TRANSFUSION ASSOCIATED DISEASE, RECALL, OR COMPLICATION INVESTIGATION POLICY

I. FATALITIES AND COMPLICATIONS ASSOCIATED WITH TRANSFUSION:

A. TRANSFUSION RELATED FATALITY:

FDA and MEDIC must be notified immediately, and subsequently in writing, when a possible transfusion related fatality occurs and is suspected to be due to an attribute of the donor or a problem with the collection, processing, storage, or shipment of the blood component.

B. TRANSFUSION RELATED SERIOUS COMPLICATION INCLUDING TRALI:

MEDIC must be notified immediately, and subsequently in writing, when a possible transfusion related serious complication occurs, and is suspected to be due to an attribute of the donor or a problem with the collection, processing, storage, or shipment of the blood component.

TRALI:

Transfusion-related acute lung injury (TRALI) also must be reported. It is a clinical syndrome associated with transfusion that typically includes dyspnea, hypoxemia, hypotension, bilateral non-cardiac pulmonary edema, and fever. Symptoms may occur during the period between the beginning of transfusion and 6 hours afterward. The severity of symptoms can range from mild to severe. However, in a large series of TRALI cases, 100% required oxygen support, and 72% also required mechanical ventilation. In this same series, symptoms resolved within 96 hours in 80% of patients. The other 20% of patients required longer support, which was associated with persistence of pulmonary infiltrates on chest radiograph. TRALI has been associated with the presence of granulocyte antibodies, HLA class 1 antibodies, HLA class II antibodies, and biologically active lipids in donor plasma. All plasma-containing blood components, including red blood cells, platelets, frozen plasma (FFP/FP-24), and cryoprecipitate have been implicated in TRALI.

MEDIC has limited the collection of large-volume transfusable plasma and platelet pheresis products to male donors, or female donors who have never been pregnant or have been tested to be HLA antibody negative since their last pregnancy.

C. SUSPECTED BACTERIAL CONTAMINATION:

1. Indications of possible bacterial contamination:

    a. Questionable appearance.

b. Bacteria present in the blood component, detected by Gram stain or culture.

c. Positive result on a bacterial detection test performed as a safety measure for platelets.

d. Patient reaction consistent with exposure to blood product with bacterial contamination.

2. The Transfusion Service should take the following steps in the case of any product suspected of bacterial contamination:

a. Immediately notify MEDIC of suspected contamination.

b. Conduct an investigation of any suspected patient reaction according to their institution's policies and guidelines.

c. If the product has been transfused, a blood culture of the recipient should be performed, if possible.

3. Follow-up actions to be taken by MEDIC for products with suspected bacterial contamination:

a. Withdrawal or return of product with suspected contamination as well as any other products associated with that donation.

b. Submission of the suspect component for Gram stain and culture.

c. Notification of Gram stain and culture results to any transfusion service that has transfused other components associated with the suspect product.

4. Platelet Pheresis monitoring by MEDIC:

a. MEDIC will monitor each platelet pheresis for bacterial contamination for at least 7 days after product collection by use of the BacT/ALERT 3D System. MEDIC's test includes aerobic and anaerobic bottles and utilizes large volume-delayed sampling (LVDS-48 hr).

b. MEDIC will notify the transfusion service if a positive BacT/ALERT result is detected on a platelet pheresis that has been shipped, with a request for return of the product if transfusion has not taken place.

c. MEDIC will have the positive culture bottle sent for a STAT Gram stain and subsequent sub-culture.

d. Results of the Gram stain will be phoned to the transfusion service if transfusion has occurred.

e. The transfusion service will be responsible for notification of the attending physician.

f. Culture reports will be called or faxed to the transfusion service as they become available, if transfusion occurred.

5. Follow-up if a clinically significant organism is present in a blood product:

a. If culturing of a blood product reveals the presence of a clinically significant organism that may have come from a bacteremic donor and the product has already been transfused, a donor investigation shall be initiated at the direction of the VP & Chief Medical Officer of MEDIC. The investigation should determine if a condition causing a bacteremia exists in the donor that may require treatment and may present reason for deferring the donor until the condition is eliminated. Such a donor investigation shall occur whether or not the recipient develops a bacteremia or sepsis following the transfusion of the contaminated product.

b. When a contaminated product containing a potentially clinically significant organism has been transfused, a report form to obtain information regarding the recipient outcome and blood culture results will be sent to the Medical Director of the transfusion service where the event has occurred. This form should be completed and returned to the VP & Chief Medical Officer of MEDIC for use in investigation of the case.

D. POST TRANSFUSION DEVELOPMENT OF INFECTIOUS DISEASE:

MEDIC is to be notified in a suspected case of transfusion transmitted infectious disease that is confirmed or **not** ruled out. For Hepatitis cases, only report cases that developed 15 to 182 days post-transfusion.

1. Initiation of investigation:

   The transfusion service is to complete the Transfusion Associated Disease Investigation form with the following information:

   a. Indicate the disease being reported
   b. Patient case number
   c. Reporting hospital name and address
   d. Transfusing hospital name and address (if different)
   e. Diagnosis at time of transfusion
   f. Date symptoms first appeared
   g. Date reported
   h. Possible exposure to hepatitis or any other risk factors
   i. Other products administered
   j. Test results for HBsAg, Anti-HBc, Anti-HCV, HIV, Western Blot, HTLV-I/II – **NOTE:** *It is up to the Transfusion Service to obtain these test results even if they were not performed in your facility.*
   k. Component information:
      1) component unit number
      2) product transfused
      3) date transfused
   l. MEDIC notified date and by.

   Forward the form to MEDIC. The investigation will not be initiated at MEDIC until all of the information requested above is received.

2. Investigation:

   MEDIC will:

   a. Review medical histories and testing records

   b. Request donors to give samples for testing (if necessary). MEDIC will notify original source to request follow-up, if the unit was from another source. The investigation is active until all involved donors have given subsequent samples **or** up to one year.

3. Completion of investigation:

   The Transfusion Associated Disease Investigation Report along with a letter acknowledging the hospital's report and investigation results will be sent to the transfusion service. Investigation results are kept on file indefinitely at MEDIC.

II. TRANSFUSION PRODUCTS MARKET WITHDRAWAL AND LOOKBACK POLICY FOR SUBSEQUENT REACTIVE TEST RESULTS:

A. TRANSFUSABLE PRODUCT MARKET WITHDRAWAL:

MEDIC will identify promptly (within 3 calendar days) in-date components from prior collections, whenever a donor has a repeatedly reactive screening test, or an initially reactive NAT result, with the following groups: HBsAg, HBV-NAT, Anti-HCV, HCV-NAT, Anti-HIV-1/2, HIV-NAT, Anti-HTLV-I/II, Anti-HBc, WNV-NAT and/or T. cruzi (Chagas):

1. Identify promptly (within 3 calendar days) in-date components from prior collections, whenever a donor has a repeatedly reactive screening test, or an initially reactive NAT result. Use the following guidelines according to test:

a. <u>HBsAg, Anti-HBc, Anti-HTLV I/II:</u>

Withdraw any in-date products collected within 12 months prior to and including last negative test and no more than 5 years from current donation whenever a donor has a repeatedly reactive screening test for HBsAg, Anti-HBc or Anti-HTLV I/II.

b. <u>HCV:</u>

1) Withdraw any in-date products collected within 12 months and less before the donor's most recent nonreactive screening test (Anti-HCV); or

2) 12 months and less before the donor's reactive HCV NAT test, whichever is the lesser period

c. <u>HBV NAT:</u>

Withdraw any in-date products collected within 12 months prior to the positive HBV-NAT.

d. <u>HIV</u>:

1) Withdraw any in-date products collected within 12 months and less before the donor's most recent nonreactive screening test (Anti-HIV); or

2) 12 months and less before the donor's reactive HIV NAT or HIV p24 antigen test, whichever is the lesser period

e. WNV-NAT:

Withdraw any in-date products collected within 120 days prior to the collection date of the reactive test.

f. Non-Discriminatory NATS:

For an Ultrio reactive donor, with negative results on discriminatory NATS, withdraw products as defined under both HIV-NAT and HCV-NAT.

g. T. cruzi (Chagas):

Withdraw all in-date components, or in a previously Chagas tested donor, products drawn within 12 months prior to the most recent negative result.

2. Transfusion service should quarantine/remove from stock any **in-date** not transfused components from prior collections as requested by MEDIC (MEDIC uses the timeframes listed in II. A. 1.

3. Repeat Reactive HIV or HCV cases with a positive or indeterminate confirmatory result (including discriminatory HIV NAT or HCV NAT or secondary HCV screen); or reactive Chagas with either a positive confirmatory test result or geographic risk factor; may also involve Lookback Notification.

B. TRANSFUSABLE PRODUCTS LOOKBACK:

1. UPON CONFIRMED REACTIVE OR INDETERMINATE GEENIUS, WESTERN BLOT, OR IFA TEST FOR ANTI-HIV-1/2 or REACTIVE HIV-NAT, MEDIC WILL:

NOTE: *If further testing results will not be available (such as inadequate sample quantity or age), follow these instructions, as if the supplemental/confirmatory were reactive.*

a. Notify by letter the Medical Director of the transfusion service receiving each component from previous donations.

b. HIV:

Do Lookback for any transfusable products collected within the 12 months prior to the repeatedly reactive NAT; and for any transfusable products collected within 12 months prior to donor's last HIV antibody negative donation, whenever a donor has a confirmed reactive or indeterminate GEENIUS, Western Blot or IFA test for Anti-HIV-1/2 or a positive test for HIV-NAT.

c. Request the hospital transfusion service to:

Contact the recipient's physician and request the physician inform recipient(s) that:

1) there is a possibility they may have been infected with HIV

2) this question may be resolved by testing a sample of the recipient's blood

3) MEDIC will perform recipient(s) testing upon request

2. UPON CONFIRMED HCV POSITIVE BY HCV-NAT AND/OR REACTIVE SECONDARY METHOD SCREENING RESULT, MEDIC WILL:

NOTE: *If further testing results will not be available (such as inadequate sample quantity or age), follow these instructions, as if the supplemental/confirmatory were reactive.*

a. Notify by letter the Medical Director of the transfusion service receiving each component from previous donations.

Use the "HCV LOOKBACK NOTIFICATION" letter if the donor has a confirmed HCV positive result.

Any required hospital notifications for lookback, including confirmatory test result, must be completed within 45 days of completing additional testing.

Use the "HCV Further Testing Notification" letter if the donor has a nonreactive/negative HCV NAT and secondary HCV antibody test result after the RR HCV antibody test, AND a call/notice had been performed to the hospital/ consignee for market withdrawal of products.

b. HCV:

1) Do lookback for any transfusable products collected within 12 months prior to and including last negative Anti-HCV test, whenever a donor has a reactive initial HCV antibody result followed by a reactive confirmatory or supplemental HCV result (NAT and/or secondary HCV antibody test).

Do lookback for any transfusable products collected within the 12 months prior to the reactive HCV NAT donation.

2) Request the hospital transfusion service (via the Lookback letter) to notify recipients as follows:

a) there is a possibility they may have been infected with HCV

b) this question may be resolved by testing a sample of the recipient's blood

c) MEDIC will perform recipient(s) testing upon request.

3. REACTIVE CHAGAS TEST:

If a donor is repeatedly reactive on the screening test, and there is additional information indicating risk of T. cruzi infection (such as information that the donor or donor's mother resided (greater than 3 months) in an area endemic for Chagas disease (Mexico, Central and South America); or as a result of other medical diagnostic testing indicating T. cruzi infection; or based on a positive result on the confirmatory test, perform the following:

a. Notify by letter the Medical Director of the transfusion service receiving each component from previous donations.

b. Encourage the hospital to notify the recipient's physician of record of a possible increased risk of T. cruzi infection for any listed blood component that was transfused.

III. PRODUCT WITHDRAWAL/RECALL FOR REASONS OTHER THAN SUBSEQUENT REACTIVE TESTS:

MEDIC will institute a product withdrawal or recall for issued components when errors or additional information are discovered that could have an adverse effect on the safety, purity or potency of the product.

A. MEDIC STAFF RESPONSIBILITY:

Staff discovering issued component with labeling or processing errors, or staff answering calls from donors that require product withdrawal or recall will:

1. Determine the location of each component involved.

2. Institute a product withdrawal or recall immediately for in-date products by contacting the transfusion service to determine the status of blood components and/or arrange for their return.

3. Document the date transfusion service was notified by phone, including name of person notified and caller's initials.

4. Photocopy the label of a product that was incorrectly labeled (blood group, Rh, expiration date, unit number, etc.) upon its return to MEDIC.

   NOTE: *If a consignee is instructed to change the label, ask them to photocopy the label before and after changes and forward copies to MEDIC.*

5. Photocopy the involved records for each product distributed.

6. Complete retesting if required.

7. VP & Chief Medical Officer and/or Quality will assess corrective action and determine:

   a. Product to be released, or

   b. Product will not be released:

      1) Quarantine product(s)

      2) Document quarantine and destruction.

B. MEDIC QUALITY DEPARTMENT WILL:

1. Assess corrective action and determine if appropriate.

2. Notify each consignee of withdrawal or recall of products with a Blood Product Notification letter.

3. Notify the Center for Biologics Evaluation and Research of the Food and Drug Administration (FDA) of any deviations occurring due to MEDIC's processing of the product that could impact the safety, purity or potency of any distributed product, and which meet the FDA's definition of reportable events.