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Document Contact	Kelly Sartor
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Warm Autoantibody Investigation - Dearborn Blood Bank

Document Type: Procedure

I. PURPOSE AND OBJECTIVE:

This document will provide guidance for the Blood Bank staff to resolve antibody investigations and provide red blood cells (RBCs) for patients with warm autoantibodies.

II. CLINICAL SIGNIFICANCE:

A. The presence of warm autoantibodies (WAAs) is associated with several diseases, including warm autoimmune hemolytic anemia (WAIHA), systemic lupus erythematosus, multiple myeloma, chronic lymphocytic leukemia, and lymphoma. Patients with WAIHA may present with shortened red cell survival, hemolysis and hemoglobinemia that is caused by the warm autoantibody coating or destroying the patient's own cells. Patients with WAAs also have a higher rate of alloimmunization than the general population.

B. Patients with WAAs can pose challenging problems for the laboratory, especially when transfusion is required. WAAs often display panreactivity, reacting non-specifically with all test red cells including the antibody screen, panel, and autocontrol. The reaction strength typically varies over time. Patients with WAAs usually have a positive direct antiglobulin test (DAT). WAA reactivity is generally enhanced by LISS, so if the WAA is reactive in the standard gel antibody screen then the 60-minute no-LISS tube method may be used. LISS is omitted in this method, so that the WAA interference is eliminated or reduced, increasing the chance to detect underlying alloantibodies that may be present.

C. When a WAA is of sufficient strength to react in the 60-minute no-LISS tube method, it may prove especially challenging to exclude underlying alloantibodies; additional testing may be required. In this case, the prophylactic use of RBCs that are phenotypically matched with the patient's RBCs is desirable. A phenotype is performed proactively on all patients with a WAA that is reactive in either the gel screen or the 60-minute no-LISS tube method. These phenotype results may facilitate crossmatching procedures, as well as antibody identification and exclusion procedures. If it is not possible to provide phenotypically matched RBCs for transfusion for patients with a WAA that is reactive in 60-minute no-LISS testing, then adsorption procedures may be indicated. Because

WAAs may interfere in crossmatching procedures (even with RBCs that are phenotypically matched) it may be necessary to transfuse RBCs that are found to be crossmatch incompatible or "least incompatible".

III. INTRODUCTION / GENERAL SUMMARY:

A. The following is a general summary of the preferred methods that the Blood Bank will use to exclude or identify underlying alloantibodies and to crossmatch RBCs for patients with WAAs.
    1. The gel method will be used to exclude underlying alloantibodies and to provide crossmatch compatible RBCs. If this proves unsuccessful, then:
    2. The 60-minute no-LISS method will be used to exclude underlying alloantibodies and to provide crossmatch compatible RBCs. If this proves unsuccessful, then:
    3. The Blood Bank will attempt to provide phenotypically matched RBCs for transfusion. Note that phenotypically matched RBCs are acceptable for transfusion, even if incompatible crossmatches are observed due to the WAA reactivity. If it proves impossible to obtain phenotypically matched RBCs, then:
    4. The Blood Bank will refer the specimen to external reference lab for adsorption studies in an attempt to exclude underlying alloantibodies. If this proves unsuccessful, then:
    5. The Blood Bank will use "least incompatible" crossmatches.

IV. DEFINITIONS / ACRONYMS:

A. **Phenotypically matched donor RBCs**: Donor RBCs that are negative for any of the following eleven antigens including Rh(D) for which the recipient is negative:
D C E c e K Fy^a Fy^b Jk^a Jk^b S and s.

B. **Least incompatible units**: The weakest reacting of multiple RBC units, that also reacts weaker than the autocontrol.

C. **Clinically significant antibody**: An antibody that is known to:
    1. Cause Hemolytic Disease of the Newborn (HDN) or shortened survival of antigen positive RBCs, **and**
    2. Requires transfusion of antigen negative red cells, **and**
    3. Is usually IgG and best detectable with antihuman globulin (AHG).

D. **Alloimmunization**: The process whereby a recipient forms antibodies in an immune response to foreign antigens on donor RBCs.

E. **Panreactive**: A patient's serum that reacts with every (or nearly every) test cell, usually including the autocontrol. All reactions are usually the same strength.

F. **CDM**: Computer Documentation Manual, computer documentation workflow.

G. **HIS**: Hospital-wide computer system.

H. **HTLA Antibody**: High Titer Low Avidity Antibody.

I. **Genotype**: Testing provided by a reference laboratory in which genomic DNA is isolated and red cell genotyping is performed to determine the patient's predicted red cell phenotype.

J. **Phenotype**: The phenotype is determined by testing the patient's red blood cells with typing anti-sera. At Beaumont, the following 11 antigens are tested for: C E c e K Fy^a Fy^b Jk^a Jk^b S and s.

V. POLICIES

A. Requirement to Obtain Patient History

1. For patients with reactive WAAs, the patient's antibody and transfusion history shall be obtained every 90 days, as described in Transfusion Medicine policy, Obtaining Patient Histories.

B. Requirement to Perform Gel Testing

1. A gel screen will be performed on all patients with a history of a WAA. However, for patients with a WAA, an antibody investigation shall be performed **each time** that a Type and Screen is performed if the WAA is reactive in the gel screen. The gel antibody screen will be assessed as follows:
    a. If the gel reactions of the **screen cells have the same or weaker reactions than previous results and**
        i. a gel panel **has** been performed within the last 90 days, then 60-minute no-LISS testing shall be performed.
        ii. a gel panel **has not** been performed within the last 90 days, then a gel panel must be performed.
    b. If the gel reactions of the **screen cells are different strengths, or the overall screen strength increased** when compared to previous screen results then a gel panel will also be performed to help assess whether underlying alloantibodies are present.
        i. If the patient has a history or underlying alloantibodies, then a selected cell panel may be tested by the gel method.
    c. If any non-reactive test cells are observed in the gel testing (screen or panel, if indicated), then gel crossmatches will be performed. The Blood Bank will attempt to exclude underlying alloantibodies in the gel method.

C. 60-Minute No-LISS Tube Testing

1. In all cases where it proves impossible to exclude underlying alloantibodies in gel testing, 60-minute no-LISS tube testing shall be performed. Most WAAs will be non-reactive in this method, making it possible to exclude underlying alloantibodies and to provide crossmatch compatible RBCs by this method.

D. 60-Minute No-LISS Testing Specifications

1. The 60-minute no-LISS testing must include an autocontrol, and will be performed as follows:
    a. For patients with a history of **only a WAA**, then a 60-minute no-LISS screen will be performed. The 3-cell antibody screen will be used for this purpose. If the reactions of the screen cells are different strengths, then a 60-minute no-LISS panel will also be performed to help assess whether underlying alloantibodies are present.
    b. For patients with a history of **both a WAA and underlying alloantibody(ies)**, then a 60-minute no-LISS selected cell panel may be performed. The cells for this panel should be selected to accomplish the following:
        i. Show whether the WAA is reactive in the 60-minute no-LISS method.

ii. Exclude other clinically significant underlying alloantibodies; test cells that are negative for the antigen corresponding to the historical, clinically significant antibody should be tested.

E. Assessment of the 60-Minute No-LISS Testing

1. If it is possible to exclude underlying alloantibodies by 60-minute no-LISS testing, then RBCs that are compatible by this method will be provided.
2. If it proves impossible to exclude underlying alloantibodies by 60-minute no-LISS testing, then additional testing will be performed; i.e., phenotypically matched RBCs, adsorption studies, or "least incompatible" crossmatches.

F. Application of Standard Transfusion Medicine Policies

1. The titers of WAAs frequently vary in strength over time, and may become non-reacitve. If it is demonstrated that the WAA is non-reactive with all test cells in gel testing, then standard Transfusion Medicine policies will be applied instead of this WAA procedure.
    a. Antibody investigations of subsequent samples will be performed only every 90 days, or if the gel screen increases in strength, as described in Transfusion Medicine policy, Antibody Screening.
2. **In order to demonstrate that the WAA is non-reactive in gel testing** and to apply standard Transfusion Medicine policies, one of the following conditions must be met:
    a. The gel screen is non-reactive, or
    b. For patients with alloantibodies and a history of a WAA, **all** antigen negative screen cells and selected cell panels are non-reactive in gel.
        i. If **any** of these test cells are reactive, then this procedure shall remain in effect. However, if only the autocontrol is reactive, standard *Transfusion Medicine policies* will apply.
        ii. If all clinically significant antibodies have been ruled out in gel, standard *Transfusion Medicine policies* apply.
        iii. If all clinically significant antibodies are **not** ruled out in gel, then this procedure will remain in effect.
3. In order to prevent unnecessary antibody investigations each time that a type and screen is performed the results must be documented correctly once it has been demonstrated that the WAA is non-reactive in gel testing. Refer to the *Test Resulting* section of this document.

G. Compliance with Transfusion Medicine policy, *Policies for Providing Red Blood Cells to Patients with Unexpected Antibodies*

1. Crossmatched RBCs for patients with both a WAA and underlying alloantibodies must also meet the requirements of Transfusion Medicine policy, Policies for Providing Red Blood Cells to Patients with Unexpected Antibodies. The donor RBCs must be negative for the antigen(s) corresponding to the patient's clinically significant alloantibody(ies).

2. Gel crossmatches must be performed on all patients with a history of unexpected antibodies (this includes historical WAAs that may be non-reactive in the current sample).

H. Direct Antiglobulin Testing

1. An autocontrol will be performed with any antibody panel or 60-minute no-LISS tube screen. If the autocontrol is positive, then a DAT will be performed as described in Transfusion Medicine policy, Direct Antiglobulin (DAT) Test by Tube Method.

I. Eluate Testing

1. It is not necessary to perform an eluate routinely as part of the WAA investigation. However, if the sample displays significant hemolysis, then an eluate may be performed after consultation with the Medical Director or designee.

J. Genotype for Patients with Warm Autoantibodies

1. A RBC genotype will be performed on patients with WAAs that are reactive in either the gel method or the 60-minute no-LISS tube method. Example: A RBC genotype will be performed on a new patient has a WAA that is pan-reactive in the gel screen and gel panel, including the autocontrol even if the 60-minute no-LISS tube screen and autocontrol is negative.
2. This RBC genotype will be referred to Versiti Wisconsin for testing. Refer to Transfusion Medicine policy, Submitting Samples to a Reference Laboratory.
3. If phenotypically matched units are required prior to the receipt of RBC genotype results:
    a. A patient phenotype will be performed at Beaumont. This phenotype will include Rh(D) testing and testing for the following eleven antigens: C E c e K Fy^a Fy^b Jk^a Jk^b S and s.

    Note: It is not always possible to perform a complete phenotype due to factors such as the patient's transfusion history, DAT results, and sample requirements. Partially phenotypically matched units will be provided with the approval of the Medical Director or designee. Refer to Transfusion Medicine policy, *Antigen Typing*.

K. Patients who Appear to be Fy^a and Fy^b Negative

1. Fy(a-b-) African American patients are generally considered incapable or making anti-Fy^b due to the GATA mutation. Transfusion of Fy^a negative units are required but typing of Fy^b is not necessary.
2. Fy(a-b-) patients that are not African American are typically capable of making anti-Fy^b. Transfusion of Fy^a and Fy^b negative units are required.

L. Providing Phenotypically Matched RBCs

1. The purpose of the performing RBC Genotyping or phenotypes for patients with WAAs is to facilitate antibody identification / exclusion procedures and to provide phenotypically matched RBCs when it proves impossible to exclude underlying alloantibodies in 60-minute no-LISS tube testing. In these cases, the use of phenotypically matched RBCs as a prophylactic measure may also help prevent alloimmunization. Phenotypically matched RBCs may be transfused, even if the crossmatch is incompatible due to the WAA reactivity.

2. Phenotypically matched RBCs may be indicated as described in the *Providing RBCs for Patients with Warm Autoantibodies* table below. It may be necessary to contact a blood supplier to get phenotypically matched RBCs if they are indicated. Phenotypically matched RBCs must be negative for any of the following 11 antigens including Rh(D) for which the recipient is negative. For example:
    a. Phenotypically matched RBCs are indicated for a patient whose phenotype follows:
    D- C- E+ c+ e+ K- Fy^a+ Fy^b+ Jk^a+ Jk^b+ S- and s+
    This patient should be provided donor RBCs that are: D- C- K- and S-.

M. Partial Phenotypes

1. In some cases, it is possible to perform only a partial phenotype on the patient, so that phenotypically matched RBCs cannot be provided. In other cases, it may be impossible to obtain donor units that are negative for all of the antigens for which the patient is negative. Additional testing (an adsorption study) sent out to a reference lab may be indicated. For example:
    a. A patient has a positive DAT; therefore the Blood Bank cannot type the patient with anti-sera that requires an indirect antiglobulin test (IAT); i.e., Fy^a, Fy^b, S and s. Versiti does not have time to genotype the patient before a transfusion is required. Therefore, it is impossible to provide RBCs that are phenotypically matched for Fy^a, Fy^b, S and s. Adsorption studies (performed at a reference lab) would be required to rule out the presence of clinically significant antibodies (including Fy^a, Fy^b, S and s).
    Note: An alternative to adsorption studies would be to use donor RBCs that are negative for Fy^a, Fy^b and s (in addition to the other antigens for which the patient is known to be negative).

N. Antibody Exclusions Based on Patient's Phenotype

1. The *Phenotype for Patients with Warm Autoantibodies* may be very helpful with antibody exclusions. In order for alloimmunization to occur, a patient's RBCs must generally be negative for the antigen corresponding to the particular antibody. For example:
    a. Testing the RBCs of a patient yields the following results:
    D- C- E+ c+ e+ K- Fy^a+ Fy^b+ Jk^a+ Jk^b+ S- and s+
    Many antibody specificities may be excluded based on these results including anti-E, anti-c, anti-e, anti-Fy^a, anti-Fy^b, anti-Jk^a, anti-Jk^b, and anti-s. Based on these results, the patient is capable of making only anti-D, anti-C, anti-Kell, and anti-S.
2. The use of the patient's phenotype to exclude antibodies should be done with caution, as some antibody specificities have been demonstrated in the patient's serum even though the patient's RBCs are positive for the corresponding antigen. Most notorious are examples of auto anti-M and warm autoantibodies with e-like specificity. Therefore, the preferable method of exclusion is the panel, not the phenotype.

O. Indications for Adsorption Studies

1. Adsorption studies are indicated only if it proves impossible to exclude underlying alloantibodies by the gel method or by the 60-minute no-LISS tube method, and
    a. The patient is an obstetrical patient. See the *Policies Specific to Obstetrical Patients with WAAs*.

b. The patient is a non-obstetrical patient, and phenotypically matched RBCs cannot be provided at the time of a required transfusion.

2. Adsorption studies are sent to Versiti Michigan Immunohematology Reference Lab. Refer to Transfusion Medicine policy, Submitting Samples to a Reference Laboratory.

P. Exclusion of Underlying Alloantibodies: Impossibility and Feasibility

1. In some cases, it will be impossible to exclude underlying alloantibodies. For example:
    a. The sample of an obstetrical outpatient contains insufficient volume for send out testing for adsorptions.
    b. A patient's strong WAA remains reactive, even when testing with autoadsorbed plasma at the reference lab.

2. In other cases, it may not be deemed necessary or feasible to exclude underlying alloantibodies. These feasibility considerations are based on the premise that phenotypically matched RBCs will be available for transfusion when transfusion becomes necessary. For example:
    a. A genotype was performed on a patient and transfusion is not required at the current time. Send outs for adsorption studies are not feasible as long as it appears likely that phenotypically matched RBCs will be available if / when transfusion becomes necessary.

Q. Policies Specific to Obstetrical Patients with WAAs

1. In addition to meeting the potential transfusion requirements of the obstetrical patient, the Blood Bank must consider the ramifications for the neonate. Therefore, if it proves impossible to exclude underlying alloantibodies for an obstetrical patient by the gel or 60-minute no-LISS method, the Blood Bank will attempt to exclude underlying alloantibodies by performing adsorption studies. Send out testing for autoadsorption studies will be performed once a month for obstetrical patients who are not transfused throughout their pregnancies. For example:
    a. An obstetrical patient has a WAA that is reactive in 60-minute no-LISS tube testing, so that underlying alloantibodies cannot be excluded. Phenotypically matched RBCs are available. Adsorption procedures should also be performed to exclude underlying alloantibodies. Note that if this patient was a non-obstetrical patient, then send out for adsorption studies would not be required as long as phenotypically matched RBCs were available.
    b. An obstetrical patient has a WAA that is reactive in 60-minute no-LISS tube testing, so that underling alloantibodies cannot be excluded. The sample contains insufficient volume for indicated adsorption studies. The Blood Bank staff must notify the patient's physician that antibody exclusions have not been performed and suggest that additional samples be sent to the Blood Bank for adsorption studies.

R. When Underlying Alloantibodies Have Not Been Excluded by any Method

1. The following applies when underlying alloantibodies cannot be excluded by any method (including

the gel method, 60-minute no-LISS method, or adsorption studies):

a. **Obstetrical patients**: The patient's physician must be notified even if transfusion is not necessary at the present time. See the *Policies Specific to Obstetrical Patients with WAAs* section of this document.

b. **Non-obstetrical patients**: The patient's physician must be notified only if phenotypically matched RBCs are unavailable at the time of required transfusion, or if RBCs with an incompatible crossmatch must be transfused.

c. This notification shall be documented as a internal comment in the Blood Bank computer and with an internal variance. Refer to Transfusion Medicine policy, Variance Reporting.

S. "Least Incompatible" Crossmatches

1. Least incompatible crossmatches are indicated only if:
    a. The WAA is reactive in all methods, so that underlying alloantibodies cannot be excluded by any method (gel, no-LISS tube methods, or adsorption studies) and
    b. Phenotypically matched RBCs are unavailable at the time of required transfusion.
    c. The patient's physician must be notified. This notification will be documented with the canned comment **INCXM** in the Blood Bank computer and with an internal variance.

T. Providing Incompatible RBCs / Notification of the Ordering Physician

1. Strong WAAs of some patients may prevent the Blood Bank from providing crossmatch compatible RBCs, even with units that are phenotypically matched. When incompatible units must be transfused, the patient's physician must be notified. This notification will be documented with the canned comment **INCXM** in the Blood Bank computer. An internal variance will also be submitted.

U. Determining Whether to Aliquot Incompatible Donor RBC Units for Patients with WAAs

1. If donor RBC units are incompatible:
    a. It is not necessary to aliquot phenotypically matched donor RBCs.
    b. It may be necessary to aliquot donor RBCs that are not phenotypically matched, or that are only "partially phenotypically matched". Consultation with the Medical Director or designee is required to determine whether issuing aliquots is recommended.

V. High Titer Low Avidity (HTLA) Antibodies

1. The presence of HTLA antibodies may present a serologic picture similar to that of a WAA; panreactivity may be present. If it is not possible to obtain compatible crossmatches, then phenotypically matched RBCs should be provided. If applicable, refer to Transfusion Medicine policy, HTLA/Bga Antibody Investigations.

W. CD38 Darzalex® (Daratumumab) Therapy

1. The Blood Bank may receive notification that a patient will be undergoing CD38 therapy with Darzalex® (Daratumumab). It is the Blood Bank technologist's responsibility to request that a Type and Screen sample and one additional pink top tube be collected before the medication is administered. The additional pink top tube should be sent to Versiti Wisconsin for a red cell genotype. See Transfusion Medicine policy, Submitting Samples to a Reference Laboratory. For information on how to work-up anti-CD38 patients, refer to the *CD38 Evaluation Flowchart*.

X. Warm Autoantibodies Displaying Apparent Specificity

1. On occasion, a WAA will display apparent specificity, most frequently a warm autoantibody with little e-like specificity or other Rh specificity. It is very important to obtain an accurate transfusion history and, if possible, to test the patient's RBCs for the corresponding antigen in order to differentiate between a WAA and an alloantibody. Refer to Transfusion Medicine policy, Obtaining Patient Histories and Transfusion Medicine policy, Antigen Typing.
2. If a WAA with apparent specificity is detected, then RBCs that are negative for the antigen corresponding to the WAA should be provided. However, if it proves difficult to obtain antigen negative units, then it is not necessary to provide antigen negative RBCs unless there is active, ongoing hemolysis. For example:
    a. A patient's panel displays WAA reactivity with apparent anti-C specificity. Testing of the pre-transfusion sample indicates that the patient's RBCs are C positive. Donor RBCs that are C negative should be provided. Anti-C should be added to the antibody field to ensure the patient receives C - negative RBCs for transfusion. The Anti-C antibody code can be removed if the WAA becomes inactive.

Y. Warm Autoantibodies with Apparent e-like Specificity

The preferred method of choice to provide product for patient with WAA with apparent e-like specificity is as follows:

First Choice	Provide gel crossmatch-compatible units that are not tested for e antigen.
Second Choice	Provide RBCs that are compatible using the 60-minute no-LISS crossmatch method, using units that are not tested for the e antigen.
Third Choice	Attempt to obtain e-negative units. Provide gel grossmatch-compatible units that are e negative.
Fourth Choice	Attempt to obtain e-negative units. Provide gel grossmatch-compatible units that are e negative.
Fifth Choice	Attempt to obtain e-negative units. Provide gel grossmatch-compatible units that are e negative.

VI. SPECIMEN COLLECTION AND HANDLING:

A. The preferred specimen is a 6 mL EDTA sample with affixed identifying label. See Transfusion Medicine policy, Triaging and Identifying Acceptable Samples for Testing.

B. If additional testing is required, then a large volume of serum, or multiple samples, may be

required.

C. If a sample will be sent to a reference laboratory, then follow their sample requirements as indicated in Transfusion Medicine policy, Submitting Samples to a Reference Laboratory.

VII. PROCEDURE:

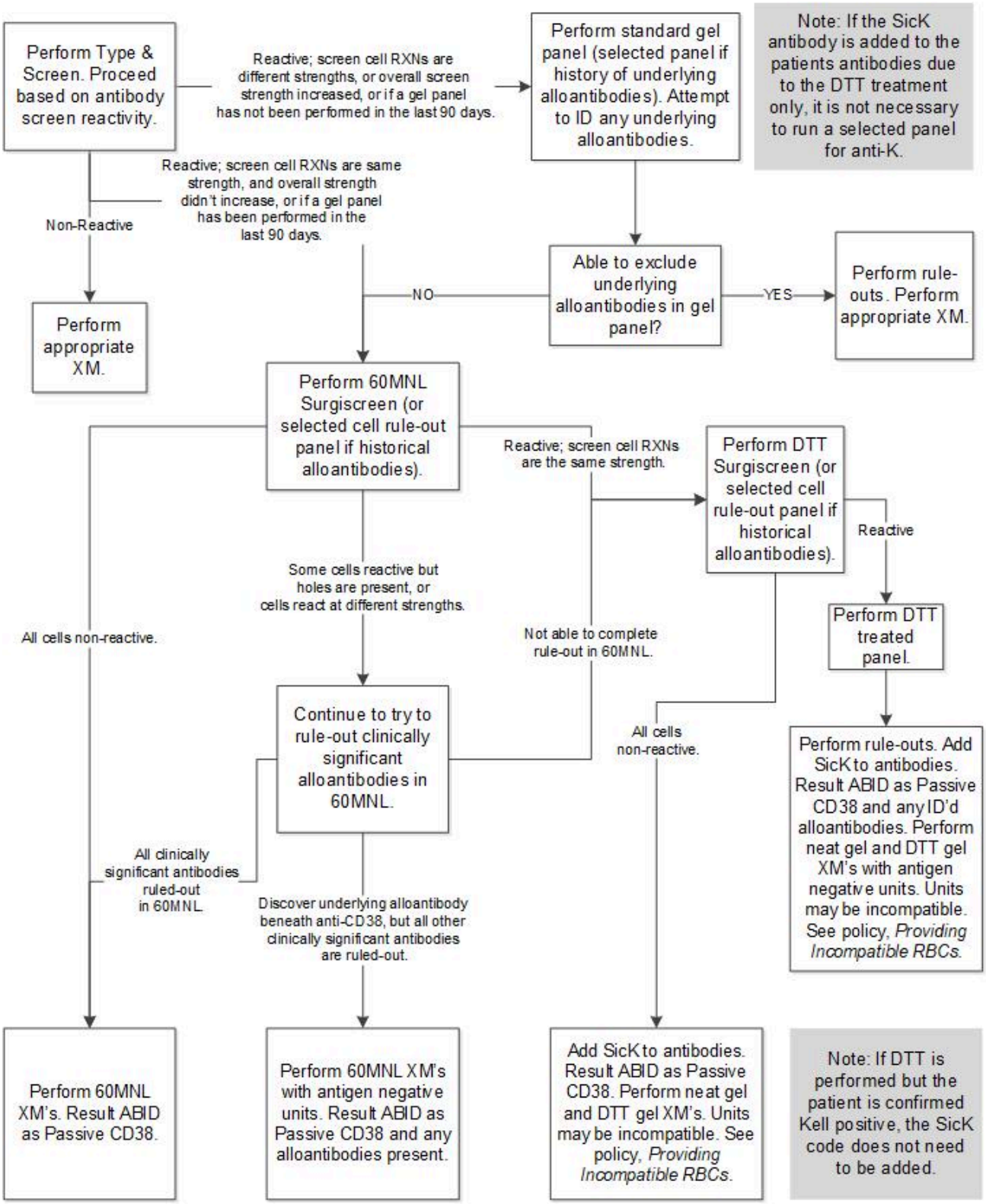
A. Differentiating Warm Autoantibodies from Other Classifications

1. Warm autoantibodies are sometimes difficult to differentiate from other antibody classifications. The reactivity of the autocontrol, DAT, the gel and 60-minute no-LISS tests, and patient antigen testing are used in making this differentiation.

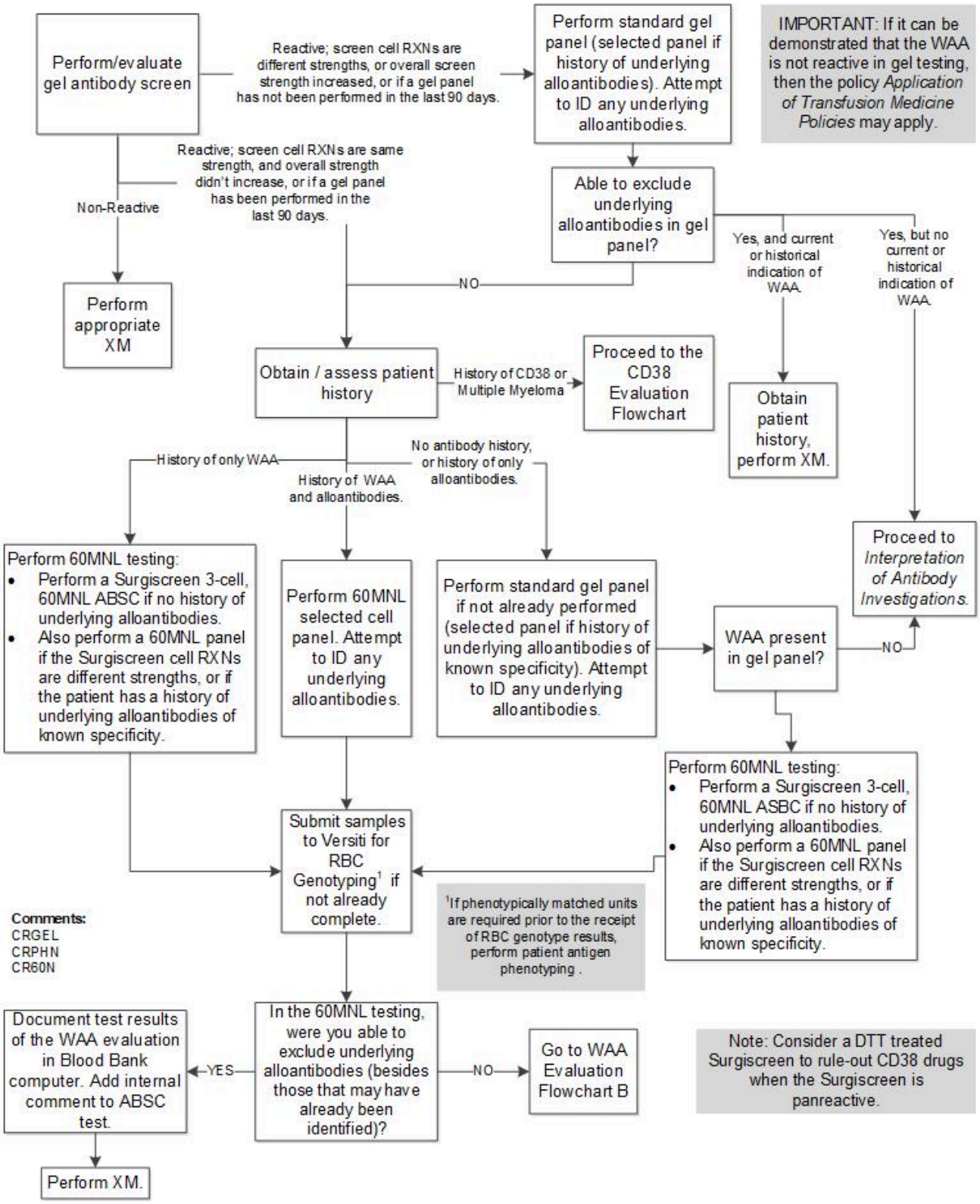
Antibody Classification	Characteristic Antibody Reactivity	Autocontrol and DAT Results	Should a patient genotype be performed?	Notes
Warm Autoantibody	Panreactivity, reactions usually all same strength. Generally cannot perform gel rule-outs.	Autocontrol and DAT are usually positive. In rare cases, they may be negative, but only if the WAA is weak.	Yes	
Alloantibody with a positive DAT; i.e. recent transfusion or reaction	Panreactivity may be present, depending on the specificity of the antibody.	Autocontrol usually positive; DAT is positive.	No (unless 3 or more alloantibodies are detected).	The patient's pre-transfusion antigen typing may be used to differentiate a WAA from an alloantibody.
Warm IgG Antibody; non-specific	Usually not panreactive. Strength is ≥ 2+. Rule-outs can be performed by the gel method.	Autocontrol and DAT usually negative, but in some cases may be positive; i.e. medications.	No	
TWTI	Usually not panreactive. Strength is ≤ 1+. Rule-outs can be performed by the gel method.	Autocontrol and DAT usually negative, but in some cases may be positive; i.e. medications.	No	
HTLA Antibody	Panreactivity likely.	Autocontrol and DAT usually negative, but may be positive; i.e. medications.	Refer to Transfusion Medicine policy, HTLA / Bga Antibody Investigation.	Differentiate WAA from HTLA antibody as described in Transfusion Medicine policy, HTLA / Bga Antibody Investigation.

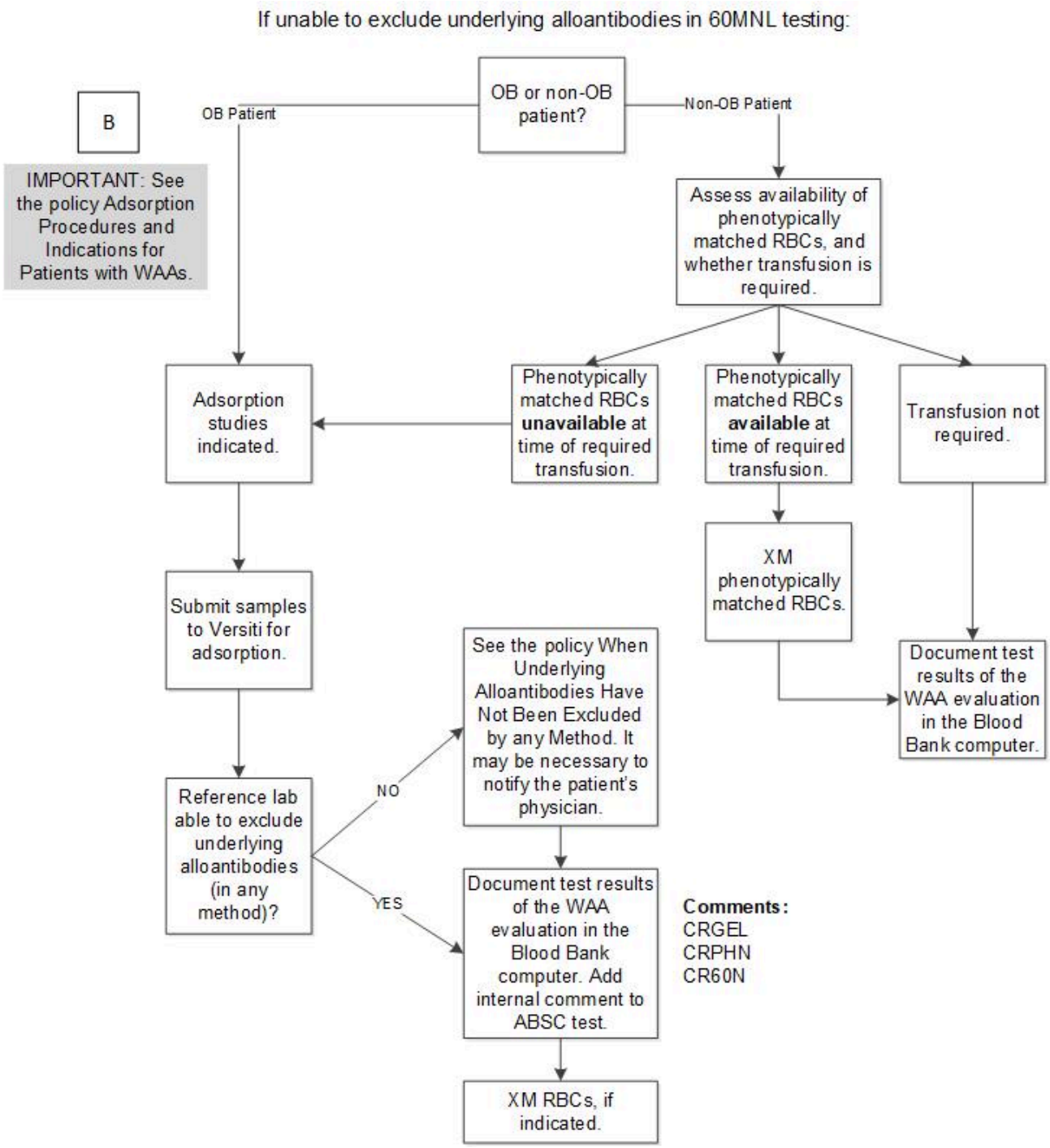
Antibody to High Frequency Antigen	Panreactivity. A specificity may be named; i.e. anti-k (cellano) or anti-Js^b.	Autocontrol and DAT usually negative, but may be positive; i.e. medications or recent transfusion.	No	See Transfusion Medicine policy, Interpretation of Antibody Investigations.
Patient undergoing CD38 treatment with Darzalex®	Panreactivity, reactions usually all same strength. Generally cannot perform gel rule-outs.	May be positive or negative, DAT is usually negative but may be positive; i.e. recent transfusions.	Yes	See the *CD38 Evaluation Flowchart* for further instructions.

B. CD38 Evaluation Flowchart



C. Warm Autoantibody Evaluation Flowchart





D. Crossmatching RBCs for Patients with Warm Autoantibodies

1. Determine the appropriate crossmatch method for patients with WAAs, based on the gel and 60-minute no-LISS testing results. If applicable, see the footnotes following this table.

Gel Testing (ABSC / Panel)	60-Minute No-LISS Testing (ABSC / Panel)	Appropriate Crossmatch Method

Negative gel antibody screen	Not tested	Provide RBCs that are compatible by the gel crossmatch method.
Some reactivity in gel testing, but all clinically significant antibodies **excluded in gel**[1].	Not tested	Provide RBCs that are compatible by the gel crossmatch method.
Some cells reactive and some non-reactive in gel testing, and all clinically significant antibodies are **not excluded in gel**[1].	Any result	**1st choice**: Attempt to provide RBCs that are compatible by the gel crossmatch method. Continue to gel crossmatch, up to a "reasonable[5] number"of units. **2nd choice**: If a "reasonable[5] number" of units are crossmatched in gel and all are found to be incompatible, then refer to the appropriate crossmatch method below.
All cells tested in gel are reactive, and clinically significant antibodies are **not excluded in gel**[1].	Negative 60-minute no-LISS antibody screen Some reactivity in 60-minute no-LISS testing, but clinically significant antibodies **are excluded in 60-minute no-LISS** testing.	Provide RBCs that are compatible by the 60-minute no-LISS method.
	Reactivity in 60-minute no-LISS testing, clinically significant antibodies **not excluded in 60-minute no-LISS** testing.	**1st choice**: Use phenotypically matched RBCs, compatible by 60-minute no-LISS crossmatch. **2nd choice**: Use phenotypically matched RBCs, incompatible by 60-minute no-LISS crossmatch[2]. **3rd choice**: Provide units that are compatible by adsorption methods[3,4] performed at Versiti. **4th choice**: Use least incompatible crossmatches[2]; see the *Procedure* section of this document.
1. If a patient has a warm autoantibody with e-like specificity, the use of e-negative RBCs may be required in some cases. 2. If an incompatible unit must be transfused, then the patient's physician must be notified and it *may* be necessary to aliquot the unit.		

3. Note that when underlying alloantibodies are excluded in an adsorption procedure, the use of phenotypically matched RBCs is still preferred (but not absolutely required) to help prevent subsequent alloimmunization.
4. If the reference laboratory indicates that a unit is compatible with homologously adsorbed plasma, then the Blood Bank must still perform a "test of record" crossmatch (60-minute no-LISS). The reference laboratory result will be added as an internal comment to the 60-minute no-LISS crossmatch in the Blood Bank computer. If this 60-minute no-LISS crossmatch is incompatible, then the patient's physician must be notified.
5. Twelve (12) is a reasonable number of crossmatches for patients with a WAA who **do not** require phenotypically matched RBCs. For patients who **do** require phenotypically matched RBCs, a reasonable number depends on the difficulty of obtaining antigen negative units.

E. Performing Least Incompatible Crossmatches

When the WAA is reactive in all methods, so that underlying alloantibodies cannot be excluded by any method (gel, no-LISS tube methods, or adsorption studies) **and** Phenotypically matched RBCs are unavailable at the time of required transfusion Least Incompatible Crossmatches will be provided.

a. Document all incompatible crossmatches in the Blood Bank computer.
b. If transfusion is required, use the "least incompatible" units for transfusion.
    a. Compare the reaction strength of the donor units to that of the autocontrol.
    b. Least incompatible units are defined as the weakest reacting RBC units as compared to other units being crossmatched;
    c. least incompatible units should also react weaker than the autocontrol.
    d. The units should be marked and issued according to the anticipated order of transfusion based on compatibility.
c. Notify the patient's physician caregiver of the incompatible crossmatches and document the notification with the canned comment INXM in the Blood Bank computer.
d. Complete an internal variance with details

VIII. TEST RESULTING:

A. All testing shall be documented in the Blood Bank Computer or on *Patient Downtime Worksheet*.
B. If the gel antibody screen is positive so that an ABID test reflexes, refer to the Blood Bank CDM - Resulting Antibody Identification.
C. Appropriate comments will be added to the patient's comment text in Blood Bank computer to include the panel results and relevant patient history, source of information and the date it was obtained. See Transfusion Medicine policy, Obtaining Patient Histories for additional information.
D. An internal canned comment will be added to the gel antibody screen. The purpose of this comment is to assist technologists who perform crossmatches at a later time / date using the current sample.
    1. **CR60N**: Perform 60-minute no-LISS crossmatches
    2. **CRGEL**: Perform gel crossmatches
    3. **CRPHN**: Use phenotpyically matched RBCs.

4. **CRAA**: Adsorption studies may be required; WAA reactive 60-min no-LISS

E. If the section *Application of Standard Transfusion Medicine Policies* applies, then document as follows:
    1. Add the internal canned comment CRGEL to indicate to perform gel crossmatches.
    2. Add a comment text to the patient's record indicating that on [date], Standard Transfusion Medicine Policies apply.

IX. NOTES:

A. WAA reactivity is enhanced by LISS. Because LISS is omitted in 60-minute no-LISS tube testing, the WAA reactivity is not enhanced, while this method is still favorable for the detection of underlying clinically significant alloantibodies. However, there may be a slight decrease in sensitivity with this method so caution should be used when excluding clinically significant alloantibodies.

X. REFERENCES:

1. AABB, *Technical Manual*, current edition.

Approval Signatures

Step Description	Approver	Date
	Jeremy Powers: Chief, Pathology	6/21/2022
Policy and Forms Steering Committe (if needed)	Gail Juleff: Project Mgr Policy [IH]	6/17/2022
Policy and Forms Steering Committe (if needed)	Kelly Sartor: Supv, Laboratory	6/14/2022
	Kimberly Geck: Dir, Lab Operations B	6/13/2022
	Kelly Sartor: Supv, Laboratory	6/9/2022
	Kelly Sartor: Supv, Laboratory	6/9/2022