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Investigation of Incompatible Crossmatches

Document Type: Procedure

I. PURPOSE AND OBJECTIVE:

This document will provide the Blood Bank staff with guidance for investigating incompatible crossmatches.

II. INTRODUCTION:

If an incompatible crossmatch (XM) is encountered, additional investigation may be required. As described in this document additional investigation may include an antibody panel, repeat antigen testing of the donor unit, repeating the XM, or a direct antiglobulin test (DAT) of the donor unit. The appropriate additional investigation is indicated in the *Procedure* section.

III. DEFINITIONS:

A. **Designee**: A Blood Bank Technical Director or transfusion medicine fellow.

B. **BBIS**: Blood Bank Information System

IV. POLICIES:

A. The Use of the *Incompatible Crossmatch Tag*

1. If an incompatible XM is observed, the technologist may attach a completed copy of the *Incompatible Crossmatch Tag* to the unit. This tag should be removed when the unit is dispensed to any patient.

Note: This tag is required at Royal Oak.

B. Incompatible Units Shall Not be Tagged or Transfused without Authorization

1. Red blood cell (RBC) units that are found to be incompatible shall never be tagged with a crossmatch tag or transfused to a patient unless specifically indicated in this document or elsewhere in the Transfusion Medicine policies, or unless authorization is obtained from the Blood Bank Medical Director or designee. Units that are not intended for transfusion (due to an incompatible XM) should be returned to available inventory immediately, and the *Incompatible Crossmatch Tag* may be attached to the unit.

C. Notification of the Patient's Physician / Incompatible Unit

1. If an incompatible unit must be transfused for any reason, the patient's physician must be notified. If a nurse or resident agrees to contact the patient's physician, then it is not necessary for the Blood Bank to also notify the patient's physician. This notification should be documented in the BBIS as a Patient Profile Note, using the **INCXM** (Incompatible Crossmatch Notification) canned message or during a downtime by completing the *Incompatible Crossmatch RBC Notification* form. The documentation should include the notifying technologist, the date / time of the notification, and the physician or nurse accepting the notification.
2. For divided aliquots of the same incompatible unit, notification of the patient's physician is only required before the first aliquot is issued, as long as all aliquots are issued within 24 hours of each other.

D. Units with a Positive Direct Antiglobulin Test (DAT)

1. An incompatible XM may be observed if the RBC unit has a positive DAT. If a unit is found to have a positive DAT, the following apply:
    a. Submit a variance
    b. Document the DAT results of the unit in the BBIS by adding a Note to the RBC unit. "Gel DAT = (reaction strength)"
    c. If the DAT result is found to be 2+ or weaker the unit may be issued to a patient who is eligible for an electronic crossmatch. However, it can not be transfused to any patient which requires an AHG crossmatch.
        i. Tag the unit with the Electronic Crossmatch only tag. This tag will remain on the unit until issued.
    d. If the DAT result is found to be 3+ or greater the unit must be quarantined.
        i. The Medical Director will review the finding and determine the appropriate disposition of the unit.

E. Repeat Antigen Typings

1. If a unit is found to have an incorrect antigen type upon repeat, then the following apply:
    a. Repeat all antigen typings from the batch in which the incorrect antigen test was originally performed.
    b. Document a variance.
2. Refer to Transfusion Medicine policy, Antigen Typing.

F. Determining Whether to Aliquot Incompatible Donor Units

1. If donor RBC units are deemed incompatible then:
    a. It may be deemed appropriate by the medical director and/or clinical caregiver in situations where no other units are available to aliquot donor units that are not phenotypically matched, or that are only "partially phenotypically matched". If necessary these units should be transferred to Royal Oak or Dearborn for aliquot preparation as directed.
    b. It is not necessary to aliquot phenotypically matched donor units.
    c. It is not necessary to aliquot donor units that are compatible by a manipulated method (e.g. using DTT-treated donor units, autoadsorped plasma, etc.) but are still considered and tagged as incompatible due to the primary compatible testing being completed at another site.

G. Incompatible Crossmatches on Patients with History of Unidentified Antibodies/ May Require Antibody Investigations More Frequently

1. If an incompatible XM is observed on a patient with a WkU (Unidentified) antibody, and a panel has not been done in the last 30 days, then a panel must be performed on the current sample.
2. In addition, if the percentage of incompatible XMs increases on a patient with a WkU (Unidentified) antibody, then a panel shall be performed, regardless of whether or not it has been done within the past 30 days, to determine if an alloantibody can not be identified.

    For example:

    a. On April 1st, a Type and Screen was performed on a patient with a WkU antibody. The antibody screen was 1+ reactive, and a work up was performed. Only one cell was reactive on Panel A, and all clinically significant antibodies were ruled out. The ABID was resulted out as a previous WkU antibody. Four gel XMs were performed on the patient. Three of the units were compatible and one was incompatible.
    b. On April 15th, a Type and Screen was performed on the same patient. The antibody screen reacted the same as it did on April 1st, and there was no increase in strength.

No antibody identification was indicated, and four gel XMs were performed. This time, only one unit was compatible, and three were incompatible.

c. Even though the patient has a WkU, and a panel was done within the last 30 days, a new work up should be performed on this patient. The percentage of incompatible XMs went up from 25% to 75%, and there needs to be confirmation that the an alloantibody can not be identified.

H. Units that are Crossmatch Incompatible by One Method, but Crossmatch Compatible by a Different Method: Use of a Different or Less Sensitive Crossmatch Method

1. In most cases, the policy *Incompatible Units Shall Not be Tagged or Transfused* applies. However, one of the few times in which the Transfusion Medicine policies specifically indicate that it is acceptable to perform a tube AHG XM on a unit on which the gel XM was incompatible is defined in the *Procedure / Incompatible Crossmatches on Patients with a WkU (Weak Unidentified) antibody.* If a unit was incompatible in one method but is compatible in a different or less sensitive method, the following apply:

   a. The Blood Bank Medical Director must be notified at the time the unit is tagged; document this notification in a variance and as an internal comment to the tube compatible XM test in the computer.

   b. Result the XM test in the computer using the results from the compatible method, so that the XM tag indicates that the unit is compatible. Note that it is not necessary to notify the patient's physician, the unit is considered compatible.

   c. Note that this policy typically applies to antigen negative units on patients with a WkU (Weak Unidentified) antibody. If gel XMs are incompatible and the patient does not require antigen negative units, then new units should be selected instead of using a different or less sensitive XM method.

I. Units that are Crossmatch Incompatible by One Method, but Crossmatch Compatible by a Different Method when Multiple Crossmatch Methodologies are Required

1. In some cases, multiple XM methodologies may be indicated for a patient. This usually occurs when a patient has an unresolved ABO discrepancy in addition to unexpected antibodies. In these situations, both immediate-spin and AHG XMs (usually by the gel method) are required as indicated in Transfusion Medicine policy, Resolution of ABO and Rh Discrepancies.

2. If the cause of the unresolved ABO discrepancy is one that will likely cause the immediate-spin XMs to be incompatible with all RBCs even when group O RBCs are used (e.g. a strong cold-reacting autoantibody), then it may be impossible to find units that are compatible at both

methodologies.

Assuming group O RBCs are being crossmatched, and that the cause of the unresolved ABO discrepancy explains the incompatible immediate-spin XM, the unit is considered compatible based off the AHG XM result. It is not necessary to contact the patient's physician, and no additional documentation or Medical Director notification is required.

In these instances:

a. The immediate-spin XM will be resulted in the BBIS first, making the unit appear as incompatible initially.

b. The AHG XM will be resulted in the BBIS second. A compatible AHG XM result will override the incompatible immediate-spin XM as the overall XM status of the unit.

c. The XM tag that is used to tag the RBC unit is the one that prints following resulting the AHG XM, so that the tag indicates that the unit is compatible with the patient.

For example:

a. A Type and Screen is performed on a patient sample that has a history of an anti-Kell. Extra reactivity is present in the reverse typing of the ABO, indicating that an all-phase tube panel is required to identify that cause of the extra reactivity. When performing the all-phase tube panel, a strong cold-reacting autoantibody (CLD) is identified that is causing panreactivity in all tube testing. A pre-warming technique is attempted to resolve the reverse typing ABO discrepancy caused by the CLD Antibody, but it is unsuccessful. The patient's blood type is resulted and Special Requirements are added as described in Transfusion Medicine policy, *Resolution of ABO and Rh Discrepancies*, and immediate-spin XMs are now required.

    a. Even when group O RBCs are used, the panreactive CLD antibody is causing all immediate-spin XMs to be incompatible, even though the same RBCs are compatible when performing gel XMs. Since it has been proven that the CLD antibody is present and it will not be possible to find RBCs that are compatible in the immediate-spin XMs, these RBCs may be used and considered XM compatible. The XM status in the Blood Bank computer and on the XM tag should indicate that the RBCs are compatible, and no notification to the patient's physician is required.

V. SPECIMEN COLLECTION AND HANDLING:

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

VI. PROCEDURE:

This *Procedure* is organized according to the specific reason that the incompatible XM was originally performed.

A. Incompatible Crossmatches on Patients with

Identified, Clinically Significant Antibodies (No History of Non-specific Reactivity)

1. Perform a gel DAT on the unit and a note to the RBC unit in the BBIS "Gel DAT = (reaction strength)".
    a. If the gel DAT is positive, the investigation is resolved. XM additional antigen negative units as described in Transfusion Medicine policy, *Policies for Providing Red Blood Cells to Patients with Unexpected Antibodies*.
    b. If the gel DAT is negative, proceed to step 2.
2. Perform a panel on the current sample (if not already performed, if performed proceed to step 2b). Verify that all antibodies have been properly excluded. Refer to Transfusion Medicine policy, *Interpretation of Antibody Investigations*.
    a. If a new antibody is identified in the panel on the current sample, then antigen type the unit (on which the incompatible XM was observed) for the antigen corresponding to the new antibody.
        i. If the unit is positive for the corresponding new antigen, then the investigation is resolved. XM additional antigen negative units.
    b. If a new antibody is not identified in the panel on the current sample, or a new antibody is identified but the unit is antigen negative for the newly identified antibody, then perform the following to attempt to resolve the investigation:
        i. Repeat the XM.
        ii. Repeat the antigen typing(s) on the unit.
3. If the investigation of the incompatible XM remains unresolved after performing the above steps, then add a WkU (Weak Unidentified) antibody to the patient's record (computer record and antibody card).

B. Incompatible Crossmatches on Patients with a WkU Antibody (With or Without Identified, Clinically Significant Antibodies)

IncXM nonspecific.jpg

C. Incompatible Crossmatches on Patients with Clinically Insignificant Antibodies of Known Specificity (e.g. Anti-M or Anti-Lea)

Note that it is not necessary to antigen type the incompatible unit(s) for the antigen corresponding to the cold reacting antibody of known specificity; however, it may be helpful if it proves difficult to find compatible XMs (e.g. for patients with anti-M).

1. Determine whether the incompatible XM is reasonably explained by the cold reacting antibody of known specificity. In making the determination, consider the following:
    a. The reaction strength of the incompatible gel XM should be similar to that of the antibody screen or panel (if performed).
    b. The percentage of incompatible XMs observed should approximate the antigen frequency of the corresponding antigen in the general population.
        i. Antibody frequencies may be found in the *AABB Technical Manual*.
2. If the incompatible XM is reasonably explained by the cold reacting antibody of known specificity, then continue to XM additional units.
3. If the incompatible XM is not reasonably explained by the cold reacting antibody of known specificity, then perform a panel on the current sample and continue to XM additional units based on the results of the new panel.
4. Examples:
    a. Incompatible XMs are NOT reasonably explained by the clinically insignificant antibody of known specificity.
        i. Four RBCs are XM'd for a patient with a history of an anti-Le^a; the patient's antibody screen was negative. Three of the units (75%) are found to be 4+ incompatible in the gel XM. The incompatible XMs are not reasonably explained by the anti-Le^a since the reaction strength of the gel XMs is much stronger than the antibody screen of the current sample, and since the percentage of incompatible units is much higher than the general antigen frequency (which is approximately 20% for the Le^a antigen).
        ii. Additional gel XMs should not be performed until an antibody investigation is performed.
    b. Incompatible XMs are reasonably explained by the clinically insignificant antibody of known specificity.
        i. Six RBCs are gel XM'd to a patient with an anti-M that was reacting w+ in the gel screen. Four of the units are weakly incompatible. The incompatible XMs are reasonably explained by the anti-M since the reaction strengths of the gel XMs are the same as the reaction strength of the antibody screen, and since four of the six units (67%) were incompatible in the gel XM. This percentage approximates the general antigen frequency (which is approximately 75% in the general population).
        ii. Additional units, which are not tested for M, may be XM'd; it is not necessary to perform an antibody investigation due to the four incompatible XMs.

D. Incompatible Crossmatches on Patients with an Antibody to a Low Incidence Antigen (The Specificity of Which Was Previously Determined)

IncXMLowIncidence 09092024.jpg

VII. REFERENCES:

1. AABB, *Technical Manual*, current edition.
2. College of American Pathologists, *Transfusion Medicine Checklist*, current edition.

Attachments

Electronic Crossmatch Only Tag 09092024.pdf

Incompatible Crossmatch RBC Downtime Notification Form 09092024.pdf

Incompatible Crossmatch Tag 09062024.pdf

IncXM nonspecific.jpg

IncXMLowIncidence 09092024.jpg

Approval Signatures

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Applicability

Dearborn, Farmington Hills, Grosse Pointe, Royal Oak, Taylor, Trenton, Troy, Wayne