

## **Analysis of FDA Guidance Document on Use of Serological Tests to Reduce the Risk of Transmission of *Trypanosoma cruzi* Infection – December 2017**

FDA's December 2017 guidance, "[Use of Serological Tests to Reduce the Risk of Transmission of \*Trypanosoma cruzi\* Infection in Whole Blood and Blood Components Intended for Transfusion](#)" (the guidance), provides recommendations to blood collection establishments regarding the use of serological tests to reduce the risk of transmission of *Trypanosoma cruzi* infection in blood and blood components. The recommendations apply to the collection of blood and blood components, except Source Plasma, for transfusion or for use in manufacturing a blood product including donations intended as a component of, or used to manufacture, a medical device.

The guidance supersedes the December 2010 guidance, "Use of Serological Tests to Reduce the Risk of Transmission of *Trypanosoma cruzi* infection in Whole Blood and Blood Components Intended for Transmission" and finalizes the November 2016 draft guidance, "Amendment to 'Guidance for Industry: Use of Serological Tests to Reduce the Risk of Transmission of *Trypanosoma cruzi* Infection in Whole Blood and Blood Components Intended for Transfusion'".

The guidance provides recommendations, consistent with the November 2016 draft guidance, for blood donor testing, deferral, notification, and donor reentry, including: (1) expanding the scope of the guidance to include the collection of blood and blood components for use in manufacturing a product, including donations intended as a component of or used to manufacture a medical device; (2) removing the recommendation to ask donors about a history of Chagas disease; (3) providing a recommendation for a reentry algorithm for certain donors deferred based on screening test results for antibodies to *T. cruzi* or deferred for a history of Chagas disease question; and (4) product management. Information regarding implementation and the circular of information is also provided.

### **Recommendations**

**The following provides a brief overview of the recommendations. Please review the guidance for relevant details.**

#### **Donor Screening**

FDA no longer recommends that the question "Have you ever had Chagas disease?" be asked to all donors at each donation because the Chagas question has no added value when all donors are tested at least once. Refer to the implementation requirements regarding this change.

#### **Donor Testing**

FDA recommends:

- one-time testing of each donor of blood and blood components as required under (21 CFR 610.40(a)(2)(iii)(A)).
- one-time testing of autologous donors of blood and blood components only when the circumstances described in §§ 610.40(d)(1) through (3) are applicable.
- a review of *T. Cruzi* testing records for a prospective donor to determine if the donor should be tested.
- donors testing non-reactive for antibodies to *T. cruzi* are qualified to return for subsequent donations without further testing for antibodies to *T. cruzi*.

## **Blood Donor Deferral, Further Testing and Notification**

### **FDA listed current requirements:**

- donors testing repeatedly reactive on a licensed screening test for *T. cruzi* antibody must be deferred (§ 610.41(a)).
- each donation testing repeatedly reactive using a licensed screening test for antibodies to *T. cruzi* must be further tested using a licensed, approved, or cleared supplemental test for antibodies to *T. cruzi* (See § 610.40(e)).
- within 8 weeks after determining that the donor was deferred based on a repeatedly reactive test for antibodies to *T. cruzi*, reasonable attempts must be made to notify the donor of the deferral and the test results, including the results of further testing required under § 610.40(e).

### FDA recommends:

- the permanent deferral of a donor testing positive or indeterminate on the licensed supplemental test.
- the deferred donor be informed of the likelihood and medical significance of infection with *T. cruzi*.
- a donor testing negative on a licensed supplemental test may be considered for reentry using the recommended algorithm and informed of the procedure to follow for reentry.

### **Reentry Algorithm for Donors Deferred on the Basis of Screening Test Results for Antibodies to *T. cruzi* or Predonation Screening Question**

Where consistent with the meaning of §§ 610.41(b) and 630.35(b), FDA considers the following to be an acceptable requalification method or process for reentry of donors deferred due to repeatedly reactive screening tests for antibodies to *T. cruzi* and for donors deferred based on an affirmative response to the history of Chagas disease question.

### FDA recommends that:

- A donor is not eligible for reentry with the following Chagas test results:
  - Positive or indeterminate with an investigational or licensed supplemental test for antibodies to *T. cruzi*.
  - Positive or indeterminate with the unlicensed *T. cruzi* RIPA test.
- A donor deferred based on the of screening test results for antibodies to *T. cruzi* may be considered for reentry based on the following test results if all other eligibility criteria are met:
  - Negative with an investigational or licensed supplemental test for antibodies to *T. cruzi*; OR
  - Negative with the unlicensed *T. cruzi* RIPA test; OR
  - Not tested with an investigational or licensed supplemental test for antibodies to *T. cruzi*, and not tested with the unlicensed *T. cruzi* RIPA test.
- Donors deferred previously based on an affirmative response to the history of Chagas disease question may also be considered for reentry if all other eligibility criteria are met.

FDA recommends using the following criteria to reenter a donor that meets all eligibility criteria as described above:

- Obtain a new blood sample from the donor (no donation is made at this time) and perform follow-up testing as follows:
  - Test sample using two different licensed screening tests for antibodies to *T. cruzi*.

Note: One of the two screening tests should be the test that was repeatedly reactive on the original donation; AND If the follow-up sample is non-reactive with the two licensed screening tests, then test the follow-up sample with a licensed supplemental test for antibodies to *T. cruzi*.

- Evaluate the results of the follow-up testing on the donor's new sample as follows:
  - If either one or both screening tests are repeatedly reactive, FDA recommends that you defer the donor permanently.
  - If the licensed supplemental test is either positive or indeterminate, FDA recommends that you defer the donor permanently.
  - If the two licensed screening tests are non-reactive and the licensed supplemental test is negative, you may reenter the donor provided all other donor eligibility criteria are met at the time of donation. Testing for *T. cruzi* is not required on future blood donations from the reentered donor.

### **Product Management** (unchanged from the recommendations of the 2010 Guidance)

#### Index Donations

FDA noted the current requirements:

- Blood and blood components that test repeatedly reactive for antibodies to *T. cruzi* must not be shipped or used unless an exception exists (§§ 610.40(h) and 630.30(b)(1)).
- Blood or blood components that test repeatedly reactive must be appropriately labeled (§ CFR 606.121), including "BIOHAZARD" legend (§ 610.40(h)(2)(ii)(B)).
- Blood and blood components determined to be unsuitable for transfusion must be prominently labeled: "NOT FOR TRANSFUSION," and the label must state the reason the unit is considered unsuitable unless the blood and blood components are intended solely for further manufacture (§ 606.121(f)).

#### **Lookback** (Product Retrieval and Consignee Notification)

FDA recommends the following within 3 calendar days after a repeatedly reactive licensed test for *T. cruzi* antibody:

- Identify all in-date blood and blood components previously donated, going back either 10 years (or indefinitely where electronic records are available), OR for donor with a prior negative test, 12 months prior to the donor's most recent negative test using a licensed test for *T. cruzi* antibody, whichever is the lesser period (the lookback period).
- Quarantine all previously collected in-date blood and blood components from the donor that remain in your inventory; and
- Notify consignees to quarantine, and either destroy or return to you, all previously collected in-date blood and blood components from that donor.

#### **Notification**

FDA also recommends that, within 12 weeks of a donor testing repeatedly reactive by a licensed screening test for *T. cruzi* and positive or indeterminate by a licensed or investigational supplemental test that, you:

- Notify consignees of all previously distributed blood and blood components collected from that donor during the lookback period; AND
- Encourage consignees to notify the recipient's physician of record of a possible increased risk of *T. cruzi* infection if those blood or blood components were transfused.

## **Autologous Donation**

FDA noted the current requirements:

- Autologous donors must be tested under §§ 610.40(d) and (e) under certain circumstances to prevent inadvertent allogeneic exposures to unsuitable units.
- The results of further testing under § 610.40(e) must be provided to the autologous donor's referring physician. (§§ 630.40(d)(1)(iii) and (d)(2)).
- Each autologous donation must be labeled as required under §§ 610.40(d)(4) and 606.121(i)(5), as appropriate.
- Autologous donations that are repeatedly reactive by a licensed test for *T. cruzi* antibody must bear a "BIOHAZARD" legend. (See § 610.40(d)(4)).

## **Circular of Information**

FDA recommends the following statement for *T. cruzi* testing in the circular of information as required in § 606.122(h):

"All blood has been collected from donors who have tested negative by a licensed test for antibodies to *Trypanosoma cruzi* either on the current donation or at least one previous donation."

## **Implementation**

### **Donor Screening**

FDA noted the current requirements:

Under § 601.12, a licensed blood establishment that makes a change to the donor history questionnaire to remove the question "Have you ever had Chagas disease?" must report the change and date of implementation in the annual report to FDA if you:

- revise your own DHQ and accompanying materials, OR
- revise a previously FDA accepted DHQ and accompanying materials.

Unlicensed establishments are required to maintain records under § 606.160 but not required to report under § 601.12.

### **Reentry of Deferred Donors**

FDA noted the current requirements:

- FDA considers the donor reentry recommendations to be consistent with §§ 610.41(b) and 630.35(b) and acceptable requalification method or process, for the reentry of donors deferred due to repeatedly reactive screening tests for antibodies to *T. cruzi* and for donors deferred based on an affirmative response to the donor history question, "Have you ever had Chagas disease?"
- Under § 601.12, a licensed blood establishment that makes a change in donor reentry based on recommendations in the guidance must report the change and date of implementation in the annual report to FDA.
- Unlicensed establishments are required to maintain records under § 606.160 but not required to report under § 601.12.
- Under §§ 610.41(b) and 630.35(b), a donor requalification method or process used to requalify a donor must be acceptable to FDA. Licensed establishments intending to use an alternative requalification method must submit a supplement for prior approval, as required under § 601.12(b).

- Similarly, before an unlicensed establishment implements an alternative requalification method or process from that described in the guidance, FDA must first find the method or process to be acceptable for such purpose (§§ 610.41(b) and 630.35(b)).

FDA has also provided a flowchart of the reentry algorithm in the appendix of the [guidance](#).