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"

Draft Guidance for Industry

This guidance document is for comment purposes only.

Submit one set of either electronic or written comments on this draft guidance by the date provided in the *Federal Register* notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

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For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
November 2016

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Contains Nonbinding Recommendations

Draft – Not for Implementation

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"

Draft Guidance for Industry

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance, when finalized, is intended to amend the document entitled "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" dated December 2010 (the "2010 Chagas Guidance") (Ref. 1) by 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, and 3) providing a recommendation for a reentry algorithm for certain donors deferred on the basis of screening test results for antibodies to *Trypanosoma cruzi* (*T. cruzi)* or on the basis of answering "yes" to the Chagas screening question.

The recommendations in this guidance apply to the collection of blood and blood components, except Source Plasma, for transfusion or for use in manufacturing a product, including donations intended as a component of, or used to manufacture, a medical device. Blood establishments are not required to test donations of Source Plasma for evidence of infection due to *T. cruzi* (21 CFR 610.40(a)(2)(ii)). Within this guidance, "you" refers to establishments that collect blood and blood components.

This guidance notifies you that *T. cruzi* is defined as a relevant transfusion-transmitted infection (RTTI) in 21 CFR 630.3(h)(1) and subject to the testing requirements in 21 CFR 610.40, the donor deferral practices in 21 CFR 610.41, and the donor notification requirements in

21 CFR 630.40. Further, this guidance notifies you that FDA has licensed a supplemental test for antibodies to *T. cruzi* and further testing of donations found repeatedly reactive to a screening test for *T. cruzi* is therefore required under 21 CFR 610.40(e).[1]

When finalized, we will update the 2010 Chagas Guidance by incorporating the new recommendations provided in this guidance into an updated final guidance. All other recommendations in the 2010 Chagas Guidance will remain unchanged.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Chagas disease is caused by the protozoan parasite *T. cruzi*. Natural infections are transmitted by infected blood sucking insects (triatomine bugs). Other primary forms of transmission include oral, congenital (mother to unborn infant), organ transplantation and blood transfusion. The disease is found primarily in Mexico and Central and South America. Several cases of natural transmission also have been reported in the United States (U.S.), which were associated with documented infections in insect vectors and reservoir hosts in the southern U.S. (Refs. 2, 3). The presence of the pathogenic agent in U.S. donors, however, has increased due to immigration of infected individuals from endemic areas. Some experts estimate that there may be as many as 300,000 persons unknowingly infected with *T. cruzi* who reside in the U.S. (Ref. 4). These individuals could serve as a potential source of transfusion-transmitted infection should they become U.S. donors. In the U.S. and Canada, 10 cases of transfusion-transmitted *T. cruzi* and five cases of infection from organ transplantation have been documented through 2013 (Refs. 5, 6).

The voluntary testing of U.S. blood donors for antibodies to *T. cruzi* was initiated in January 2007, subsequent to FDA licensure of the first blood donor screening test. As stated above, in 2015,[2] FDA defined *T. cruzi* as a RTTI and, as of May 23, 2016, blood establishments must test for *T. cruzi* consistent with the requirements in 21 CFR 610.40, subject to the exceptions found in 21 CFR 610.40(c) and (d). Additionally, consistent with 21 CFR 610.40(a)(2)(iii)(A), FDA currently recommends one-time testing of each donor of allogeneic units of blood using a licensed test for antibodies to *T. cruzi* (Ref. 1). This guidance document, when finalized, will extend FDA's recommendations relating to one-time testing of donors to 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. An online report of the AABB Chagas'

[1] See Requirements for Blood and Blood Components Intended for Transfusion or for Further Manufacturing Use; Final Rule (80 FR 29842, May 22, 2015), effective May 23, 2016.
[2] See footnote 1.

Biovigilance Network (http://www.aabb.org) dated May 1, 2015,[3] showed that between January 1, 2007 and May 1, 2015, 10,575 donors gave collections that were repeatedly reactive on a licensed screening test for antibodies to *T. cruzi*. Of those collections, 2,046 (19.3%) were reported as confirmed, 8,010 (75.7%) negative, 427 (4.0%) indeterminate, and 92 (0.9%) cases were pending at the time the report was generated. FDA's 2010 Chagas Guidance recommends that all donors whose collections test repeatedly reactive on a licensed test for *T. cruzi* antibodies should be deferred indefinitely and notified of their deferral.

A. Donor Screening for History of Chagas Disease

FDA's 2010 Chagas Guidance recommends asking the question "Have you ever had Chagas disease?" to all donors at each donation, to identify donors with a history of Chagas disease. The 2010 Chagas Guidance also recommends that donors who answer "no" to the question should be tested with a licensed screening test for antibodies to *T. cruzi*, and donors who answer "yes" to this question should be deferred indefinitely and notified of their deferral. In a recent study, Steele, et al., identified 34 donors deferred because of a history of Chagas disease as revealed by the question among approximately 76 million qualified donors screened by the American Red Cross (ARC) between January 2000 and August 2011 (Ref. 7). In comparison, ARC identified 488 donations positive by the unlicensed supplemental Radioimmunoprecipitation Assay (RIPA) among approximately 21 million donations tested between January 2007 and August 2011. The 488 *T. cruzi* RIPA positive donors had not responded in the affirmative to the Chagas history question during the predonation screening process. This report also showed that only one of the six who provided a follow-up sample, among the 34 donors deferred based on the Chagas disease history question, had a repeatedly reactive result with a licensed screening test. This donor was also *T. cruzi* RIPA positive on further testing. The authors concluded that the Chagas question has no added value when all donors are tested at least once.

Based on this study, the clinical sensitivity of the two currently licensed screening tests (Refs. 8, 9), the low (0.8%) risk of transfusion-transmitted *T. cruzi* infection in the blood donor population (Ref. 10), and the observation that *T. cruzi* RIPA positive donors are likely not aware of their infection, we are recommending that one-time testing alone, without donor questioning for history of Chagas disease, is adequate to identify donors at risk for Chagas disease. We explain in section III of this guidance that the recommendation in the 2010 Chagas Guidance to ask the question "Have you ever had Chagas disease?" to all donors at each donation is no longer recommended, and the question can be removed from donor history questionnaires.

[3] Facilities report their data intermittently; consequently, the numbers reported represent what was available in the database at the time.

B. Supplemental Testing of Donors Repeatedly Reactive with a Licensed Screening Test for Antibodies to *T. cruzi*

Consistent with 21 CFR 610.40(e), you must further test each donation found to be reactive by a donor screening test using a licensed, approved or cleared supplemental test, when available.[4] In November 2011, FDA licensed a supplemental test for antibodies to *T. cruzi*. This test is intended for use as an additional, more specific test for human serum or plasma specimens found to be repeatedly reactive using a licensed screening test for antibodies to *T. cruzi*.

A positive test result on the licensed supplemental test indicates that antibodies to *T. cruzi* were detected, providing further confirmation of the repeatedly reactive screening test result. It is FDA's view that donors whose blood samples are found to be repeatedly reactive on a licensed screening test, but negative on a licensed supplemental test, may be considered for reentry as set forth in section III.D of this guidance.

C. Donor Reentry

The reentry of donors deferred on the basis of screening test results for antibodies to *T. cruzi* was discussed at the July 31, 2014 Blood Products Advisory Committee (BPAC or the Committee) meeting (Ref. 11).

FDA presented an analysis of donor follow-up studies used to develop a proposed donor reentry algorithm and four alternative scenarios. In these follow-up studies, donors whose collections were repeatedly reactive on a licensed screening test for antibodies to *T. cruzi* and negative on a licensed supplemental test for antibodies to *T. cruzi* on their initial donation were further evaluated to determine their eligibility for requalification/reentry as donors. Follow-up testing was performed to assess their most likely *T. cruzi* infection status and determine those who could safely be reentered.

Results of the follow-up studies showed that 117/238 (49.2%) of donors in the FDA analysis had follow-up samples that were non-reactive with the two licensed screening tests. Among the 117 donors with negative screening tests on follow-up, 115/117 (98.3%) had non-reactive results with the licensed supplemental test. Conversely, 2/117 (1.7%) of these donors had indeterminate results with the licensed supplemental test.

It is FDA's current thinking that it would not be safe to reenter a donor with any reactivity with a licensed supplemental test given the higher analytical sensitivity of the currently licensed supplemental test compared with the licensed screening tests and the consequent uncertainty regarding the donor's infectious status. FDA currently considers donors whose follow-up samples are tested with all three currently licensed tests and show no reactivity with any of the three tests to be eligible for reentry, provided all other donor eligibility criteria are met. A least burdensome approach to identifying potentially

[4] See footnote 1.

eligible donors would be to perform sequential testing. The donors' follow-up samples would be first tested with the two licensed screening tests, which are run on automated instruments. Only specimens which are non-reactive on both screening tests would be subsequently tested with the manual licensed supplemental test.

It is FDA's current thinking that previously deferred donors who have had positive test results with either the unlicensed *T. cruzi* RIPA test or with an investigational or licensed supplemental test for antibodies to *T. cruzi* are not eligible for reentry and therefore should not be considered for reentry using the recommended algorithm (See section III.D of this guidance). The *T. cruzi* RIPA test has a long history of being used to identify individuals infected with *T. cruzi*. In a study by ARC of *T. cruzi* RIPA positive donors, a high proportion, 74.5% (117/157), were born in a *T. cruzi* endemic country (Ref. 12). Data from the licensed supplemental test clinical trial showed high concordance, 98.7% (151/153), between *T. cruzi* RIPA positivity and licensed supplemental test positivity among screening test repeatedly reactive donors (Ref. 13). Similarly, previously deferred donors who have had an indeterminate test result with either the *T. cruzi* RIPA test or with an investigational or licensed supplemental test are not eligible for reentry and therefore should not be considered for reentry using the recommended algorithm. These donors represent a small percentage of currently deferred donors (4.0%, according to an online report of the AABB Chagas' Biovigilance Network (http://www.aabb.org) dated May 1, 2015, as stated in section II of this guidance) and because their infectious status is unclear due to low level antibody reactivity to *T. cruzi* specific antigens, FDA considers them not eligible for reentry.[5] Only deferred donors with negative test results on the unlicensed *T. cruzi* RIPA (if so tested) and the investigational or licensed supplemental test for Chagas (if so tested), and deferred donors who have never been tested by *T. cruzi* RIPA or an investigational or licensed supplemental test should be considered for reentry using the recommended algorithm. FDA recommends that deferred donors who previously answered "yes" to the predonation screening Chagas question also be considered for reentry using the recommended algorithm provided that they have had no positive or indeterminate test results on the unlicensed *T. cruzi* RIPA or on the investigational or licensed supplemental test for Chagas.[6]

Donors who may be considered for reentry using the recommended algorithm may provide a follow-up blood sample for testing after a minimum of 6 months since the time of their last deferral. Although all *T. cruzi* positive U.S. blood donors identified since testing was initiated in 2007 have shown evidence of a long term rather than recent infection, the six-month time period prior to reentry testing would add a safeguard by allowing time for maturation of an early antibody response in a donor with low level

[5] FDA may reconsider in the future the eligibility of donors with an indeterminate test result using the unlicensed *T. cruzi* RIPA test, or an investigational or licensed supplemental test for antibodies to *T. cruzi* based on newly acquired supporting scientific evidence that these donors are not infected.

[6] If donors participated in follow-up studies, those with a positive or indeterminate test result with an investigational or licensed supplemental test for antibodies to *T. cruzi* or with the unlicensed *T. cruzi* RIPA test should not be considered eligible for reentry.

antibodies at the index donation due to recent infection. Six months would also allow for resolution of potential cross-reacting medical conditions that may have produced the repeatedly reactive screening test result.

While the BPAC did not take a formal vote on the donor reentry algorithm proposed by FDA at its July 31, 2014 meeting, the Committee discussed this approach and did not express concerns about the adequacy of this plan as a reentry algorithm (Ref. 11).

III. RECOMMENDATIONS

The recommendations set forth below are intended to update the recommendations in FDA's 2010 Chagas Guidance at section III.A and section III.C. The recommendations regarding product management in section III.B of the 2010 Chagas Guidance are unchanged.

These recommendations apply to the collection of blood and blood components, except Source Plasma, for transfusion or for use in manufacturing a product, including donations intended as a component of, or used to manufacture, a medical device.[7]

A. Donor Screening for History of Chagas Disease

We no longer recommend that the question "Have you ever had Chagas disease?" should be asked to all donors at each donation. The question may be removed from your donor history questionnaire.

B. Donor Testing

You must test donations for evidence of *T. cruzi* infection using a licensed test for antibodies to *T. cruzi* (21 CFR 610.40(a)), subject to the exceptions found in 21 CFR 610.40(c) and (d). We recommend one-time testing of each donor of blood and blood components (21 CFR 610.40(a)(2)(iii)(A)). We recommend one-time testing of autologous donors of blood and blood components only when the circumstances described in 21 CFR 610.40(d)(1) through (3) are applicable.

Donors who test non-reactive are qualified to return to donate without further testing of subsequent donations for antibodies to *T. cruzi*.

C. Donor Deferral and Counseling

Donors who test repeatedly reactive on a licensed test for *T. cruzi* antibody must be deferred (21 CFR 610.41(a)).

[7] Blood establishments are not required to test donations of Source Plasma for evidence of infection due to *T. cruzi* (21 CFR 610.40(a)(2)(ii)).

You must further test each donation which tests repeatedly reactive using a licensed test for antibodies to *T. cruzi* with a licensed, approved, or cleared supplemental test for antibodies to *T. cruzi* (See 21 CFR 610.40(e)). Further, you must make reasonable attempts to notify any donor that tests repeatedly reactive for antibodies to *T. cruzi* of their deferral and of their test results including the results of further testing required under 21 CFR 610.40(e) within 8 weeks after determining that the donor is deferred (See 21 CFR 630.40).

Donors whose blood tests positive or indeterminate on the licensed supplemental test should be deferred permanently and informed of the likelihood and medical significance of infection with *T. cruzi.* Donors whose blood tests negative on a licensed supplemental test may be considered for reentry using the recommended algorithm and informed of the procedure to follow for reentry.

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

1. FDA recommends that donors with the following Chagas test results are not eligible for reentry:

    a. Positive or indeterminate with an investigational or licensed supplemental test for antibodies to *T. cruzi.*

    OR

    b. Positive or indeterminate with the unlicensed *T. cruzi* RIPA test.

2. Donors deferred on the basis of screening test results for antibodies to *T. cruzi* who had (at the time of the donation that prompted the deferral) the following Chagas test results may be considered for reentry using the recommended algorithm below, provided that they do not meet any of the ineligibility criteria described in item 1 above:[8]

    a. Negative with an investigational or licensed supplemental test for antibodies to *T. cruzi.*

    OR

    b. Negative with the unlicensed *T. cruzi* RIPA test.

[8] Effective May 23, 2016, blood collection establishments must use a licensed supplemental test for *T. cruzi* in accordance with 21 CFR 610.40(e). Accordingly, only donors who were deferred prior to May 23, 2016 should be considered for reentry on the basis of Chagas test results, at the time of the donation that prompted the deferral, with the investigational supplemental test for antibodies to *T. cruzi* or with the unlicensed *T. cruzi* RIPA test.

OR

c. Not tested with an investigational or licensed supplemental test for antibodies to *T. cruzi*, and not tested with the unlicensed *T. cruzi* RIPA test.

3. Donors deferred on the basis of answering "yes" to the predonation screening question "Have you ever had Chagas disease?" may also be considered for reentry using the recommended algorithm, provided that they do not meet any of the ineligibility criteria described in item 1 above.[9]

4. To reenter a donor who meets the criteria described in 2 or 3 above, we recommend that you do the following (also see algorithm in the Appendix):

   a. At least 6 months after the date of deferral, obtain a new blood sample from the donor (no donation is made at this time) and perform follow-up testing as follows:

      i. Test sample using two different licensed screening tests for antibodies to *T. cruzi.*

      If applicable, one of the two screening tests should be the test that was repeatedly reactive on the original donation.

      AND

      ii. 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.*

      Note: As part of this reentry algorithm, FDA recommends that only follow-up samples that are non-reactive with the two licensed screening tests should be tested with a licensed supplemental test.

   b. Evaluate the results of the follow-up testing on the donor's new sample as follows:

      i. If either one or both screening tests are repeatedly reactive, we recommend that you defer the donor permanently.

[9] If donors participated in follow-up studies, those with a positive or indeterminate test result with an investigational or licensed supplemental test for antibodies to *T. cruzi* or with the unlicensed *T. cruzi* RIPA test should not be considered eligible for reentry.

ii. If the licensed supplemental test is either positive or indeterminate, we recommend that you defer the donor permanently.

iii. 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.

IV. IMPLEMENTATION

Note: This guidance is being issued for comment purposes only. Implementation of the recommendations contained herein is not recommended at this time.

A. Donor Screening

If you hold an approved biologics license and you remove the "Have you ever had Chagas disease?" question from your donor history questionnaire (DHQ), you must report this change under 21 CFR 601.12, as follows:[10]

- Revision of your own DHQ and accompanying materials: report in your annual report consistent with 21 CFR 601.12(d), noting the date the question was removed from your DHQ and accompanying materials.

- Revision of a previously FDA accepted DHQ and accompanying materials: report in your annual report consistent with 21 CFR 601.12(d), noting the date the question was removed from the accepted DHQ and accompanying materials.

B. Reentry of Deferred Donors

We consider the recommendations in section III.D for donor reentry in this guidance to be an acceptable requalification method or process, within the meaning of 21 CFR 610.41(b), for reentry of donors deferred due to repeatedly reactive screening tests for antibodies to *T. cruzi* and within the meaning of 21 CFR 630.35(b)[11] for donors deferred for previously answering "yes" to the donor history question, "Have you ever had Chagas disease?"

Licensed establishments implementing the recommendations for donor reentry must report this change to FDA as required under 21 CFR 601.12. Specifically, licensed establishments must submit a statement of this change in an annual report under

[10] See 21 CFR 601.12(a)(3).
[11] See footnote 1.

21 CFR 601.12(d), indicating the date that the revised standard operating procedures were implemented.[12] Unlicensed establishments implementing recommendations for donor reentry in this guidance in their entirety and without modification are not required to report this change.

Sections 610.41(b) and 630.35(b) require that a donor requalification method or process used to requalify a donor be acceptable to FDA. Accordingly, before you implement an alternative requalification method or process from that described in this guidance, FDA must first find the alternative method or process to be acceptable for such purpose. Licensed establishments intending to use an alternative requalification method must submit a supplement for prior approval, as required under 21 CFR 601.12(b). Similarly, FDA must find an alternative requalification method proposed by an unlicensed establishment to be acceptable before it is implemented (21 CFR 610.41(b) and 630.35(b)).

[12] See 21 CFR 601.12(a)(3).

V. REFERENCES

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3. Garcia, M. N., et al., "Case Report: Evidence of Autochthonous Chagas Disease in Southeastern Texas." *Am J Trop Med Hyg* 92(2): 325-330 (2015).

4. Bern, C. and Montgomery, S. P., "An estimate of the burden of Chagas disease in the United States." *Clin Infect Dis* 49 e52-54 (2009).

5. Benjamin, R. J., et al., "*Trypanosoma cruzi* infection in North America and Spain: evidence in support of transfusion transmission." *Transfusion* 52: 1913-1921 (2012).

6. Kirchhoff, L.V., "Epidemiology of American trypanosomiasis (Chagas disease)." *Adv Parasitol* 75: 1-18 (2011).

7. Steele, W. R., et al., "Donors deferred for self-reported Chagas disease history: does it reduce risk?" *Transfusion* 54(8): 2092-2097 (2014).

8. *Trypanosoma cruzi* (*T. cruzi*) Whole Cell Lysate Antigen, ORTHO *T. cruzi* ELISA Test System, Package Insert (2009). http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/ucm085846.htm.

9. *Trypanosoma cruzi* (*E. coli*, Recombinant) Antigen, ABBOTT PRISM Chagas, Package Insert (2010). http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/ucm210158.htm#.

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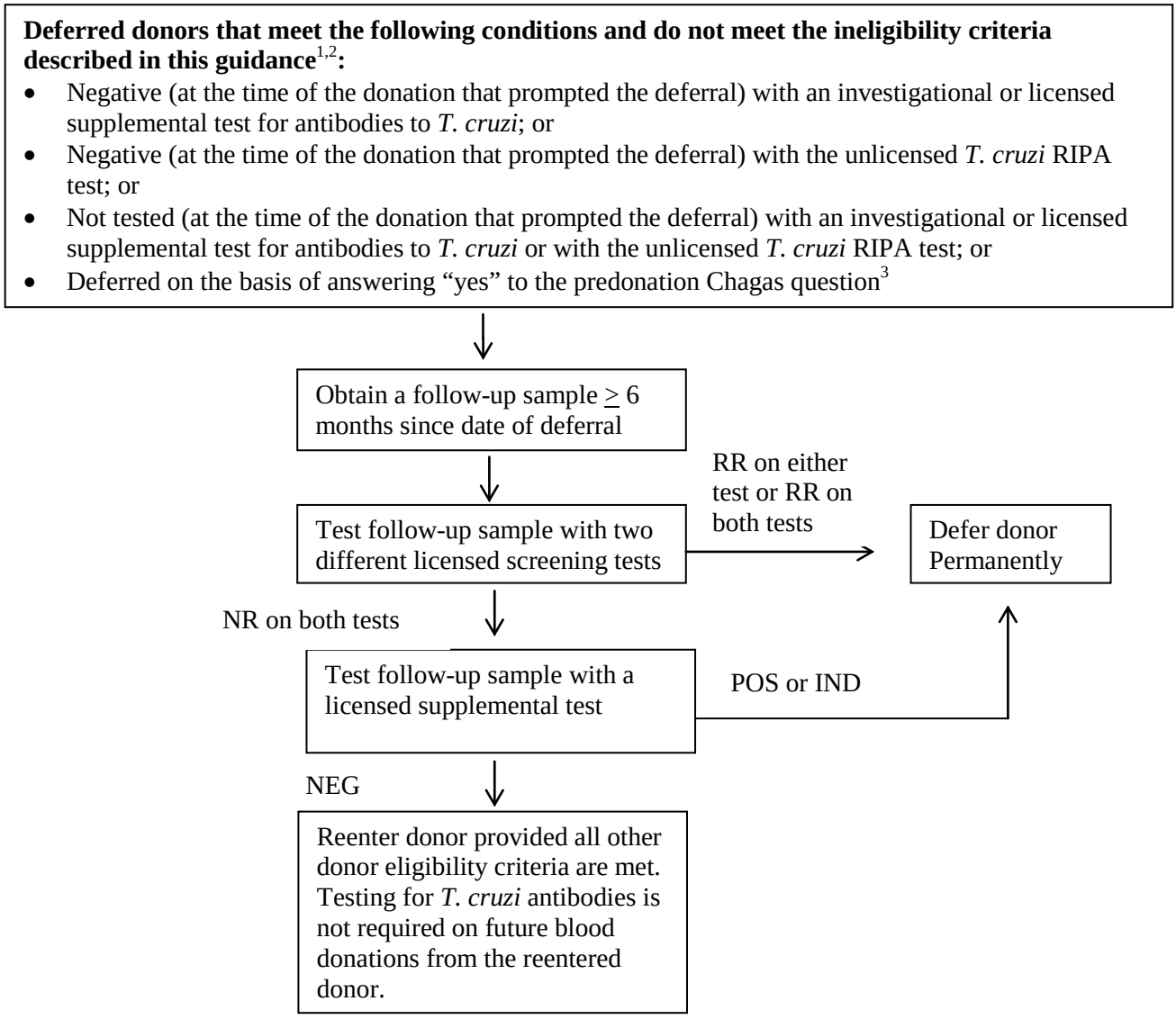
11. FDA Blood Products Advisory Committee "Reentry of blood donors deferred on the basis of screening test results for antibodies to *T. cruzi*." July 31, 2014. http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/BloodProductsAdvisoryCommittee/ucm386681.htm.

12. FDA Blood Products Advisory Committee "Potential Testing Strategies for *T. cruzi* Infection in Blood Donors." April 1, 2009. http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/BloodProductsAdvisoryCommittee/ucm155529.htm#.

13. *Trypanosoma cruzi* (*E. coli*, Recombinant) Antigen, ABBOTT ESA Chagas, Package Insert (2011). http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/ucm280719.htm.

APPENDIX

RECOMMENDED REENTRY ALGORITHM FOR DONORS DEFERRED ON THE BASIS OF SCREENING TEST RESULTS FOR ANTIBODIES TO *T. CRUZI* OR PREDONATION SCREENING QUESTION



RR = repeatedly reactive; NR = non-reactive; POS = positive; NEG = negative; IND = indeterminate

[1] Effective May 23, 2016, blood collection establishments must use a licensed supplemental test for *T. cruzi* in accordance with 21 CFR 610.40(e). Accordingly, only donors who were deferred prior to May 23, 2016 should be considered for reentry on the basis of Chagas test results, at the time of the donation that prompted the deferral, with the investigational supplemental test for antibodies to *T. cruzi* or with the unlicensed *T. cruzi* RIPA test.

[2] FDA recommends that donors with the following Chagas test results are not eligible for reentry: (1) Positive or indeterminate with an investigational or licensed supplemental test for antibodies to *T. cruzi* or (2) Positive or indeterminate with the unlicensed *T. cruzi* RIPA test.

[3] If donors participated in follow-up studies, those with a positive or indeterminate test result with an investigational or licensed supplemental test for antibodies to *T. cruzi* or with the unlicensed *T. cruzi* RIPA test should not be considered eligible for reentry.