety and efficacy studies of rejuvesol Solution treated RBCs, specifically during a pregnancy, have not been performed. The use of rejuvenated RBCs is a clinical judgment of the prescribing physician.

18. **Are rejuvenated RBCs better than fresh RBCs?**
   Rejuvenation of RBCs with rejuvesol Solution restores 2,3-DPG and ATP of liquid stored RBCs to “fresh” levels.26

19. **Is this the same rejuvesol Solution I previously ordered from Cytosol Laboratories (enCyte Systems, Inc.)?**
   Yes, the product and rejuvenation process remain the same.

20. **Does rejuvesol Solution contain latex?**
   No, rejuvesol Solution is latex free.

21. **What is the acceptable tolerance for the temperature of the 37°C water bath used to incubate the RBCs / rejuvesol Solution mixture?**
   The water bath temperature control should be set at 37°C and capable of holding the temperature at ±1°C.

**Pricing / Returns**

1. **How much does rejuvesol Solution cost?**
   rejuvesol Solution (PN7012) is distributed as a 12 unit pack. Pricing is available via Citra Labs Customer Service at 1-800-299-3411.

2. **What is the return policy for rejuvesol Solution?**
   Contact customer service at 1-800-299-3411 for returned goods authorization (RGA) Guidance.

**Regulatory**

1. **What type of clearance does rejuvesol Solution have in the US?**
   The Federal Drug Administration approved rejuvesol Solution on February 27, 1997. It is approved for use as a drug. It currently falls under jurisdiction of Center of Biologics Evaluation and Research (CBER) which regulates biological products for human use. For additional details, refer to FDA Approval Statement in this handbook.

2. **What type of clearance does the Y-Type Rejuvenation Set have in the US?**
   The Y-Type Rejuvenation Set is cleared under a 510k. For additional details, refer to FDA Approval Statement in this handbook.

3. **Are rejuvesol Solution and the Y-Type Rejuvenation Set available outside of the United States?**
   rejuvesol Solution and the Y-Type Rejuvenation Set are only approved for use in the United States.

4. **Can I purchase rejuvesol Solution and the Y-Type Rejuvenation Set for shipment to (country X)?**
   No, rejuvesol Solution and the Y-Type Rejuvenation Set are only approved for use in the United States.
Quality

1. **Who should I notify if I have a product experience or complaint to report?**

   Please promptly report any experiences or concerns to Citra Labs Customer Service at 1-800-299-3411 or via email at CitraCS@Biomet.com.

Company

1. **Where is rejuvesol Solution manufactured?**

   rejuvesol Solution is manufactured for Citra Labs by Grand River Aseptic Manufacturing, Inc., located in Grand Rapids, MI.

2. **Is Citra Labs part of Biomet?**

   Yes, Citra Labs, LLC is a wholly owned subsidiary of Biomet, Inc. and Biomet Biologics, LLC.

3. **What happened to Cytosol Laboratories and enCyte Systems?**

   Biomet, Inc. and Biomet Biologics, LLC purchased certain assets of Cytosol Laboratories, Inc., Citra Anticoagulants, Inc., and enCyte Systems, Inc., and transferred and assigned those assets to Citra Labs, LLC, a wholly owned subsidiary of Biomet, Inc. and Biomet Biologics, LLC.

Samples

1. **Is it possible to obtain samples of rejuvesol Solution and the Y-Type rejuvenation set?**

   Yes, visit rejuvesol.com to request samples and view the sample policy.
Appendices

Appendix A: Materials and Equipment Checklist

**Materials/Equipment (As suggested or equivalent)**

- [ ] An FDA cleared cell washer/washing system*
- [ ] Temperature-controlled (circulating) water bath
- [ ] Integral tubing sealer
- [ ] Sterile alcohol swabs (70%)
- [ ] One sterile vial (50 mL) of rejuvesol Solution (Citra PN 7012)
- [ ] Y-type Rejuvenation Set (Citra PN 7212)
- [ ] Two watertight plastic overwrap bags and weights
- [ ] Waterproof tape
- [ ] Overwrap bag impulse sealer (optional)
- [ ] Sterile Docking Device (SCD)

*Required for immediate use only*
Appendix B: Training Presentation

Refer to rejuvenol.com for on-line training presentation/video.

Questions or comments? Please contact us:

Citra Labs Customer Service
p: 1-800-299-3411
e: CitraCS@Biomet.com

Product Quiz Answer Key

1. A
2. A
3. B
4. A
5. A
6. B
7. A
8. A
9. D
10. D
References

4. Valeri CR, CG Zaroulis, JJ Vecchione, et al.; Therapeutic effectiveness and safety of outdated human red blood cells rejuvenated to restore oxygen transport function to normal, frozen for 3 to 4 years at –80 °C, washed, and stored at 4 °C for 24 hours prior to rapid infusion. Transfusion 1980; 20: 159-70.
7. Boston University School of Medicine/Naval Blood Research Laboratory, Boston, MA Standard Operating Procedure—Red Blood Cells Collected in the CPDA-1 800 mL Primary PVC Plastic Collection Bag System and Stored for 3 to 35 Days (Indated-Rejuvenated) or for 36 to 38 Days (Outdated-Rejuvenated), Biochemically Modified with PIPA Solution Prior to Glycerolization in the Primary 800 mL Bag with the Special Adaptor Port Using 40% W/V Glycerol and Storage at –80 °C, Washed in the Haemonetics Blood Processor 115, and Stored at 4 °C for 24 Hours Prior to Transfusion (Revised 5/91).
26. Instructions for Use (IFU); rejuvenesol red blood cell processing solution.

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