Status **Scheduled** PolicyStat ID **13078544**

Origination	6/10/2022	Document Contact	Kelly Sartor: Supv, Laboratory
Last Approved	2/21/2023	Area	Laboratory-Blood Bank
Effective	3/7/2023	Applicability	Dearborn, Taylor, Trenton, Wayne
Last Revised	2/21/2023		
Next Review	2/20/2025		

Rh Immune Globulin Evaluation - Blood Bank

Document Type: Procedure

I. PURPOSE AND OBJECTIVE:

This document will provide Blood Bank policies relating to Rh Immune Globulin (RhIG) candidacy and the preparation of RhIG.

II. CLINICAL SIGNIFICANCE:

Rh(D) immunization in pregnancy most commonly results from the fact that, at delivery, a variable volume of fetal blood enters the maternal circulation when the placenta separates from the uterine wall. Rh(D) immunization may result if the mother produces antibodies that are directed at antigens present on the fetal red blood cells (RBCs) but absent on the maternal RBCs. Rh(D) negative mothers delivering Rh(D) positive infants are most susceptible. In most cases, Rh(D) immunization can be prevented by the administration of Rh Immune Globulin (RhIG) within 72 hours from the time of delivery. One standard 300 µg dose of RhIG is generally sufficient to prevent immunization when up to 30 ml of fetal whole blood (approximately 15 ml of RBCs) have entered the maternal circulation.

III. SCOPE:

A. This document is applicable for the following patients:
    1. Postpartum and antepartum patients for whom a Rh Immune Globulin evaluation is ordered by a physician; e.g., a pregnant patient in the emergency room, or a post-partum patient

B. At Beaumont Health (BH) the patient caregivers will order one of two available tests:
    1. Rh Immune Globulin Evaluation – Antepartum (**RHGAN**) ; a complex test code ordered in EPIC using order code LAB5288, and comprised of:

a. Maternal ABO/Rh
b. Maternal Antibody Screen
c. RhIG Candidacy Report (**RHIGC**)

2. Rh Immune Globulin Evaluation - Postpartum (**RHGPP**); a complex test code ordered in EPIC using order code LAB5287, and comprised of:
    a. Fetal Cell Screen (**FCS**)
    b. RhIG Candidacy Report (**RHIGC**)

IV. DEFINITIONS/ACRONYMS:

A. Current Sample: a sample that was collected no more than 3 days before the current date. For example, if a sample is drawn on Monday (day 0), then the sample remains "current" all day Mon., Tues., Wed., and Thur.

B. Delivery: as used in this document this term refers to the cessation of all pregnancies greater than 18 weeks gestation including full-term births and pregnancies that are terminated or interrupted for any reason.

C. CAP: College of American Pathologists

D. Designee: a Blood Blood Technical Director or Blood Bank fellow.

E. RHGAN: The Blood Bank computer test code assigned to the Rh Immune Globulin - Antenatal profile.

F. RHGPP: The Blood Bank computer test code assigned to the Rh Immune Globulin - Postpartum profile.

G. RHIGC: The Blood Bank computer test code assigned to the RhIG Candidacy report.

H. RhIG: Rh Immune Globulin

I. Rhogam®: Trade name for Rh Immune Globulin produced by Kedrion Biopharma Inc.

J. RhIG Control Card: 3 part form provided by the manufacturer as part of the RhIG insert, for each vial of RhIG used to document immunization details.

K. FMH: Fetal Maternal Hemorrhage

L. FCS: refers to the qualitative fetal cell screen test that is performed in the Blood Bank. This test is called the FMH Rapid Screen; see the package insert provided by Immucor/ Gamma®. FCS is the computer test code for this Blood Bank test.

M. FRBCG: The EPIC Beaker test code assigned to the quantitative flow cytometry test for Fetal RBC Assay.; LAB6413

N. ACDEL: The EPIC Beaker test code assigned to the Hematology Acid Elution test by Kleihauer Betke method; LAB5135

V. SPECIMEN COLLECTION AND HANDLING:

A. The preferred sample is a 6ml EDTA sample with affixed identifying label. Refer to Transfusion Medicine Policy, Triaging And Identifying Acceptable Samples For Testing

B. Postpartum testing requires a blood specimen collected from the mother after delivery of all products of conception. It is best to wait about an hour after delivery to allow any fetal RBCs to mix thoroughly in the maternal circulation, but the sample should be collected as soon as possible thereafter.

VI. POLICIES:

A. **Indications for Antepartum RhIG Administration**

1. It is the responsibility of the patient's physician to determine whether antepartum RhIG is indicated. If the physician orders antepartum RhIG, the Blood Bank will set up the RhIG as described in attachment *Antepartum Determination of RhIG Candidacy*.
2. Possible reasons that the patient's physician may order antepartum RhIG include:
    a. 28 week prophylaxis
    b. Threatened miscarriage or vaginal bleeding
    c. Ectopic pregnancy, placenta previa, or abdominal trauma
    d. Known or suspected fetal-maternal hemorrhage
    e. Invasive obstetrical procedures (amniocentesis, chorionic villus sampling, percutaneous umbilical cord sampling [PUBS], and manipulative procedures such as an external cephalic version)

B. **Maternal Compatibility Testing**
Before assessing maternal RhIG candidacy, the maternal ABO/Rh and antibody screen should be completed on a current sample. Antibody identification studies should also be completed, if applicable.

C. **Determination of Neonatal Rh(D)**
Before assessing postpartum maternal RhIG candidacy, neonatal Rh(D) testing should be completed on a sample from the current admission. Neonatal Rh(D) is determined as described in Transfusion Medicine Policies *Cord Blood Evaluation, Typing of Neonatal Samples to Assess Maternal RhIG Candidacy and* Forward Typing Determination Of Neonatal ABO and Rh for Patients Less Than Four Months of Age By Tube Method.

D. **Requests for Add On Testing**
If there is a request to add Rhogam Eligibility to a previously collected specimen, the technologist must confirm if the specimen is eligible for add on.

1. The delivery status of the patient must be confirmed. Post partum rhogam can not be added to a predelivery specimen.
2. Clinical staff must be instructed to place either the antenatal or post partum orders based on this status.
3. RhIG action codes can not be added to previously collected specimen that does not include the appropriate RHIGC and Fetal Screen order codes (if indicated).

E. **Maternal Rh(D) Sensitization /Requirement for Medical Director Review.**
Mothers who are previously sensitized to Rh(D) are not candidates for RhIG. However, in some cases it may be difficult to determine whether the mother is truly sensitized to Rh(D). For this reason:

1. All RhIG evaluations that are interpreted as Ineligible and resulted with the canned comment code **RNCSD** (Not Rh Immune Globulin Candidate; Patient is sensitized to the Rh (D) Antigen) should be reviewed as soon as possible by Medical Director or designee.
2. All RhIG evaluation cases for patients in which there is any question as to whether Anti- D specificity is due to recent RhIG administration or to alloimmunization (**DUNK** antibody determination) shall be considered RhIg candidates. Final determination whether RhIG is to be given is to be made by the ordering physician.

   Refer to Transfusion Medicine Policy, Policies Specific to Patients with Passive Anti-D (Due to Recent RH Immune Globulin Administration).

F. **Maternal Fetal Cell Screening**

1. Fetal cell screening is performed as described in Transfusion Medicine Policy, Fetal Cell Screening Using the FMH Rapid Screen Kit.
2. The FCS may be performed only on a sample from a Rh(D) negative mother after the delivery of a Rh(D) positive neonate. It is not performed on antepartum patients. The specimen used to perform the FCS test must be collected after delivery of all products of conception.
3. The FCS is a qualitative test only, and is used to determine whether one vial of RhIG is sufficient or if quantitative FMH testing is required to determine the total number of vials of RhIG that are indicated.

G. **Fetal Maternal Hemorrhage Flow Cytometry (FRBCG)Testing**

1. Fetal RBC Assay testing is performed in the following situations:
   a. When the FCS test is positive.
   b. When the mother or baby is weak D / partial D positive.
   c. When the Rh(D) of the mother or neonate / fetus cannot be determined or if a sample cannot be obtained for any reason; e.g., intra-uterine fetal death (IUFD), medical interruption of pregnancy (MIP), when an unresolved Rh(D) discrepancy is present, for cases greater than 18 weeks gestation.
   d. When delivery has not yet occurred; e.g., in antepartum cases greater than 18 weeks gestation as described in attachment *Antepartum Determination of RhIG Candidacy.*
2. When indicated a sample will be sent to the Flow Cytometry laboratory for the quantitative Fetal RBC Assay test (FRBCG). The test is available on the day shift Monday through Saturday except holidays. The results of this test are used to determine the total number of vials of RhIG that are indicated.
3. If the Fetal RBC Assay test is indicated for any reason as described in attachments, one vial of RhIG should be prepared as soon as possible; do not wait until the flow cytometry is complete.

H. **Acid Elution by Kleihauer-Betke Method (ACDEL)**

1. If the FRBCG test cannot be performed when indicated then the Kleihauer Betke

stain is used as an alternative method.

2. It is performed only for patients seen in the emergency room or for mothers being discharged at Dearborn, Taylor, Trenton or Wayne before the Flow Cytometry laboratory will reopen with the approval of the Medical Director.
3. The blood bank at Dearborn performs this test on behalf of Hematology department at Dearborn. Blood Bank must communicate with the hematology department about the status of this test when ordered as the test code appears on the Hematology Outstanding List.

I. **Ordering the FMHA test code**

1. Whenever the RBC Fetal Assay is indicated the SoftBank test code FMHA should be ordered regardless of whether the sample will be sent to flow cytometry or hematology. This will appear on the Pending Test Report as a place order until all testing is complete.
2. The FMHA is cancelled upon completion of the RBC Fetal Assay/Kleihauer Betke.

J. **Determining RhIG Dose**

1. RhIG dosage is determined based upon the the % Fetal Cells determined by the results of the Fetal RBC Assay or Kleihauer Betke methods as indicated in the following table:

Rh Immune Globulin Dosage	
% Fetal Cells	Vials of RhIg Indicated
0.0 to 0.2	1
0.3 to 0.8	2
0.9 to 1.4	3
1.5 to 2.0	4
2.1 to 2.6	5

2. The CAP (College of American Pathologists) has provided a calculator that may also be used to determine the required number of RhIG vials. This calculator may be applied for postpartum or antepartum RhIG assessment. As indicated in the calculation, if the the maternal height and weight are not supplied a maternal blood volume of 5000 mLs is assumed. The % fetal cells (from the FMH or KBT) are entered in the calculator, and the full dose of RhIG (number of vials) is calculated. The CAP calculator can be accessed via Blood Bank Share Point.

K. **Refusal of Rhogam**

If a patient or the patient's physician refuses to administer RhIG when indicated, as described in this document, the refusal should be documented and a variance report should be submitted.

1. A comment text should be added to the patient's record with details.

L. **Timing of RhIG Administration**

1. Postpartum RhIG administration should occur within 72 hours from delivery, or as

soon as possible after delivery.

2. Antepartum RhIG should be administered after known or potential exposure to Rh(D) positive red blood cells, within 72 hours or as soon as possible after the known or potential exposure.
3. If the FMH test is indicated for any reason, one vial of RhIG should be prepared and dispensed as soon as possible; do not wait until the FMH is complete.
4. The Blood Bank will supply prophylactic RhIG at 28 weeks gestation when ordered by the patient's physician, as described in attachment: *Antepartum Determination of RhIG Candidacy*.
5. Once the Blood Bank prepares RhIG for patients, the vials are placed in the designated area in the refrigerator.
6. Whenever possible, the Blood Bank should issue RhIG within approximately 24 hours from the time that it was set up. Therefore, each morning, a technologist will verify that all allocated vials were dispensed from the Blood Bank. If any vials have not been dispensed, the patient's caregivers should be notified. This verification and any required notifications will be documented on the Communication bench/board.
7. If a dose of RhIG is indicated but is not administered within 72 hours:
    a. The dose should be administered as soon as possible; it may still be beneficial to administer the indicated RhIG dose for up to approximately 21 days. The half-life of RhIG is about 24 days.
    b. A variance report should be submitted.

M. **Disposition of the RhIG**
A RhIG vial that is dispensed by the Blood Bank will be issued in the Blood Bank Computer.

N. **Return of Unused RhoGAM® Vials to the Blood Bank**
There may be instances when an unused vial of RhoGAM® is returned to the Blood Bank after it was issued for a patient. In these situations, the RhoGAM® will be inspected to determine whether or not it should be discarded or can still be used.

1. If the returned RhoGAM® vial was not opened and the integrity is not in question (i.e. there is no visible damage to the RhoGAM®, the plunger was not pushed into the vial, the needle cover was not removed, etc.), the RhoGAM® may be set up and used again, as long as it is has been returned within 6 hours.
2. If the returned RhoGAM® is clearly damaged or the vial has been opened, it should be discarded in a sharps biohazard container and a variance should be submitted.
3. If the RhoGam® vial has been returned after 6 hours and/or the integrity of the RhoGAM® is in question for any reason, it should be placed into quarantine until it is reviewed by the Medical Director. This should be documented on department communication logs or white boards where applicable.

O. **Return of the RhIG Control Form to the Blood Bank**

1. In most instances the completed RhIG Control Form is scanned into Epic Chart and not returned to Blood Bank. However, a copy of the RhIG Control Form may be returned to the Blood Bank, indicating that a vial has been injected to the patient.

2. Upon return, the Blood Bank will proceed as follows:
    a. Confirm the RhIG vial is issued in the Blood Bank computer and then file the RhIG Control form with the daily product dispense forms.

VII. SUPPLIES:

A. Rh Immune Globulin, 300 µg
B. F-1564 Blood Product Dispense Form
C. RhIG Control Form

VIII. PROCEDURE:

A. Perform maternal compatibility testing.
Complete the maternal ABO/Rh, antibody screen, and antibody identification (if applicable). Refer to Transfusion Medicine Policies, Determining The ABO and RhD Of Patients Who Are At Least Four Months Old, Antibody Screening, Antibody Identification and Routine Testing on the Ortho Vision Analyzer

B. If RhIG is ordered post partum, initiate/complete neonatal Rh(D) testing if the mother is Rh(D) negative, weak D/partial D, or if the Rh(D) of the mother is undetermined.
    1. Access the neonate's record in EPIC to verify that you are testing the correct baby, to check for multiple births etc. Refer to the Blood Bank CDM, Viewing Mother Bay Link in EPIC.
    2. Perform ABO/Rh of baby and include weak D testing if the Rh(D) reaction at immediate spin is negative. Refer to Transfusion Medicine Policy, Weak D Testing

C. Fetal Cell Screening.
    1. Determine whether FCS testing is indicated.
        a. FCS testing is indicated only for a Rh(D) negative mother after the delivery of a Rh(D) positive neonate or the cessation of pregnancy with a gestation of greater than 18 weeks.
        b. If the RhIG evaluation is ordered antepartum and it is determined the pregnancy is greater than 18 weeks, then fetal cell screen is not indicated. Quantitative FMH testing must be performed.
        c. If the RhIG evaluation is ordered postpartum and the fetal screen is not indicated cancel the FCS test as described in Blood Bank CDM - Cancelling Orders in SoftBank.

        Refer to attachments *Antepartum Determination of RhIG Candidacy* & *Postpartum Determination of RhIG Candidacy*

    2. If Indicated, perform Fetal Screen testing as described in Transfusion Medicine Policy, *Fetal Cell Screening Using the FMH Rapid Screen Kit.* FCS testing is documented in the computer under Patient/ Orders/ Results as described in the Blood Bank CDM - Resulting the Fetal Cell Screen (FCS).

D. Fetal Maternal Hemorrhage (FMH) Testing

1. Order a RBC Fetal Assay if indicated (and not already ordered by the patient's physician) as described in the Blood Bank CDM, Ordering the RBC Fetal Assay.
    a. Fetal Cell Quantitation is indicated if:
        i. Gestational age > 18 weeks
        ii. Fetal screen is positive or Mother or Infant is Weak D Positive
2. If the RBC Fetal Assay is indicated but cannot be performed (e.g., flow cytometry is closed) order and submit a sample for Kleihauer-Betke Testing. Refer to the Transfusion Medicine policy, Acid Elution by Kleihaeur Method.
3. One vial of RhIG should be prepared as soon as possible as described in step F; do not wait until the FMH is complete.
   Refer to Transfusion Medicine Policy, Fetal Cell Screening Using the FMH Rapid Screen Kit.

E. Resulting RhIG Candidacy Report

1. If RhIg evaluation is ordered antepartum, result the RHIGC (RhIG Candidacy Report) using the Blood Bank CDM - Resulting the RhIG Candidacy Report and the computer codes indicated in the attachment *Antepartum Determination of RhIG Candidacy*.
2. If RhIg evaluation is ordered postpartum, result the RHIGC (RhIG Candidacy Report) using the Blood Bank CDM - Resulting the RhIG Candidacy Report and the computer codes indicated in the attachments *Postpartum Determination of RhIG Candidacy.*

F. If the patient is a RhIG candidate, prepare and document a copy of the RhIG Control Form as described below. This copy will serve as temporary documentation until such time the vial is ready for dispense.

CONTROL FORM **Rh(D) Immune Globulin (Human) RhoGAM®**
Hospital: Beaumont Health System

ATTENTION LABORATORY
Document Patient's Name, Hospital No., and Room No.
Using an accession label, or document manually

- ✓ Patient is Rh negative / Current Date
- ✓ Baby's Rh(D) type is positive or unknown / Current Date
- ✓ FMH screening test performed, if indicated / Current Date

LOT NO. of RhoGAM issued: Lot Number EXP. DATE: Exp. Date
Tech: Initials

G. Obtain required number of vials of RhIG from the refrigerator.

1. Add an action for each vial of RhIG required (i.e. RHG, RHG2, RHG3, etc) to the appropriate test code using the Blood Bank CDM - Ordering RhIG Action Code .
2. Reprint and attach accession labels to each vial of RhIG , unless the patient name, hospital number and room number will be documented manually. Refer to the Blood Bank CDM - Reprint RhIG Accession Labels.
3. Place the RhIG vial and the completed RhIG Control form in the designated area in the refrigerator.

H. When the dispense form is received for the RhIG, issue each vial of RhIG that has been allocated for the patient.

1. Using Blood Bank CDM - Issuing RhIG generate and affix the RhIG sticker that is printed with computer workflow to the plastic bag of the product.
2. Remove and document document the 3 copies of the RhIG Control Form for each vial of RhiG as described.
3. Attach the Rh Immune Globulin Product tag that prints at issue to the plastic bag.
4. Retain the dispense copy of the tag in the blood bank and the lab copy of the RhIG Control Form for each vial of RhIG issued.

I. When the dispense form is received for the RhIG, issue each vial of RhIG that has been allocated for the patient

J. If FMH testing was indicated, upon completion of the RBC Fetal Assay test (or Acid Elution by Kleihauer Betke tests) perform the following:

1. Obtain the RBC Fetal results from EPIC. Refer to the Blood Bank CDM - Viewing Fetal RBC Assay Results in EPIC.
2. Finalize the RHIGC report with the Fetal RBC Assay results. Refer to Blood Bank CDM - Finalizing the RhIG Candidacy Report After Completion of the Fetal RBC Assay.
3. Cancel the FMHA test. Refer to Blood Bank CDM - Cancelling Tests in Soft Bank.
4. Based on the Fetal RBC Assay results (or KBT), if additional RhIG vials are required then prepare and document the Control Form for each vial of RhIG. Refer to step F of this Procedure.
5. Notify the patient's caregivers that the additional RhIG vials are ready, and document this notification as a comment to the RHIGC report.

IX. SPECIAL NOTES:

A. It is not necessary to obtain informed consent for a blood transfusion in order to administer Rh Immune Globulin (RhIG is not considered a blood product).

B. The Blood Bank typically dispenses RhIG for postpartum patients who delivered at Beaumont Health, or for antepartum patients in Labor & Delivery. However, if RhIG is requested from the Blood Bank for any patient in any location at this facility, the Blood Bank will supply the RhIG.

C. The dispense of RhIG should not be delayed while waiting for FCS or Fetal RBC Assay testing

to be completed. For example, in situations where physician intends to discharge the patient prior to completion of testing.

D. The Blood Bank should not refuse to dispense RhIG if the patient's physician or caregiver refuses to order or collect the tests required in this document. For example, physician refuses to order/collect a specimen on a patient with recent miscarriage. If RhIG is requested the fetus is considered Rh Positive, for RhIg purposes, and one vial of RhIG should be issued. The technologist should submit a variance report and a comment text should also be added to the patient's record.

X. REFERENCES:

1. Ortho Clinical Diagnostics Rh(D) Immune Globulin (Human RhoGAM® insert).
2. College of American Pathologists Transfusion Medicine Checklist, current edition.
3. AABB Technical Manual, current edition.
4. AABB Standards for Blood Banks and Transfusion Services, current edition.
5. Transfusion Therapy: Clinical Principles and Practice, 2nd ed. Mintz PD, ed.Bethesda, MD: AABB Press, 2005.
6. Memo from Robin Mofle, Director of Quality, Kedrion Biopharma, December 14, 2017.

Attachments

Antepartum Determination of RhIG Candidacy

Postpartum Determination of RhIG Candidacy

Approval Signatures

Step Description	Approver	Date
Medical Director	Muhammad Arshad: Physician [GJ]	2/21/2023
Medical Director	Jeremy Powers: Chief, Pathology	2/8/2023
	Fatima Bazzi: Medical Technologist Lead	2/8/2023
Policy and Forms Steering Committee Approval (if needed)	Kelly Sartor: Supv, Laboratory	2/3/2023

Policy and Forms Steering Committee Approval (if needed)	Ilene Hirsch: Project Mgr Policy	2/3/2023
	Ashley Beesley: Mgr Laboratory	2/2/2023
	Hilary Morey: Medical Technologist Lead	2/2/2023
	Michele Ferla: Medical Technologist Lead	2/2/2023
	Katherine Persinger: Mgr Laboratory	2/2/2023
	Kristen Lafond: Mgr Laboratory	2/2/2023
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	Kelly Sartor: Supv, Laboratory	2/2/2023